NEUROPSYCHOLOGY AND NEUROIMAGING IN

DIFFUSE BRAIN DAMAGE

A STUDY OF VISUAL EVENT PERCEPTION

A thesis

submitted in fulfilment

of the requirements of the degree

of

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DEDICATION

This thesis is dedicated to my parents and all those who believed that education might bring us a better world.

ABSTRACT.

The aims of this project were (1) to investigate two forms of event perception: perception of movement and perception of sudden appearance, (2) to develop event perception procedures which could be applied to testing clinical populations, and (3) to relate event perception to abnormalities shown by neuroimaging. In addition issues relevant to each of the particular clinical populations involved were addressed.

Event perception tasks used stimuli consisting of a background of randomly selected dots of light. In one task a dot was added to the display (appearance), in the other a dot started to move (movement onset). Four laboratory experiments were conducted examining the ability to detect and locate these events under varying conditions in healthy controls. Results indicated that neuronal coding strategies were different for appearances and movement onset.

Laboratory tasks were adapted for clinical application and administered to groups of patients with different neurological conditions. Five studies were conducted to assess sensitivity and specificity of the Event Perception tasks in clinical settings. The groups studied were chronic solvent abusers, detoxified alcoholics, patients suffering from optic neuritis, and patients with traumatic brain injury. Event Perception tasks were found to be differentially sensitive to neurological conditions and showed dissociations and double dissociations both within and between neurological conditions. Relationships with Magnetic Resonance Imaging (MRI) and Single Photon Emission Computed Tomography (SPECT) were investigated in patients with head injury. Patterns of brain damage differed significantly for patients with impaired performance on the movement task.

It is concluded that Event Perception tasks are of value in the assessment of neurological patients: They allow assessment of functions which are not usually evaluated in neuropsychological examinations, facilitate detection of subtle deficits and deficits which may present at an early stage, and offer greater specificity and sensitivity than many traditional neuropsychological test procedures. Event Perception tasks are easy to administer and do not suffer from training effects on repeated administration to the same degree as many traditional measures. It is also argued that tests with a theoretical basis are better suited to clinical research in neuropsychology than many traditional tasks because they potentially allow a more precise explanation and assessment of the abnormal processes under investigation.

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GENERAL INTRODUCTION.

Test procedures in clinical and experimental neuropsychological research are designed to provide a means of assessing behaviour quantitatively in subjects with neurological abnormalities. Clinical evaluation has the purpose of identifying and mapping deficits as well as locating spared capacities; one aim of research is to establish relationships between particular deficits and the nature or location of neurological abnormalities. One of the drawbacks in this attempt is that a majority of the tests in use were not specifically designed for this purpose and are lacking a firm theoretical basis. These tasks are often rather vaguely defined with respect to the individual functions they are supposedly measuring. For instance, a broad division is used for the Wechsler Adult Intelligence Scales (Wechsler, 1955) separating them into verbal and non-verbal tasks with some, but not particularly specific, distinctions of what each of the subtests in either category is measuring. Explanations as to their intrinsic validity is usually given on a post hoc basis. Nevertheless, attempts have been made to use such tasks in the localisation of brain damage by relating performance on particular subtests to individual lobes in the brain (McFie, 1975). However, many of the traditional tests even within their specific domain tend to address a fairly broad spectrum of cognitive functions and processes. Another drawback of many traditional measures lies in their lack of repeatability with few, if any, parallel measures to allow serial assessments without a considerable training effect. However, in many conditions it is desirable to measure disease progress, recovery, or the efficacy of intervention.

One of the aims in this thesis is to develop neuropsychological test procedures which are based on and rooted in the knowledge amassed in neuropsychological, physiological and psychophysical research of visual event perception. Information processing speed has been found to be affected by a variety of neurological conditions. Although the idea of reduced information processing speed is commonly encountered, it is often poorly defined. In many neurological conditions the central nervous system as a whole or parts of various subsystems may be affected to varying degrees and result in decreased efficiency of information processing. This may be studied in a graded approach with specifically designed tests aiming at assessment of function of early levels of visual information processing such as appearances or disappearances and movement of visual stimuli, or at later stages with the introduction of more complex, symbolic information, and in its final stage with the introduction of tasks involving semantic processing. It is sometimes assumed that there is an upward relationship between basic and higher order processes and that impairment in basic processes will affect performance in more complex processes. Any tasks aimed at assessment of such early processes which are considered suitable as clinical tools should be highly specific in addressing individual psychological processes as independently as possible, and they should be highly sensitive to allow detection of abnormal processes at an early stage.

The first chapter gives a review of some of the theoretical background to visual event and movement perception. Clearly, with such a vast and rapidly expanding area of research only the most relevant aspects relating to the general aim of this thesis can be addressed. The major aim of the thesis is to test the suitablity of applying visual event perception tasks to a variety of patients with neurological disorders. Discussion

of the event perception literature will therefore be limited to that necessary for understanding the rationale for task design and analysis. The results from a number of laboratory experiments are reported and a neuronal model of visual event perception is developed which is based on work by Phillips & Singer (1974), Singer & Phillips (1974) and Wilson (1981, 1983). Computerised visual event procedures are developed to allow measurement of perception of appearances and movement onset of light stimuli under varying conditions. Phenomenologically the two tasks seem to be almost identical. Detection of appearances and movement onset seem at first glance to operate on similar principles. However, under certain conditions detection of movement onset is found to be much more difficult than detection of appearing stimuli. This leads to the conclusion that there might be fundamental differences in the neural coding processes in response to appearing stimuli compared with movement onset of stimuli. Specific parameters are manipulated to establish these differences in healthy human subjects. On the basis of these findings a set of event perception tasks is developed for application in clinical settings. The first two tasks are set against a background of approximately 50 randomly selected dots of light in a 10 by 10 matrix. In the first task which will be called Event Perception Appearance an additional dot appears with a fixed stimulus onset asynchrony (SOA) of 2 secs. The second task which is otherwise identical to the previous task has a variable SOA based on a staircase procedure and allows assessment of the minimum temporal separation between background onset and target appearance required by individual subjects to allow target identification. This task will be called Event Perception Threshold and performance is measured in milliseconds as the average amount of temporal separation required on 50% correct identification of the targets. The third task which will be called Event Perception Movement is set against a background of 100 dots of light arranged in a 10 by 10

matrix and one of these dots selected at random produces a single lateral movement. Performance on this task is measured as the number of targets correctly identified out of a specified number of trials. The term 'Event Perception tasks' will be used to refer to these tasks collectively.

Research into most neurological conditions under investigation in this thesis has been extensive and the selection of literature reviewed is guided by their perceived relevance to visual event perception. The aim is not to cover all these conditions in their clinical and phenomenological width but to assess the sensitivity and specificity of the event perception tasks for a selected spectrum of neurological conditions. In all clinical investigations the emphasis is placed on performance on the Event Perception tasks but a number of other measures, both traditional and novel computerised tasks, were used for comparison except in the study in chapter 4.

Chapter 2 gives a review of the literature of solvent abuse concentrating mainly on both clinical and experimental findings of mental and physical impairment following exposure to toluene and n-hexane. A single case study is reported, and a study of 12 chronic solvent abusers whose performance is compared to 12 non-solvent abusing matched controls. Four solvent abusers were followed up over a period of 12 months. All subjects were inmates from a young offenders institution. Magnetic Resonance Imaging and neurological investigations were obtained for the single case study. The relevance of findings on Event Perception tasks and their relationship with neurotoxic changes resulting from chronic inhalation of solvents in these subjects is discussed.

Chapter 3 reports a study of 40 detoxified alcoholics and 40 matched controls. Alcoholics were assessed after a mean of 9 days after ceasing consumption of alcohol. Twenty-four alcoholics and 12 controls were reassessed after a mean of 27 days. The relationship between performance on Event Perception tasks and the neurotoxic effects of alcohol is discussed and the implications for the proposed model of event perception are evaluated.

Chapter 4 reports a study of 5 patients suffering from optic neuritis and compares performance on the Event Perception tasks with patterned visual evoked potentials (VEPs) and contrast sensitivity assessments obtained from the same patients. Findings are related to reports from the literature using VEPs and sinosoidal gratings in the assessment of abnormalities found in patients with optic neuritis and multiple sclerosis. The implications of findings in this study for the model of visual event perception proposed in chapter 1 are discussed.

Chapter 5 gives a review of the literature on neuroimaging after traumatic brain damage concentrating on reports from Computed Tomography (CT) and Magnetic Resonance Imaging (MRI). Studies attempting to establish relationships between neuroradiological indices of brain abnormalities and neuropsychological function are critically evaluated. The results from a study of 47 patients with traumatic brain damage and 16 orthopaedic controls are reported. An attempt is made to find neuroradiological correlates to performance on Event Perception tasks.

In chapter 6 a study of cerebral bloodflow (CBF) abnormalities in 24 patients with traumatic brain damage is reported using Single Photon Emission Computed

Tomography (SPECT) in combination with the tracer ^{99m}Tc-hexamethyl propyleneamine oxime (HM-PAO). Performance is compared with the controls from the previous study. The relationship between CBF abnormalities and performance on the Event Perception tasks is examined.

In chapter 7 a summary of findings and a general discussion of the clinical application of Event Perception tasks is provided.

1.0 VISUAL EVENT PERCEPTION.

1.1 INTRODUCTION.

Visual event perception, particularly movement perception, has attracted a great deal of attention in the neurosciences as a central issue to human perception. Movement perception in phylogenetic terms has been referred to as one of the most primitive forms of vision (Walls, 1942) and it is often assumed that the study of such basic processes would ease the way for tackling more complex aspects of human cognition. The ability to detect and efficiently process events such as onset and offset of stimuli or appearance, disappearance, and movement of objects has been interpreted as being advantageous from a developmental and evolutionary point of view (Walls, 1942). A behavioural response may be required to appearing, disappearing or moving objects which in nature may take the shape of prey or predator even while the relevant part of the visual field is temporarily obscured by some other object moving across the line of sight or when a moving subject fixates objects seen through trees or other vegetation. It has been suggested that under certain conditions movement can be detected when it is defined only by the difference in position of some part of a pattern in eg. random-dot patterns in two successively presented stationary fields (eg. Julesz 1971; Pollack 1972; Braddick 1973).

1.1.1 Anatomical considerations

Early work by Hubel and Wiesel (1961; 1962) initially led to the assumption that processing of visual information is based entirely on hierarchical principles with input being processed sequentially in many stages of ever increasing complexity and convergence along the visual pathways. Hubel and Wiesel have identified cells in Brodman's areas 17, 18 and 19 whose receptive field properties differed greatly in their complexity and degree of selectivity. On the basis of their observations they proposed a model suggesting that after synapsing in the lateral geniculate nucleus (LGN) input was relayed to simple cells, complex cells, hypercomplex cells and, at the highest stage, higher order hypercomplex cells. This model represents the simplest form of hierarchical organisation, with information being processed in an exclusively serial fashion. However, more detailed studies of the visual pathways provided evidence contradicting a strictly serial scheme of organisation in visual processing. Hubel and Wiesel (1965) discovered subsequently to their earlier studies that area 17 projects simultaneously to several cortical areas (18, 19 and lateral suprasylvian cortex) thus demonstrating parallel outputs from a single area. Other findings (Lennie, 1980; Stone, Dreher & Leventhal 1979; Gilbert, 1985; Geisert, 1985) may be summarised as follows (cf.Van Essen & Maunsell, 1983, p. 371): there are (1) direct projections from LGN to areas 18, 19 and lateral suprasylvian cortex as well as to area 17; (2) projections from areas 18 and 19 back to area 17; (3) direct LGN inputs into complex cells as well as simple cells; and (4) distinct retinal ganglion cell classes, the X, Y and W cells, whose output remains partially segregated at cortical as well as subcortical levels. This evidence suggests that information processing in the visual system is not exclusively hierarchical and at least to some degree processed in a

parallel fashion. Van Essen and Maunsell (1983) have proposed a view that has gained considerable recognition implying that visual cortex might be organised as a complex network in which distinct hierarchical levels of processing do not exist. However, subsystems, even if not hierarchical in their internal organisation, may nonetheless be members of a larger hierarchical system whose other members consist of similar multicellular groups. It may be possible that in the visual system different areas are related to one another in a hierarchical fashion irrespective of whether individual areas are internally organised as hierarchies. It is generally assumed that separate channels mediate object and spatial vision (Newcombe & Russell, 1969). These two types of visual perception have initially been linked to the geniculostriate and tectofugal systems, respectively, rather than to separate channels diverging from a common striate origin. However, Mishkin, Ungerleider & Macko (1983) argued that there is now sufficient evidence - at least in primates - that all forms of visual perception, as distinguished from visuomotor functions, are more heavily dependent on the geniculostriate than the tectofugal system. They found that even complete bilateral destruction of the superior colliculus would not produce a reliable loss in retention of visually presented material.

Cortical models of event perception assume movement analysis to take place beyond V1, the striate or primary visual cortex, presumably even as far as the medial/superior temporal area for short range movement and beyond that for long range movement (Van Essen & Maunsell 1983). One pathway identified to be responsible for motion perception involves the middle temporal (MT) and medial superior temporal area (MST) (Maunsell & Van Essen, 1983c). Zeki (1974) found evidence for a high incidence of direction selective cells in a region of the superior

temporal sulcus which is part of the middle temporal area. In addition it has been found that the majority of MT neurons are selective not only for the direction of motion, but also for speed and binocular disparity (Maunsell & Van Essen, 1983a, b). These cells were found to show little or no selectivity for shape or colour. At least three parallel pathways originating in layer IVb of V1 converge in the medial temporal area. Each of these converging paths has its own distinctive characteristics, in (1) direction selectivity (2) disparity selectivity and (3) in wavelength selectivity. DeYoe and Van Essen (1988) investigated why these three streams or pathways might converge in this particular area and came to the following conclusion: (1) they may cooperate to establish cue-invariant representations of trajectory and distance, and (2) enhance the accuracy of motion perception compared to that attainable using only a single computational strategy. MT is assumed to be the lowest area in the cortical hierarchy in which a selective emphasis on motion analysis is found. However, basic properties of selectivity for direction, speed and disparity have been found to be present in a substantial percentage of cells in V1 and V2 (Dow, 1974; Fischer, Boch & Bach, 1981; Hubel & Wiesel, 1968; Poggio & Talbot, 1981; Zeki, 1978). Directionally selective cells in V1 are especially concentrated in layer IVb (Dow, 1974), which is the major source of projection from V1 to MT (Lund, Lund, Hendrickson, Bunt & Fuchs, 1976; Maunsell & Van Essen, 1983b). The difference between cells in V1 and MT is reflected in a high degree of convergence in this pathway: receptive fields are approximately twice the size in MT compared to V1. It is assumed that these larger receptive fields are related to functional capacities not found in V1. An example is the range of preferred speeds for the overall population of cells which is nearly an order of magnitude greater in MT than in V1 (Fischer, Boch & Bach, 1981; Maunsell & Van Essen, 1983a). This increased range is seen as being

potentially important for the analysis of rapid motion in the visual field. A further important difference demonstrated in MT of the owl monkey (Miezen, McGuinness & Allman, 1982) is the presence of pronounced surround interactions in which responses to stimulation within the excitatory receptive field can be inhibited by motion in other parts of the visual field. Cells with this property are capable of signalling information about relative motion.

The research reviewed above takes little or no account of subcortical processing of movement. However, it is well known that early or primitive forms of vision and in particular movement detection need not involve cortical pathways at all. Studies of 'blindsight' - a term coined by Weiskrantz (1978) - in both humans and animals have identified subcortical pathways involved in movement perception. These pathways known as the tectofugal system involve the tectum and the superior colliculi which form part of a secondary visual system. Phylogenetically, this system would more correctly be called the 'first' visual system given its importance in invertebrates. However, in mammals this system is primarily involved in visual reflexes and reactions to moving stimuli. Nerve fibres of the retinotectal system pass directly to the pretectum and the tectum without synapsing in the LGN. These fibres begin as portions of the optic nerve and tract; after they pass the LGN they continue as the brachium of the superior colliculus and proceed to the pretectum and tectum. It is believed that direct input from the retina to the superior colliculi becomes progressively less important with phylogenetic ascent to man. There are nevertheless cortical connections with areas V2 and V3 via the occipito-mesencephalic tract. This pathway subserves reflex pursuit eye movements in any non-horizontal direction. The paired pretectal nuclei receive direct photic input from the retinas, as well as input from the

contralateral pretectal nucleus via the posterior commisure. This aspect is of importance in two ways: (1) it involves fewer synapses and may thus result in a decrease in reaction times in response to moving or flashing stimuli and (2) it allows perception of simple stimuli in cases of cortical blindness. This system known as the tecto-oculomotor system is believed to involve cerebellar and vestibular pathways and is connected with oculo-motor nerves. Horizontal pursuit eye movements are mediated by the occipito-pontine pathways to the paramedian pontine reticular formation bypassing the superior colliculi. In response to photic stimulation the tectospinal tract is involved in reflex head and trunk movements.

Studies in blindsight have shown that patients suffering from large scotoma or visual field deficits may nevertheless be capable of perceiving light stimuli displayed in their perimetrically blind fields (Weiskrantz, Warrington, Sanders & Marshall, 1974; Weiskrantz, 1980; Weiskrantz, 1987; Zihl & Von Cramon, 1980; Zihl, 1980). Moreover, Ruddock and colleagues (in: Braddick, 1980) have demonstrated that one of their patients was also capable of perceiving movement in his blind fields. Campion, Latto & Smith (1983) in a comprehensive review article have criticised the phenomenon as an artifact and as a result of inadequate investigation techniques. In a number of peer comments accompanying the article their position was criticised as untenable and later investigations (Zihl & Werth, 1984a,b; Marzi, Tassinari Aglioti & Lutzemberger, 1986; Weiskrantz, 1987) have shown that Campion's et al. criticism was inappropriate in dismissing the phenomenon as merely representing spared cortical vision and scattered light.

Patients with damage to the geniculostriate visual pathway do not report any visual sensation when stimulated in their perimetrically blind field region. They can, however, locate a light stimulus and direct their gaze or point to it under forced choice conditions. Two major hypotheses have been proposed to explain this phenomenon: (1) stimuli which are presented in an area of the visual field which is perimetrically blind are still processed by some spared geniculostriate function which may not have been detected or be undetectable by conventional perimetric testing (Campion, Latto & Smith, 1983). (2) The second hypothesis suggests that the visual capacities demonstrated after striate cortex damage (ablation or surgical removal in some cases) are mediated by the retinal projection via the superior colliculus and the posterior thalamus. This hypothesis has been supported by a number of animal studies but in particular in an investigation by Mohler & Wurtz (1977) who showed that monkeys lose the ability to detect and locate visual stimuli when the superior colliculus ipsilateral to the striate lesion was also damaged. It appears from this study that, in the absence of striate cortex, the superior colliculus is the crucial structure for the execution of these visual capacities. Most investigators seem to believe that the tectofugal system has a rather limited capacity which is mainly restricted to identifying movement or light spots or bars. This view was born out in an investigation by Weiskrantz (1987) on a patient previously investigated by the same author and his colleagues (Weiskrantz et al., 1974). Weiskrantz found that the intact visual field was superior to the blind field for form discrimination but there were particular conditions when the blind field was actually superior to the intact field for detection tasks. Weiskrantz concluded that his findings fitted the general framework of 'two visual systems' by "allowing extrastriate routes a capacity for mediation of detection, location and orientation of a visual event, but requiring integrity of striate cortex (together with

other more anterior cortical structures, especially the temporal lobes, to which striate cortex projects over several synapses) for its identification" (Weiskrantz, 1987, p.90). Marshall & Halligan (1988) on the other hand reported a patient who was apparently capable of extracting more complex information from a line drawing when presented to her left homonymous hemianopic field. The line drawings consisted of two identical houses except that the one presented to her blind field was 'on fire'. Asked which house she preferred to live in the patient scored persistently above chance level deciding not to want the burning house without being able to describe verbally the reasons for her decision. This study would suggest that form discrimination may be possible to some extent using the tectofugal system.

From the research reviewed above it would appear that the importance of the tectofugal visual system might have been played down by adherents of cortical models and investigation techniques, perhaps more than appropriate for human event perception, and one of the aims in future research should be an attempt at integration of geniculo-striate and tecto-fugal models of early visual perception.

1.1.2 Physiological and psychophysical aspects of event perception

It has long been known that appearing stimuli produce transient bursts of neuronal activity with firing or spike frequencies much greater than the sustained response to the continued presence of the stimulus (Adrian & Matthews, 1927; Hartline, 1938; Winters & Walters, 1970; Brooks & Huber, 1971; Singer & Phillips, 1974). Winters & Walters (1970) were able to divide both transient and steady state stimulus-response curves into two segments based on single cell recordings in the cat's optic fibre tract: a monotonic increasing portion for low-contrast levels and a non-monotonic decreasing segment for high contrast levels. One of their conclusions was that more information about intensity changes is signalled during the transient phase than during the steady state phase of the response. It has been concluded that for human movement perception different cell types like those detected in the cat's visual system (Hubel & Wiesel 1962; Enroth-Cugell & Robson, 1966; Cleland, Dubis & Levik, 1971), and whose existence was at least partly confirmed for the monkey's visual system (De Monasterio 1978) might play a vital role in the human visual system (Todd & Gelder 1979). The assumption was that X cells with slower conduction velocities producing mainly sustained responses might serve as a feature analyser whereas Y cells with faster velocities and exclusively producing transient responses might be more concerned with movement perception (Tolhurst 1973; Kulikowski & Tolhurst 1973; Breitmayer & Ganz 1976, 1977). However, Ikeda and Wright (1973) found X cells to have shorter latencies when stimulated by spots of light. Lennie (1980) has shown that the distinction and specialisation attributed to X and Y cells is not as clear as originally assumed. He found that both cell types can mimic the properties of the other type under certain circumstances. Lennie concluded that even though conduction velocity in

Y cells is higher than in X cells, the important functional aspect is not conduction time but a cell's latency of response to light. Another characteristic distinction between X and Y cells is the difference in response pattern of the neuronal signal they produce. It is believed that Y cells produce transient signals only but X cells can produce both transient and sustained signals. It is also commonly believed that noticeability of visual events is dependent on transient neuronal responses (Wilson, 1981, 1983; Stelmach, Bourassa & DiLollo, 1984). In the following context the use of the terms 'transient' and 'sustained' is not restricted to certain cell types: 'transient' is used to signify any neuronal signal with a high spike frequency in neuronal firing and with a decay rate of some milliseconds (<100 ms); 'sustained' is used for any neuronal response with lower spike frequencies and more equal levels of firing which persists for at least a few seconds. These concepts are used to describe responses of cell groups rather than single cell responses.

Abruptly appearing or disappearing stimuli are noticed very easily. The precondition for this capacity is attributed to one of the fundamental properties of visual processing: the emphasis on change and suppression of constancy. Wertheimer (1912) and Korte (1915) mapped out the temporal and spatial intervals which gave optimal apparent movement using simple line and dot stimuli. However, when using more elaborate stimuli such as pairs of complex pictures increased complexity demanded more elaborate models.

Julesz (1971) was one of the first investigators to use computer generated random-dot patterns as stereoscopic stimuli in psychophysical investigations. In a typical experiment the two patterns of a display are identical except for a region of dots (or all

dots) in the second pattern which is laterally displaced in one pattern with respect to its position in the other. When one pattern is presented to each eye, the displaced region is retinally disparate and appears in a different stereoscopic depth plane from the rest of the pattern. The displacement region is only defined by the relationship between the patterns: each pattern taken on its own is a homogeneous random array. If the two random-dot patterns are exposed alternately at at suitable rate, the displaced region appears to oscillate laterally back and forth (Anstis, 1970) thus creating the phenomenon of visual apparent motion. An advantage of random-dot patterns over more traditional stimuli for apparent movement is that the limiting conditions for apparent movement are more unambiguously defined (Braddick, 1973). With random-dot patterns a much easier distinction can be made between the appearance when the shifted region is visible as a discrete entity with clear boundaries, and when no such region can be recognised. Close observation of small parts of the pattern may still reveal that they are being displaced, but such displacement, as distinct from perceived movement, does not lead to segregation of the perceptual field (Braddick, 1973). This means that even isolated spots within a random-dot pattern can be assigned apparent movement function. The paradigm lends itself much better to the naturalistic study of apparent motion perception than traditional models since movement rarely occurs in isolation in a natural environment but is usually highly dependent upon surroundings which can be either stationary or moving at differential rates.

Braddick (1974) conducted a series of experiments using uniformly displaced random-dot patterns to induce perception of apparent movement. He found that segregation of patterns and coherent movement were only perceived when the displacement was small. The limit on the displacement and perception of coherent

movement was found to be approximately 15 min/arc. The range of 15 min/arc for the perception of apparent movement found in Braddick's experiments differs considerably from classical studies (Neuhaus, 1930; Zeeman & Roelofs, 1953) who had reported apparent movement for visual angles of up to 18 deg/arc and more (Smith, 1948). However, using random-dot patterns differs considerably from classical displays typically employing single dots or lines. The dense array in random-dot patterns might be expected to provide alternative interactions not present with isolated stimuli. Braddick therefore suggested that two different processes might be assumed for apparent movement perception: A low-level motion detecting process with a very limited spatial range and a higher level process which may lead to the perception of motion from the succession of two or more widely separated stimuli. Braddick felt that there was a temptation to equate the low-level short-range process with the activity of directionally selective neurons in the visual pathway which in species other than human are known to respond to suitable discontinuous sequences of retinal illumination. He thought that long-range apparent motion might involve more complicated processes of interpretation of stimulus configurations.

Anstis (1980) expanding Braddick's ideas distinguished between two systems responsible for motion perception: (1) a simple point-by-point mechanism based on hard wired motion detectors operating within a short spatial range (up to approximately 15 min/arc; Braddick, 1974) which stimulates neural motion detectors (Gruesser & Gruesser-Cornehls, 1973) and (2) a more 'cognitive' system which extracts edges or forms before it processes motion for a long spatial range up to tens of degrees, which does not stimulate motion detectors. In his experiments Anstis employed patterns of random dots and more complex configurations which could

either stimulate the one or the other system or both systems simultaneously. Anstis' view is shared by Farrell (1983) who acknowledged that apparent movement over short distances is directly sensed by motion detecting mechanisms whereas long-range apparent movement is "presumably generated by a central process dependent on prior computation of the positions of stimuli in three dimensional space" (p.85).

Perception of onset and offset of visual stimuli can be isolated from perception of a steady state background by using stimuli consisting of the appearance and disappearance of elements in complex patterns. In a series of psychophysical experiments Phillips and Singer (1974) have shown that subjects can detect appearances and disappearances which occur during temporary interruptions. Subjects were presented with two random-dot patterns separated by an inter stimulus interval (ISI). Patterns were identical except that on 50% of trials at random a single dot was added or deleted in the second pattern. The subject's task was to report whether the second pattern was identical to the first. The ISIs over which this was possible were found to be longer than those for an interruption to be detectable. The appearance of an additional light spot was detectable with ISIs of up to 120 ms, and disappearance with ISIs of up to 60 ms. The authors argued that their findings depend upon sensory processes since their paradigm involved small changes in a complex field and depend upon sensory conditions. They suggested that these processes could involve the transient components of ON & OFF activity of cell groups producing a signal which stands out against the background of ongoing activity. Ability to detect the added element was thought to be determined by the interaction of transient neural events caused by the offset of the first display and the onset of the second display. Lengthening the duration of the ISI was believed to weaken progressively the

magnitude of interactions, and thus cause poorer performance at longer ISIs. In their physiological experiments Singer & Phillips (1974) using a paradigm similar to that in their psychophysical experiments were able to corroborate their model using single unit recordings in the cat lateral geniculate nucleus (LGN). They could establish a correlation between performance and transient activity which is taken as support for their interpretation of their psychophysical results.

The action of reciprocal inhibition of ON and OFF responses in overlapping visual fields provides an important link for the model advanced by Phillips & Singer (1974). A consequence of reciprocal inhibition is a reduction in the ON and OFF responses to interruptions. The Phillips & Singer model can also be applied to explain neural coding in apparent motion perception. Apparent movement could produce ON and OFF activity with each apparent shift in location. Technically speaking this means a light source is switched off at one location and turned on at another ie. a set of discrete stimuli which are flashed in a sequence. In the case of a light disappearing and 'reappearing' at another location within the range of a few minutes of visual angle it may be possible that no transient bursts of neuronal firing are produced as a result of lateral spread of reciprocal inhibition of ON and OFF centre cells. Instead of signalling each ON and OFF event a small increase in the sustained signal may be produced which will be combined with the sustained background signal. This is only expected to be the case for short-range movement (Singer & Phillips, 1974; Braddick 1974). According to this model it would be predicted that as soon as the lateral movement of the background pattern exceeds a certain limit of visual angle and reaching the limits of the field of reciprocal inhibition, perception of coherent movement will break down and appear jerky. As movement distance increases beyond the area of reciprocal

inhibition events become, in terms of their neuronal response, separated into appearances and disappearances producing transient responses.

The aims in this chapter are: (1) to extend the Phillips & Singer paradigm of psychophysical event perception to movement perception and (2) to develop a set of psychophysical event perception tasks for use with various clinical populations with possible visual pathology.

To achieve these aims a set of experiments is required to answer the following questions:

(1) Is the onset of movement detectable in a complex random pattern forming a stationary background?

(2) What is the detection rate of an appearing stimulus in a pattern of continuously moving background?

(3) What is the detection rate of movement onset in a pattern in which half of the background is moving and half is stationary, and the stimulus is already part of the stationary pattern?

(4) How does detection rate for appearances and movement onset change under

(a) varying temporal conditions?

(b) varying spatial conditions?

1.2 GENERAL METHODS AND APPARATUS.

General paradigm. In the following experiments patterns of rectangularly shaped light stimuli are produced to form a matrix of dots providing a background pattern. These background patterns are used to mask for additional lights appearing on the screen which are the targets in the appearance condition or to mask for onset of movement of any of the lights which already form part of the background pattern which are the targets in the movement onset condition. Patterns and stimuli are generated by a microcomputer and displayed on a VDU. In the first three experiments the background is formed by randomly selecting approximately 50 lights in a 10 by 10 matrix. In the last experiments patterns are formed by 100 dots of light which are arranged in a 10 by 10 matrix. The target always appears or moves after a manipulable delay or stimulus onset asynchrony (SOA). Performance is measured by counting the number of correctly identified targets out of a given number of trials.

Subjects. Subjects for all experiments in this section were volunteers recruited amongst postgraduates and members of staff of the Psychology Department at Stirling University except for the last experiment where undergraduates served as subjects in fulfilment of a course requirment. Subjects included both males and females and were in the age range of 17-46 years with normal or corrected-to-normal vision.

Apparatus and stimuli. The same conditions applied for all experiments unless stated otherwise. Stimuli were presented on a visual display unit equipped with a P49 fast phosphor which ensured rapid onset and offset of all displays (luminance decay was < 1ms). A second video display was connected allowing the experimenter to

monitor displays and exert control over the entire experimental process. Displays were viewed binocularly at a distance of 30 cm from the retina to a 290 by 215 mm display screen. The display occupied a field of 185 by 130 mm which subtended 31 degrees horizontally and 23 degrees vertically of visual angle at this distance. Patterns were formed by randomly selected rectangular elements of 2x5 mm in a 10 by 10 matrix. The probability for an element to appear in any pattern was 0.5 and a new random selection was made for each trial. The number of rectangles and configuration of patterns was therefore variable with a mean of 50 elements in any pattern. Elements were separated from each other by at least the width of one element. A single element subtended an angle of 0.5 deg horizontally and 1 deg vertically. Eccentricity from fixation measured on average 3, 6, 9, 12 and 15 deg/arc horizontally and 2, 4.5, 7, 9.5 and 12 deg/arc vertically in either direction. Thus for a full 10 by 10 display there would be 4 elements at 3 deg/arc, 12 at 6 deg/arc, 20 at 9 deg/arc, 28 at 12 deg/arc and 36 elements at 15 deg/arc. For appearing targets with a pattern probability of 0.5 there were on average 50 empty random locations at which the target could appear resulting in an overall chance performance of 1/50 or 2%. For movement onset chance distribution would be different since the target - by definition - would have to be one of the non-moving elements already displayed at onset of the background pattern. With a selection probability of 0.5 and half of those elements moving, the resulting average number of non-moving background elements would be 25 plus the target. This results in an average chance detection of 1/26 or 3.8%.

Horizontal and vertical coordinates of the matrix were marked on the bottom and left edge of the array. Coordinates of target stimuli were entered into the computer by the experimenter for later analysis. A chinrest was used to minimise accidental head

movements and to keep viewing distance constant. Ambient background illumination was provided by a 60W desklamp located behind the VDU. Brightness and contrast on the VDU could be adjusted and calibrated allowing constant luminance levels. Stimuli were generated by an Apple II microcomputer. Timing of stimulus displays was achieved by reference to the 50 hz refresh rate of the VDU and was in 20 ms intervals employing hardware modifications recommended by Cavanagh & Anstis (1980). The term movement refers to apparent horizontal movement with a constant distance and an oscillation rate of 2.5 hz unless stated otherwise. Patterns were refreshed every 20 ms. During the refresh interval, rectangles were plotted at the maximum rate of the computer.

General procedure. Subjects were instructed to place their head into the chinrest and to make themselves as comfortable as possible. They were asked to maintain a steady gaze at the fixation point at the centre of the screen. At the beginning of each trial a priming "Ready" appeared on the screen briefly replacing the fixation point and after an interval of 1 sec the background pattern was displayed. Subjects had to locate the target with their finger as soon as they had identified it. If subjects failed completely to identify a target they were asked to make a guess. Forced choice was applied to reduce response categories to hits and misses. Feedback was provided after each trial by displaying the correct coordinates of the target.

1.2.1 Experiment 1: Detectability of appearance versus movement onset.

This experiment was conducted to establish whether there are any differences in a subject's ability to detect appearing targets which were not previously part of the background in a complex but steady background compared to detection of movement onset of targets against a background in which half of the lights are moving and the other half are not moving; the target in the latter condition is randomly selected from the non-moving half of the background. If detection rates were found to be significantly different for the two conditions it could be assumed that two different neuronal processes are involved in the processing of these tasks.

Subjects. This experiment employed six male and female postgraduate students and members of staff with normal or corrected to normal vision and an age range of 23 to 46 years.

Procedure. Two different experimental conditions were employed:

(1) Appearance of a target: target appeared at an empty random location after display of the background pattern;
(2) Movement onset: 50% of the elements forming the background pattern moved continuously from onset of the display; the target which in this case was already part of the display started to move after varying intervals.

The experiment consisted of 2 conditions with 4 different levels for each

condition. Ten trials were assigned to each condition requiring subjects to perform a total of 80 trials. The background in the appearance condition was steady state ie. background elements did not move at any point under this condition. For movement onset background elements and target moved at a rate of 2.5 hz. Stimulus onset asynchronies (SOA) were 20, 60, 100 and 10^4 ms for both conditions. Subjects were given an unspecified number of practice trials until they felt confident understanding the requirements of the task. A two minutes break was given between each set of ten trials. The entire session lasted for approximately 45 minutes. Table 1.1 gives a summary of the conditions in all experiments.

Results. Figure 1.1 shows the pooled results for all subjects. Since there were no general differences in performance between individual subjects it appeared justified to pool the results. Detection of an appearing target proved to be rather easy but difficult for movement onset. The mean for correct responses in the appearance condition was 60% and 5.8% for movement onset. A repeated measures analysis of variance was performed both for conditions and levels. The analysis indicated that the difference between conditions (Appearance x Movement) was highly significant ($F(1,5)= 193$ $p<0.001$). Differences between levels (SOAs) were also highly significant ($F(3,15)= 49.9$ $p<0.001$). Analysis of variance for the appearance condition between levels (SOAs) showed a significant difference between SOAs of 20 ms and SOAs of 60 ms ($F(1,5)= 139.8$ $p<0.001$) and 60 ms and 100 ms ($F(1,5)= 52.5$ $p<0.001$); there were no statistically significant differences between SOAs of 100 ms and 10^4 ms. Except for the shortest SOA of 20 ms differences in SOAs for movement onset did not alter detection rate to any significant degree and detection proved to be difficult over the whole range of SOAs. Individual performance never

exceeded 20% correct identification of the target and was on average 5.8%. Analysis of variance between the four levels of SOA for the movement condition revealed a significant difference between level 1 (20 ms) and level 2 (60 ms) ($F(1,5)= 7.5$ $p<0.05$) but differences for other SOAs were not significant. Despite its low mean of 5.8% performance was still slightly above chance level of 1/26 or 3.8%.

Discussion. The results showed a highly significant difference in detection rate between appearance and movement onset of a target in a background of sustained movement. This finding supports the hypothesis that two different ways of neuronal coding might be involved in the processing of the two tasks. The proposed strategy for appearing targets was that they would produce a brief transient signal which is easily noticeable and for movement targets to produce merely a slight increase in the sustained signal to the background pattern. However, there could be an alternative possible interpretation of these findings. Perhaps movement detectors do give transient responses at stimulus onset but transient ON & OFF responses may also be produced by the moving target at each new position. These ON & OFF responses would then mask any transient responses produced by the target. This possibility is particularly plausible for experiments using apparent rather than real motion.

1.2.2 Experiment 2: Appearances versus movement onset against a moving background.

Experiment 1 showed that detection of motion onset is poor under the conditions of the experiment. One possible explanation suggested for the difference in detection between appearances and movement onset was that the moving background is continuously producing transient bursts of ON and OFF activity particularly as apparent movement was used rather than real continuous movement. If this is the case then a target appearing in either the moving pattern or the non-moving background will also be poorly detected because the transient burst that it produces will be lost in the complex array of transient bursts being produced by the background. To test this prediction the following experiment was conducted to establish whether detection of appearing targets would decrease in a background of continuous movement. The hypothesis was that detection of appearing targets would be poor in a background of sustained movement if background movements produce transient ON & OFF responses at each new position.

Subjects. This experiment employed 7 postgraduates including males and females with an age range of 23 to 32 years with normal or corrected to normal vision.

Apparatus and Procedures. Conditions were identical to those described in general procedures. Similar to the previous experiment there were two different conditions: for the appearance condition a target which was not part of the background pattern appeared after a SOA of 2 secs and started to move in synchrony with the elements forming the background pattern. All other parameters were held constant.

The second condition was movement onset of a target already belonging to the background pattern and was identical to experiment 1 except for the SOA being held constant at 2 secs as for the appearing target. For both conditions oscillation rate was 2.5 Hz, movement distance was 9 min/arc, and display time after target appearance was 2 secs. An experimental session consisted of 5 blocks of 10 trials per condition requiring each subject to perform 100 trials. There was a break of one minute between blocks extending the experimental session to approximately 30 minutes.

Results. Figure 1.2 shows the pooled results for all seven subjects. Mean performance for appearance was 63% and for movement onset 26%. An ANOVA revealed a highly significant difference in detection rate between the two conditions ($F(1,6)= 75.7$ $p<0.001$). No significant differences were found for the five blocks in the appearance condition. For movement onset a significant difference in detection rate was observed between blocks 1 and 3 ($F(1,6)= 10.8$ $p<0.02$).

Discussion. Detection rates for appearances were considerably lower than for the equivalent conditions in the previous experiment and clearly affected by backgound events. This did not prevent detection rates from reaching levels well above chance and significantly above the detection rates for movement onset. It may be possible that activity in the background pattern can lead to some reduction in the transient signal produced by the target in terms of interaction of signals or competition in neural processing. However, the interaction and resultant reduction in detection rate does not appear to be severe enough to suggest that the background pattern produces transient signals which would compete directly with transient signals from the target. It appears therefore justified to reject the suggested alternative interpretation and it is assumed

that at the level of the nervous system responsible for detection of movement onset moving background stimuli do not produce transient ON & OFF responses at each new position. Likewise, it may also be assumed that the sustained response to movement does not completely mask ON responses produced by an appearing ('new') target as reflected by the detection rate for appearing targets.

A further implication of the findings in this experiment is that movement of a target to a new position (movement onset) inhibits the ON response which would otherwise be produced by the appearance of a stimulus at that position possibly in response to inhibition by the OFF signal produced by the 'same' target. However, it is known from other studies that this form of reciprocal inhibition has spatial limitations which are explored in the following experiment.

1.2.3 Experiment 3: Lateral spread of reciprocal inhibition.

Experiments 1 and 2 have provided evidence for the assumption of different neuronal coding for targets appearing and targets starting to move in a complex array. Experiment 2 has shown that the sustained response to a moving background does not mask ON signals produced by an appearing target but it was assumed that reciprocal inhibition would suppress ON signals of a movement onset target since detection rate would otherwise be similar to that for appearing targets. This form of reciprocal inhibition is known to have spatial limitations. In Braddick's (1974) experiments these limits were found to be around 15 min/arc. The following experiment was conducted to test this hypothesis and establish the spatial limits of reciprocal inhibition for the

present conditions. If the rationale for these experiments were correct it is assumed that detection rates will drop markedly for appearing targets at a certain level of lateral separation of the moving stimuli ie. when lateral separation has reached the limits of the field of inhibition.

Subjects. Subjects in this experiment were 13 undergraduate and postgraduate psychology students and members of staff including both sexes with an age range of 20 to 47 years.

Procedure. Apparatus and procedure were the same as outlined in the general description. The experiment consisted of two conditions (appearances and movement onset) with 5 levels of discretely varying movement distances and 10 trials at each level. Movement distance of the target was 9, 27, 45, 81 and 120 min/arc at a viewing distance of 30 cm. All other variables were kept constant: SOA was 2 secs; oscillation rate was 2.5 hz; and display time after target onset was 2 secs. Each subject performed 100 trials in total and the whole experiment lasted for approximately one hour.

Results. An ANOVA revealed a significant difference in detection rate between the two experimental conditions (Appearances x Movement) ($F(1,12)= 28.8$ $p<0.001$). Differences between levels (movement distance) for both conditions were also highly significant ($F(4,48)= 27.8$ $p<0.001$). The overall mean for correct detection of appearances was 53% and for movement onset 35%. Figure 1.3 shows the results of an analysis of different levels ie. movement distances. Detection rate of appearances worsened with increasing lateral spread. Breakdown of perception of continuous movement occurred between 27 and 45 min/arc. At distances above 81

min/arc the impression of continuous, smooth movement was completely disrupted and detection dropped to <40%. For these distances detection rate for appearances was approximately the same as for movement onset. Detection rate for movement onset was very similar at all levels apart from the 27 min/arc condition for which detection was higher at 46%. The difference was statistically significant at $p<0.01$ using a Scheffe test when compared to the 28% detection rate for the 9 min/arc condition.

A quadrant analysis and an analysis of eccentricity were performed to investigate any possible abnormalities of visual fields or sensitivity in individual subjects. Percentages for the whole group and each level of lateral spread were calculated and compared to the distribution for each quadrant and each range of eccentricity. For the appearance condition three instances occurred where performance deviated more than 10% for quadrants from the overall mean and for the movement onset condition this happened twice (see tables 1.2 and 1.3). Randomisation of target locations which was achieved by using the computer random function generator worked satisfactorily; the largest deviations were found for appearances with an expected/obtained difference of 11 trials. For eccentricity analysis the two positions nearest to fixation can be ignored because of their low target frequency. Targets in second position from the periphery ie. at 12 deg/arc horizontally and 9.5 deg/arc vertically showed persistently lower percentages compared to the mean for each level of lateral spread. On two occasions for appearances was the deviation well beyond 10% and when all levels were collapsed the difference was 11% lower than expected compared with the overall mean. For movement onset the overall mean for the 12/9.5 deg/arc range was also 11% lower than the grand mean and there were three instances where the deviation was greater than 10% (see table 1.3).

Discussion. In this experiment the prediction that detection rate in the appearance condition depends on lateral movement distance of the background pattern is supported and in quantitative agreement with other measures. It was found that detection rates deteriorated significantly between 27 and 45 min/arc. It is therefore concluded that the field of reciprocal inhibition for the present conditions was around 30 min/arc. This is in approximate agreement with Braddick's (1974) findings of inhibitory fields comprising 15 min/arc for short-range apparent movement considering that experimental conditions were slightly different. The observation that the impression of smooth, continuous movement was lost at distances of 45 min/arc and beyond is interpreted as being due to the production of transient signals for each individual ON and OFF event requiring separate processing. This increased demand on processing capacity is seen as a reason for decreased detection rates since new events (appearances) are now competing almost equally with the processing of ongoing background activity. Thus, a transient signal produced by a "new" event no longer standsout against the signals produced by the background pattern at movement distances beyond the field of reciprocal inhibition. No conclusive explanation can be provided for the significantly higher detection rate in the movement onset condition at 27 min/arc but it could be argued that this might reflect a specific property (latencies?) of retinal cells at this particular distance. For the current conditions this range appears to be the boundary between short-range and long-range apparent movement. This result may support Baker & Braddick's (1985) findings of higher displacement values for short-range apparent movement in the periphery which will be discussed further. When scrutinising table 1.3 this particular argument is strengthened by the observation of three instances for which detection rates are higher than the mean in the most eccentric location in the movement onset condition.

There are at least three possible explanations for a lower detection rate of targets located at 12/ 9.5 deg/arc: (1) A difference in the lateral spread of cell types in the retina has been reported: transient cells are found only sparsely in the fovea but more concentrated in peripheral regions; the ratio of transient to sustained cells increases from the fovea to the periphery of the retina (Breitmeyer and Ganz ,1976). However, this does not fully explain why there should be a selective drop in this particular location. (2) Perhaps a more plausible explanation might be a contour-contrast difference: since the most eccentric elements form the boundaries of the pattern its uniformity is discontinued and the edges of the screen (as blanks) provide a different contrast to this particular area. Thus targets appearing or moving in this area might be detected more easily than those in the adjacent (inner) ring because they have a contrast profile aiding detection. (3) A further possible explanation could be based on findings by Baker & Braddick (1985) who established that maximum displacement values of moving stimuli in the periphery are higher than for the fovea for short-range apparent movement. The drop in performance in the current experiment does indeed occur just at or beyond the boundaries of central vision ie. in the 12 deg/arc condition. To answer this question unequivocally a separate experiment would be required in which element size remains the same but a larger display and a larger matrix would be employed. This could show whether there is a linear relationship between eccentricity of targets and performance, or whether it is invariably the most eccentric elements for whom detection rate is highest.

1.2.4 Experiment 4: Movement onset against a steady state background.

Movement - even within a very small area of the visual field - is nevertheless noticeable and of high survival value. The ability to "freeze" within the environment and to remain motionless on the one hand and to detect subtle movement on the other is of utmost importance to many species. The natural equivalent of short-range movement can be parallelled with a scenario in which an insect - after having remained motionless for some time in the foilage of a tree - gives itself away by a subtle movement sufficient to signal its presence and position to its predator. The following experiment attempts to mimick this situation by measuring detection rate of movement onset in a steady background to establish how noticeable brief movements smaller than 27 min/arc are.

The previous experiments have provided evidence for the assumption that short-range apparent movement produces sustained rather than transient responses. Short - range movement for the present conditions was found to extend to between 27 and 45 min/arc. Detection of appearing stimuli within this range was found to be relatively high at about 60%. On the other hand detection of movement onset was rather poor under most conditions when it occurred within a moving background (<35%). This difference was thought to be due to different neuronal coding. In the paradigm by Phillips & Singer (1974) it was assumed that appearing targets produce transient signals which within the framework of a busy neuronal infromation processing system tend to attract attention easily. From the experimental evidence obtained so far it would appear that for short-range movement only a discrete rise in sustained firing is

produced and that no transient signals are required to attract attention. This is in some conflict with the general notion that transients are a necessary prerequisite to attract attention and it might be possible that movement signals from the background are responsible for poor detection of movement onset. This alternative interpretation could be plausible since apparent rather than real continuous movement is used and the perception of movement is induced by switching the target off at one location and switching it on at a new, albeit proximate, location. It is in this respect that the movement onset task resembles appearances and disappearances of targets in the Phillips & Singer paradigm, and it is possible that transient signals are produced at each off and on event even for the detection of movement in a steady background.

Subjects. Subjects in this experiment were 25 male and female psychology undergraduates.

Procedure. The stimulus pattern in this experiment was different from previous experiments: Instead of selecting 50 elements randomly the display was filled with 100 elements in a 10x10 matrix. However, elements were not forming straight rows or columns but each element was randomly displaced by the width of at least its own size. The background pattern was steady state during experimental displays. The target made a single move to either left or right after a randomly variable SOA ranging from 1 to 6 secs. Movement distance was 9 min/arc and oscillation rate was 0.5 hz. This particular speed was chosen because it gave the best impression of smooth, coherent movement at this distance as assessed on a series of (informal) trials. Each subject performed 50 trials in a single block. The whole procedure lasted for approximately 40 minutes.

Results. Mean detection rate for the entire group was 79%. Individual performance varied from a 62% to 100% detection. An additional analysis including close misses defined as any element next to the target gave an overall detection rate of 86%. The inclusion of close misses appeared justified since detecting movement immediately surrounding the target still represents performance far beyond chance. A quadrant analysis failed to show any significant field abnormalities but eccentricity analysis revealed a similar but less dramatic tail-off as observed in experiment 3 for the two most eccentric conditions of 12/9.5 and 15/12 deg/arc (see table 1.4; figure 1.6).

Discussion. In experiments 1 to 3 detection rate of movement onset was very low because it was assumed that target onset was masked by ongoing activity of the background pattern. The assumed absence of transient signals in response to target onset within a spatial range of approximately 30 min/arc was seen as a possible factor for low detection rates. However, it was argued that short-range movement perception in a natural environment is nevertheless possible and of high survival value. The last experiment has shown that detection of movement onset is indeed easy in a steady state background. If neuronal coding is similar to the previous experiments it can be concluded that a small increase in the sustained response to the background pattern is sufficient to attract attention. However, this finding is in conflict with the idea that a transient signal is required to attract attention (Breitmeyer & Ganz, 1976) in a busy information processing environment. Allman, Miezen & McGuiness (1985) studied the response properties of direction selective neurons in area MT of the owl monkey and found that movement of the background of an array of dots in the same direction as a moving group of target dots caused a 75% suppression of the firing response. Movement of the background in the opposite direction caused facilitation of the

response by 50%. In applying these findings to the current experiment this could be interpreted to mean that in the absence of any background movement there is no suppression of signals produced by movement of the target. In other words transients could have been produced in response to movement onset even in the previous experiments but they were suppressed by the ongoing activity of the moving background; high detection rates in the current experiment would then be a result of transients which are not suppressed by surround movement.

1.3 GENERAL DISCUSSION.

A series of four experiments has provided psychophysical evidence for differences in neural coding to appearing and moving targets. In experiments 1 and 2 it was shown that detection rates were much higher for appearing targets than for movement onset for all SOAs ranging from 20 ms to $1x10^4$ ms. Better detection of appearing targets was thought to result from transient signals produced by ON responses to appearance of a new target which would stand out clearly against the background signal of sustained firing. These differences were thought to depend upon a mechanism of reciprocal inhibition of ON and OFF responses. Reciprocal inhibition suppresses transient signals which would normally be produced in response to a target "changing" positions. In experiment 3 these differences in neuronal coding were found to apply only to short-range apparent movement which for the present condition was limited to approximately 30 min/arc. Beyond these limits transient signals were assumed to be produced for both appearances and movement onset as reflected by highly similar detection rates. Finally, experiment 4 demonstrated that even small

movements of less than 27 min/arc can attract attention. Two possible explanations were sought for these findings: (1) no transient signals are produced in response to movement onset within short-range apparent movement and a small rise in the sustained signal to background activity may be sufficient to attract attention; (2) movement signals from background activity may mask movement onset of the target and reduce the level of firing in response to target onset.

A phenomenon reported spontaneously by many subjects for experiments 1 to 3 in the appearance condition but also observed by Singer & Phillips (1974) was the perception of the appearing stimulus as being brighter at onset and thus clearly standing out against the background pattern. However, luminance levels for appearing stimuli were technically exactly the same as for background elements and the phenomenon was never reported for movement onset under short-range conditions. This observation would further the argument that neuronal coding for the two conditions is intrinsically different within the limits of the short-range process: the transient peak produced by an appearing target would clearly stand out against the sustained background signal and at the processing level responsible for luminance analysis the strength of the two signals would be compared. The decaying sustained response representing the background pattern would be smaller in absolute spike frequency than the new transient signal representing the oncoming target; the arithmetic absolute difference in spike frequency might be perceived as increased luminance. This interpretation is in agreement with Phillips & Singer's (1974) findings of a declining detection rate for increasing ISIs when displays were interrupted. The OFF response at pattern offset would inhibit ON responses at re-display when the same retinal spots are hit again by identical dots. At short ISIs this

would result in a marked decrease in perceived luminance but the target, appearing at a place not inhibited, would appear brighter since its transient signal was not inhibited by a previous OFF response. The time course of these interactions has been studied in detail by Wilson (1981, 1983). It would be possible to devise an experiment in which luminance levels of the target are manipulated eg. reducing target luminance until it is perceived isoluminant to the background pattern on appearance. From the present study and from the Phillips & Singer model a strong relationship between ISI and reduction in perceived brightness would be expected but also a deterioration in detection rate as (perceived) stimulus luminance approaches (perceived) background luminance as transients are reduced to the size of the sustained signal or simply no longer strong enough to elicit a transient response (Brooks & Huber, 1972). The accuracy of this prediction was partly confirmed in a study by Bourassa, Stelmach & DiLollo (1985). They adapted the Phillips & Singer paradigm and manipulated luminance levels in a way similar to that suggested above. For long ISIs they reduced luminance of the background pattern during the ISI by a much smaller amount than for short ISIs to match the perceived difference in luminance at redisplay of the pattern. The authors found that by adjusting luminance levels in this way detection rates could be kept constant at the level corresponding to the ISI to which luminance was matched. However, Wilson & Phillips (1987) pointed out that Bourassa, Stelmach & DiLollo had not adjusted luminance levels for the target. This meant that target luminance was proportional to (general) background illumination but not to the adjusted background pattern luminance. Hence detection rate would still depend on a higher absolute difference in transient spike frequency.

A similar effect of perceived variations in luminance was observed in a study by

Wilson (1983) who investigated effects of stimulus luminance and duration on responses to onset and offset. Wilson used random-dot patterns in which bigrams could either appear (onset) or disappear (offset). Onset of bigrams was marked by additional dots appearing in the pattern after varying delays; these additional dots would stand out very clearly and appear brighter than the surrounding background pattern. It seems that this effect was stronger with longer ISIs although this point was not specifically under investigation. The Phillips & Singer model would provide a reasonably convincing explanation for the phenomenon: Decaying sustained signals to the background pattern would be contrasted with transients from the oncoming dots and be perceived as a differential in luminance.

Indirect support for the current model can also be derived from a post hoc analysis of an experiment conducted by Kolers (1972). Kolers described an experiment in which he displayed vertical lines on a cathode-ray tube (CRT) to induce apparent motion. He was able to vary the number of lines in the display from 2 to 1024. Lines were switched on and off in succession to induce a sensation of movement. Kolers observed that "two lines on the screen yielded good apparent motion, and thirty-two lines did also; but the intermediate values of four, eight, and sixteen lines produced degenerate displays in which a sense of motion was always available, but not a sense of continuity. Moreover, the brightness and compellingness of the 'moving' line varied markedly: the illusory line between the flashes was always paler than the flashes themselves. This sharp waxing and waning of brightness destroyed for the observers tested any acceptable equivalence between the sense of motion ... . The successive appearances produced a clear sense of something moving, but not of a continuously visible moving object" (Kolers, 1972 p. 37-38). Kolers believed that the failure to

obtain perception of smooth motion at these intermediate values of density demonstrated that the motion system is not linearly connected. He felt that in the case of intermediate density he was dealing with "near threshold conditions in which motion signals are not quite strong enough to induce a well-formed perception, but are not entirely absent; the motion signals are 'subliminal' " (p.38). The results from the current experiments together with Braddick's (1974) study can provide a good explanation for Kolers' observations: (1) It appears from Braddick's findings that the motion detection system is indeed not linearly connected but falls into a short-range and long-range system. Kolers' conditions of 2, 4, 8 and 16 lines correspond to 7.5, 3.7, 1 and 0.5 deg/arc. His 32 line condition was at 14 min/arc which corresponds precisely to Braddick's spatial limits for short-range apparent movement. (2) Consequently, perceived conformity of movement within these limits would be within the range of reciprocal inhibition producing only sustained signals whereas those beyond the limits would produce transient signals for each onset and offset leading to reported luminance fluctuations. The fact that two lines produced "good" motion may be due to spatial separation of 7.5 deg/arc activating the cognitive apparent motion system (Anstis, 1980; Braddick, 1980).

1.4 APPLICATION OF PARADIGM IN CLINICAL POPULATIONS.

The experiments in this chapter have clearly established that there are fundamental differences in the detection of appearances and of movement onset and detection rates differed significantly over a wide range of conditions between appearance and movement onset tasks. The status of the explanations proposed to account for these differences in terms of neural models remains hypothetical since assumptions were based on psychophysical experiments which require verification by neurophysiological means. However, if it is the case that the two neuronal coding strategies proposed to explain differences in detection rates of appearances and movement onset of stimuli are distinct, the model should lend itself to a double dissociation test. The problem lies in finding clinical populations in whom performance on the appearance tasks would differ significantly from performance on the movement onset tasks. For instance, a population showing decreased amplitudes in their neuronal response to visual stimuli might be expected to perform better on a task involving noticing of appearing than of moving targets because the transient responses to the former would still be expected to stand out against the sustained activity produced by the background pattern. Movement onset in this case might be expected to go unnoticed because the increase by the target in the sustained response being already fairly small in a normal population would be even smaller in a clinical population with weakened neuronal signals. In a clinical condition resulting in increased background noise in neural channels which could be caused by toxic or viral factors performance on both tasks would be expected to deteriorate for short SOAs. For longer SOAs performance should improve on the appearance task since longer temporal separation would allow the sustained response to the background pattern to

decline sufficiently - even if disturbed by minor peaks and valleys of erratic, spontaneous firing - which is followed by a clear transient peak from the target. The same erratic firing pattern from an affected nerve fibre could easily mask the response from a movement onset target given the small overall increase in the neural response occasioned by such a target. A third possible clinical condition would produce significant latency variations of the neuronal signal. This would mean that performance at short SOAs on the appearance task deteriorates as a result of insufficient reduction in the sustained firing pattern to background onset by the time the transient signal arrives. In other words the transient signal would arrive before adaptation has occurred and would be "swallowed" by the sustained signal. Much longer SOAs may be required to make detection possible. For movement onset both background onset and target onset signals would be delayed accordingly and should therefore allow detection at almost normal levels. The problem with most clinical populations is that abnormalities rarely occur in isolation and in the case of neurotoxic or viral conditions all three types of nerve fibre dysfunction are frequently observed: decreased amplitudes and increased latencies and noise often tend to co-occur.

If the assumption is correct that detection of appearances and movement onset are mediated by distinct neuronal processes then this can be tested by examining whether motion detection and detection of appearances dissociate in clinical populations. For this purpose adaptations of the tests used in this chapter were produced for clinical application and are described in the following section.

Event Perception Appearance. The stimulus display consisted of an array of small rectangles; after 2 secs a single rectangle was added to the display and the

subject's task was to point to this additional rectangle. The display was generated by randomly lighting rectangles in a regular 10 by 10 array; the probability of each rectangle being lit was 0.5 and therefore, on average, there were 50 rectangles in the display. The overall size of the array was 185 mm by 105 mm; each rectangle measured 5 mm horizontally by 3 mm vertically. A fixation point was provided at the centre of the display and subjects were instructed to maintain fixation until they were ready to respond. Responses were made using a light pen and subjects were given feedback on each trial. Subjects completed 25 trials.

Event Perception Threshold. The previous task can be performed almost perfectly by normal controls; the second task was designed to be free of a ceiling effect. The task and stimulus display were identical to those used in the first procedure. However, an adaptive tracking procedure was used (Corwin, Kintz & Beaty, 1979). With each correct response the task was made more difficult by decreasing the interval between the onset of the array and the onset of the target by one refresh cycle (= 20 ms): in the limit, target onset was masked by the onset of the array. With each incorrect response the task was made easier by increasing the interval. The programme kept track of the intervals at which reversals occurred and vice versa. The test ended when 16 reversals had been completed, and the intervals at which the final eight reversals occurred were averaged to give a threshold value. The threshold is an estimate in milliseconds of the time needed between the onset of the array and the onset of the target for 50% correct performance. The shorter this time the better the performance.

Event Perception Movement. A 10 by 10 array of small vertically oriented

rectangles was displayed. The array measured 185 mm by 130 mm, and each rectangle measured 5 mm vertically by 2 mm horizontally. After a variable interval one rectangle was deleted, and redisplayed 1 mm away horizontally. The subjective impression created by the display was of a sudden movement of one rectangle. The subject's task was to point to the rectangle which appeared to move. Subjects were given 25 trials. Before the task commenced subjects were familiarised with the test using a version in which the movement was repeated and the number of repetitions successively reduced on each trial.

TABLES AND FIGURES

Table 1.1 Conditions for experiments.

	Experiment 1	Experiment 2	Experiment 3	Experiment 4
Appearance	**Yes**	No	No	No
Appearance & Move	No	**Yes**	**Yes**	No
Movement Onset	**Yes**	**Yes**	**Yes**	**Yes**
Background moving	**No/Yes**	**Yes**	**Yes**	**No**
SOA (ms)	**20, 60, 100, 10^4**	$2x10^3$	$2x10^3$	$1x10^3$ to $6x10^3$
Distance (min/arc)	9	9	**9, 27, 45, 81, 120**	9
Rate (hz)	2.5	2.5	2.5	2.5

SOA = stimulus onset asynchrony; Variables under investigation are printed in bold

Table 1.2 **Experiment 3: Effect of movement distance on detection rate for *appearing* targets: Eccentricity and Quadrants**

	N_{exp}	9 min/arc			27 min/arc			45 min/arc			81 min/arc			120 min/arc			All distances			
$E_{deg/arc}$		N_{obt}	$\%_{cor}$	%dif	N_{obt}	$\%_{cor}$	%dif	N_{obt}	$\%_{cor}$	%dif	N_{obt}	$\%_{cor}$	%dif	N_{obt}	$\%_{cor}$	%dif	N_{exp}	N_{obt}	$\%_{cor}$	%dif
3 / 2	5	8	87	- 6	5	100	+ 27	2	100	+ 55	8	50	+ 25	3	66	+ 37	**26**	26	**76**	+ 23
6 / 4.5	**16**	14	100	+ 7	15	86	+ 13	17	35	- 10	20	30	+ 5	18	38	+ 8	**78**	84	**44**	+ 9
9 / 7	**26**	30	93	0	33	81	+ 8	27	40	- 5	28	35	+ 10	22	18	- 11	**130**	140	**57**	+ 4
12 / 9.5	**36**	31	90	- 3	36	52	- 21	42	45	0	35	8	- 17	43	25	- 4	**182**	187	**42**	- 11
15 / 12	**47**	47	93	0	41	75	+ 2	42	50	+ 5	39	25	0	44	31	+ 2	**234**	213	**56**	+ 3
Totals	**130**	130	**93**	---	130	**73**	---	130	**45**	---	130	**25**	---	130	**29**	---	**650**	650	***53***	---
Upper left	**32.5**	34	94	+ 1	38	71	- 2	21	33	- 12	29	27	+ 2	31	29	0	**162.5**	153	**54**	+ 1
Upper right	**32.5**	35	100	+ 7	28	57	- 16	33	48	+ 3	42	23	- 2	38	36	+ 7	**162.5**	176	**51**	- 2
Lower left	**32.5**	33	84	- 9	32	87	+ 14	37	51	+ 6	34	23	- 2	21	33	+ 4	**162.5**	157	**57**	+ 4
Lower right	**32.5**	28	92	- 1	32	75	+ 2	39	43	- 2	25	28	+ 3	40	20	- 9	**162.5**	164	**50**	- 3

$E_{deg/arc}$ = eccentricity in degrees of visual arc; N_{exp} = expected target frequency; N_{obt} = obtained target frequency; $\%_{cor}$ = % targets correctly identified % dif = difference from total percentage for condition

Table 1.3 **Experiment 3: Effect of movement distance on detection rate for *movement* onset targets: Eccentricity and Quadrants**

	N_{exp}	9 min/arc			27 min/arc			45 min/arc			81 min/arc			120 min/arc			All distances			
$E_{deg/arc}$		N_{obt}	$\%_{cor}$	%dif	N_{obt}	$\%_{cor}$	%dif	N_{obt}	$\%_{cor}$	%dif	N_{obt}	$\%_{cor}$	%dif	N_{obt}	$\%_{cor}$	%dif	N_{exp}	N_{obt}	$\%_{cor}$	%dif
3/2	**5**	5	60	+32	4	75	+29	2	50	+20	4	75	+39	2	50	+16	**26**	17	**64**	+29
6/4.5	**16**	14	28	0	12	66	+20	11	45	+15	18	44	+ 8	21	42	+ 8	**78**	76	**44**	+ 9
9/7	**26**	28	21	- 7	21	42	- 4	28	28	- 2	26	26	-10	34	41	+ 7	**130**	137	**32**	- 3
12/9.5	**36**	31	25	- 3	33	39	- 7	32	15	-15	31	16	-20	27	22	- 12	**182**	154	**24**	-11
15/12	**47**	52	30	+ 2	60	45	- 1	57	36	+ 6	51	49	+13	46	32	- 2	**234**	266	**39**	+ 4
Totals	**130**	130	**28**	---	130	**46**	---	130	**30**	---	130	**36**	---	130	**34**	---	**650**	650	***35***	---
Upper left	**32.5**	34	38	+10	24	41	- 5	28	17	-13	27	44	+ 8	37	40	+ 6	**162.5**	150	**36**	+ 1
Upper right	**32.5**	33	24	- 4	37	40	- 6	39	35	+ 5	36	47	+11	34	26	- 8	**162.5**	179	**35**	0
Lower left	**32.5**	32	21	- 7	32	40	- 6	34	29	- 1	28	28	- 8	27	33	- 1	**162.5**	153	**30**	- 5
Lower right	**32.5**	31	29	+ 1	37	59	+13	39	37	+ 7	39	28	- 8	32	37	+ 3	**162.5**	168	**38**	+ 3

$E_{deg/arc}$ = eccentricity in degrees of visual arc; N_{exp} = expected target frequency; N_{obt} = obtained target frequency; $\%_{cor}$ = % targets correctly identified % dif = difference from total percentage for condition

Table 1.4 Experiment 4: Effects on eccentricity and Quadrants

$E_{deg/arc}$	N_{exp}	N_{obt}	$\%_{corr}$	$\%_{diff}$
3 / 2	**50**	37	89	+ 10
6 / 4.5	**150**	146	88	+ 9
9 / 7	**250**	239	87	+ 8
12 / 9.5	**350**	351	73	- 6
15 / 12	**450**	477	76	- 3
Totals	**1250**	1250	**79**	
Upper left	**312.5**	299	76	- 3
Upper right	**312.5**	333	78	- 1
Lower left	**312.5**	332	80	+ 1
Lower right	**312.5**	276	82	+ 3

$E_{deg/arc}$ = eccentricity in degrees of visual arc; N_{exp} = expected target frequency; N_{obt}= obtained target frequency; $\%_{cor}$ = % targets correctly identified; % diff = difference from total percentage for condition.

Figure 1.1 Results of experiment 1: Appearance and Movement Onset

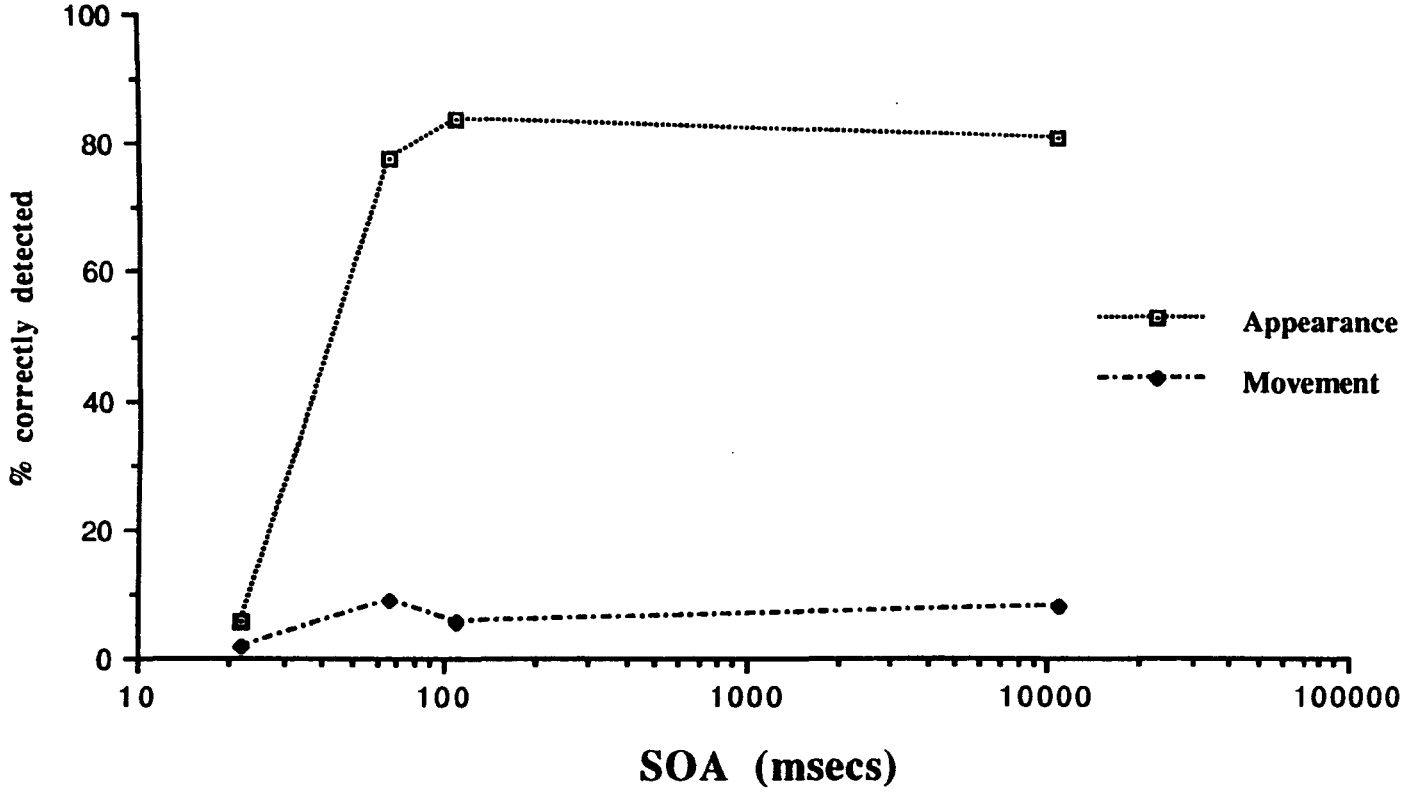


Figure 1.2. Results of experiment 2: Appearance and Movement Onset

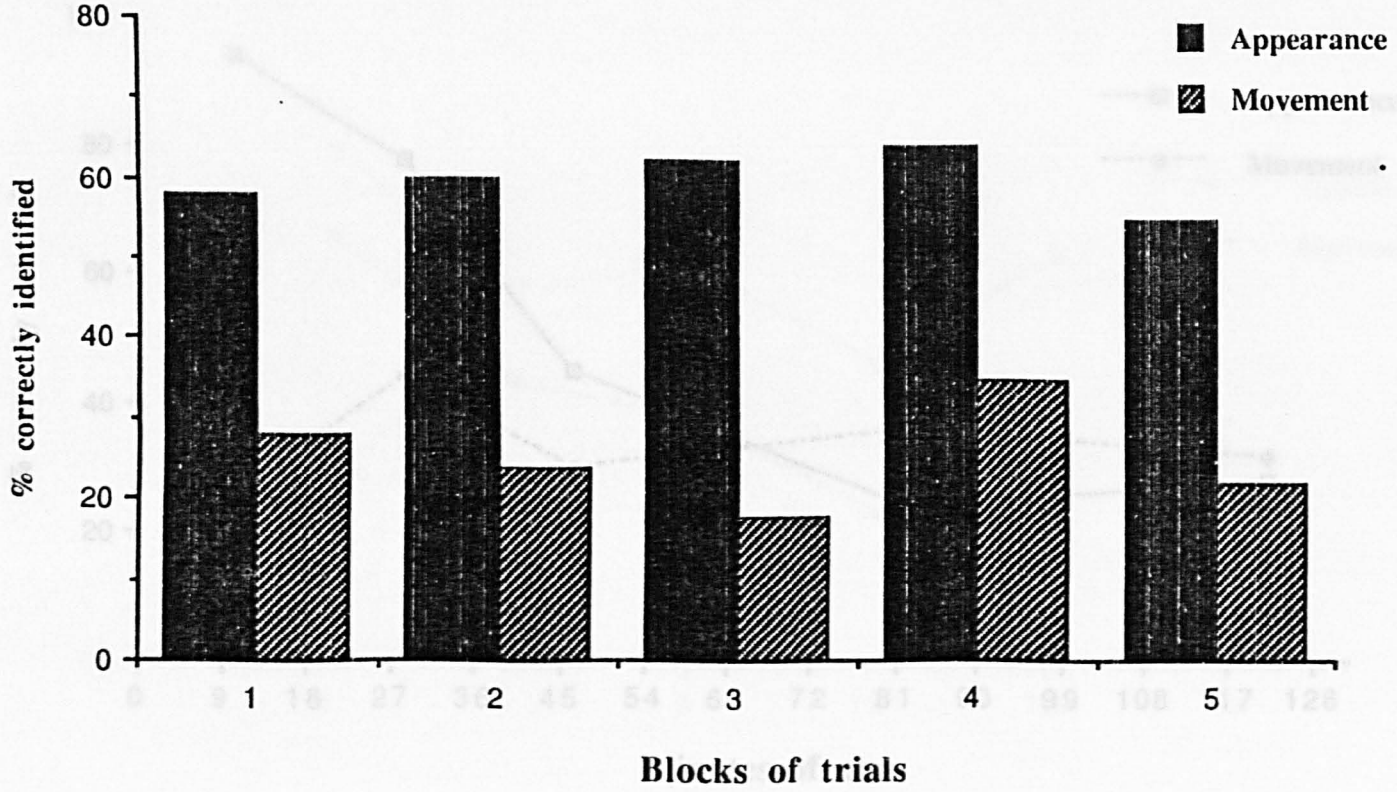


Figure 1.3. Results of experiment 3: Lateral spread of reciprocal inhibition

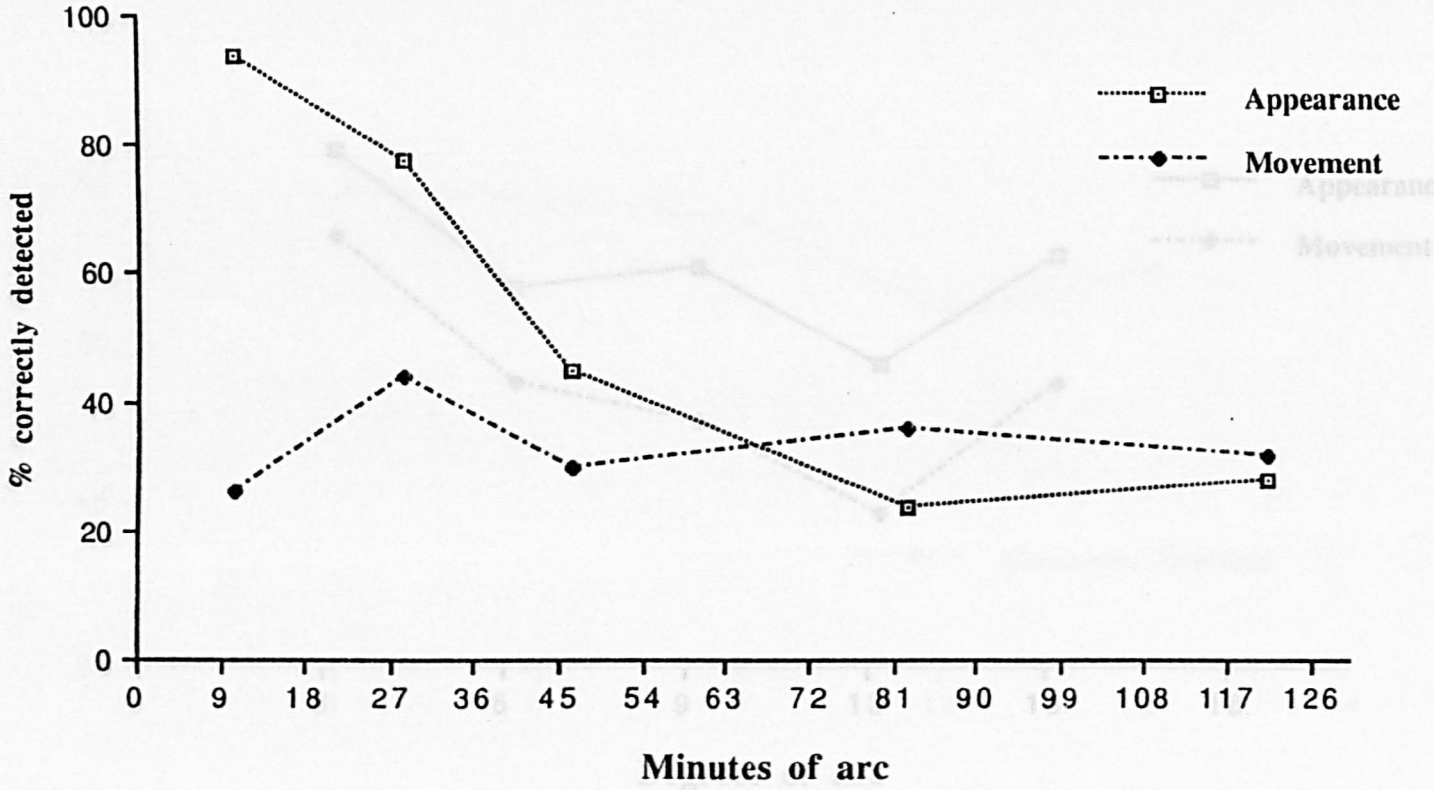


Figure 1.4. Analysis of eccentricity for results in experiment 3

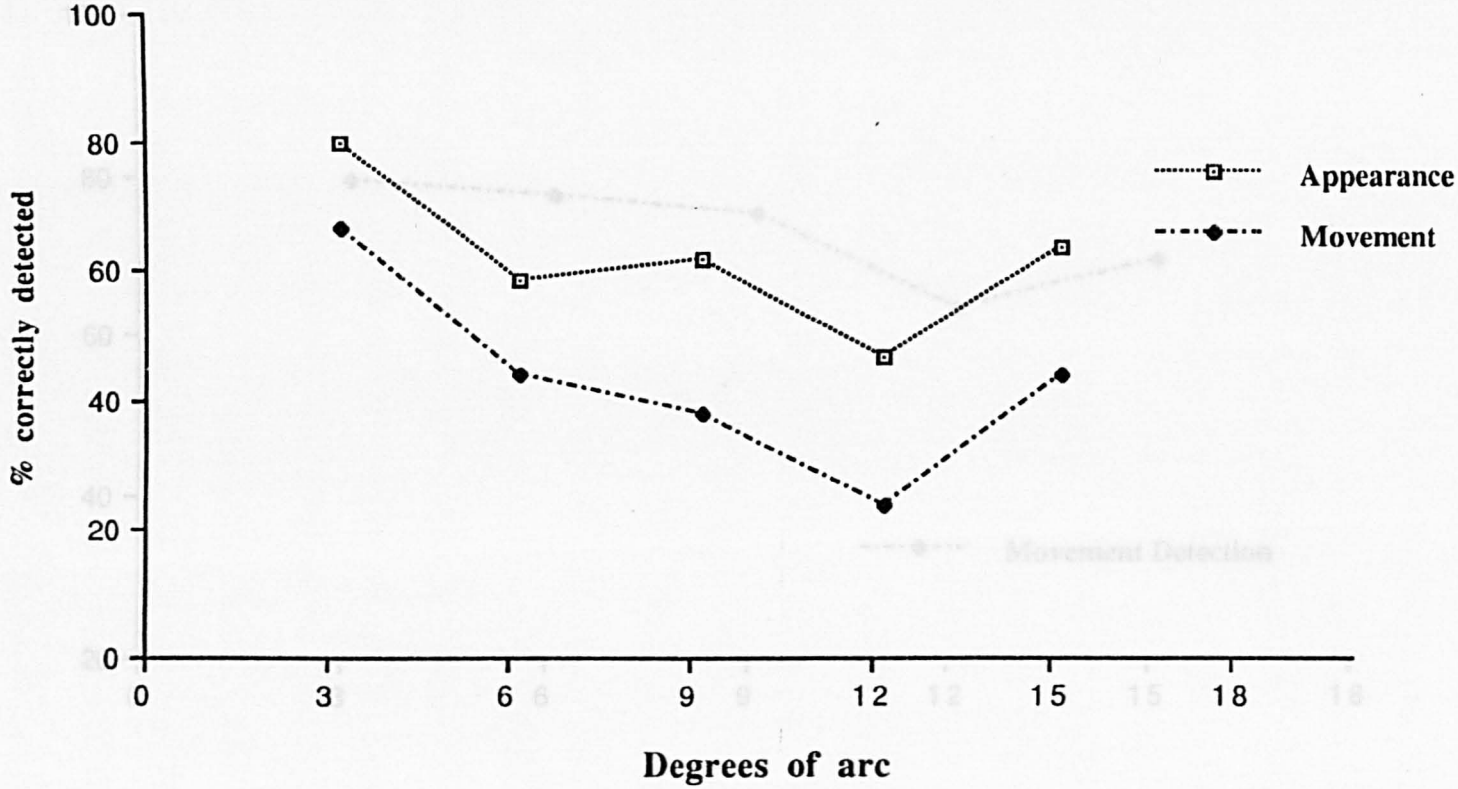
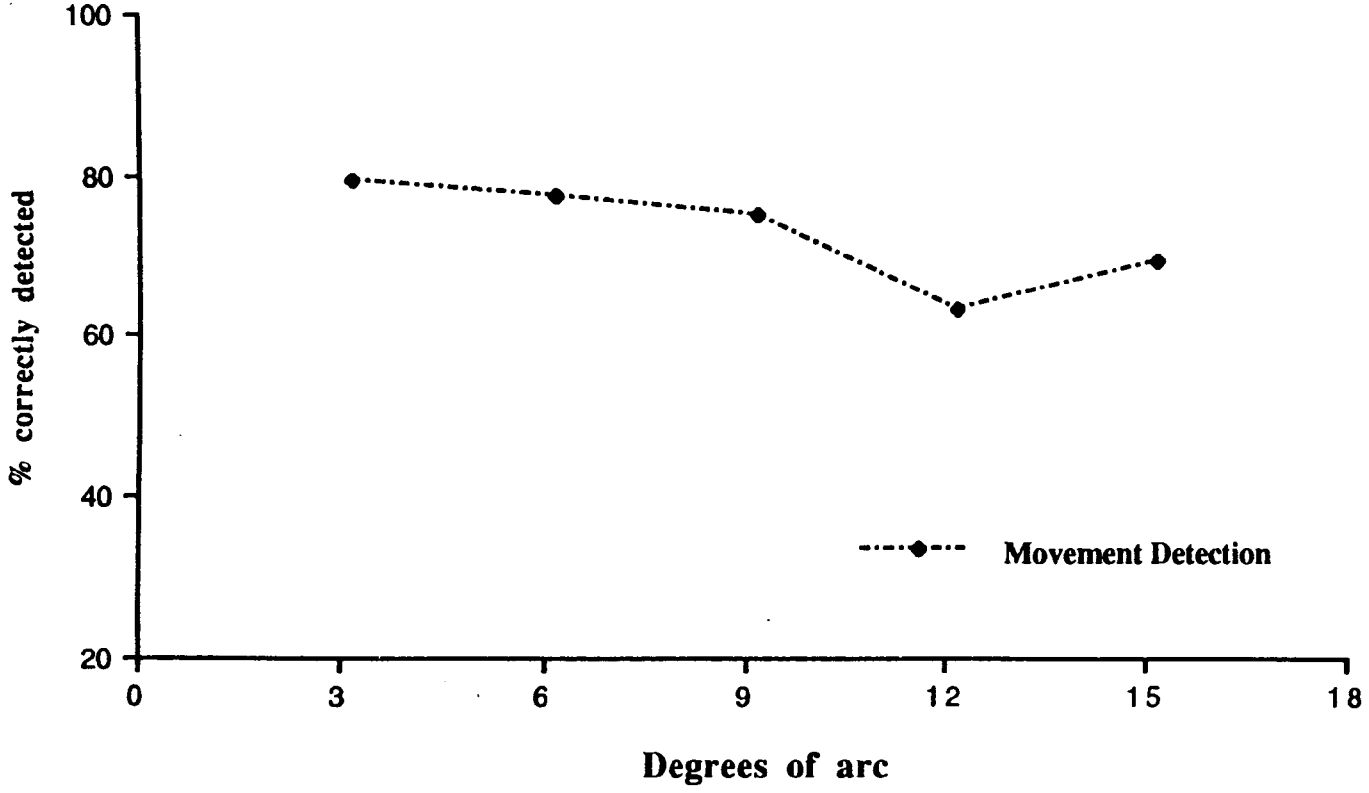


Figure 1.5. Analysis of eccentricity for results in experiment 4



2.0 SOLVENT ABUSE

Solvent abusers were thought to be an appropriate group for evaluation of the specificity and sensitivity of the Event Perception tasks because visual and related attentional processes are known to be affected by prolonged solvent inhalation. In addition, as the literature review will show, there is a suggestion of potentially differential involvement of the peripheral and the central nervous system depending on the substances used.

2.1 INTRODUCTION.

Accidental poisoning by organic solvents has been reported long before solvents became fashionable agents for recreational use/abuse. Solvents - especially toluene and n-hexane - are ubiquitous substances in modern industry and in the home. Although a heterogeneous group, most solvents are volatile, lipophilic, and have central nervous depressant effects. Solvent "sniffing" is by no means a recent phenomenon; misuse by adults of nitrous oxide, ether, and chloroform was fashionable as early as the 19th century. An epidemic like increase in voluntary inhalation of solvents by children and teenagers has swept many parts of the world from the early sixties and continued to present a problem throughout the eighties. The use of solvents for 'kicks' enjoyed increasing popularity amongst children and teenagers generally of the lower socio-economic classes mainly for their ease of availability and use combined with low cost and rapid intense effects. Press and Done (1967) published an early comprehensive account concerning the physiological effects as well as the socioeconomic background

and geographical distribution of solvent abuse amongst young Americans. As with most substances of abuse disruptive social and clinical effects were soon discovered and became a matter of increasing concern as the number of fatalities rose and individuals with apparently irreversible neurological conditions were identified. Apart from self-destruction and antisocial acts associated with acute intoxication the gravest aspect of solvent abuse lies in the occasional occurrence of sudden death and permanent neurological deficit. In 1970 Bass reported on a phenomenon labelled 'Sudden Sniffing Death' (SSD) relating to the deaths of a number of young people following voluntary solvent inhalation and some sort of exercise or stressful situation. Sudden death has been attributed to the precipitation of cardiac arrhythmias possibly due to sensitisation of the myocardium to adrenaline (Bass, 1970; Winek & Collom, 1971). However, death also occurs from accidental suffocation as a result of using the popular method of placing a plastic bag over head and mouth to increase the effects of rapid intoxication, and from aspiration of vomit. In the UK between 1970 and 1977 forty deaths of young people could be positively linked to solvent abuse (Oliver & Watson, 1977). By 1980 1300 new cases of solvent abuse were reported to the police in one year in Scotland alone in a secondary school population of almost half a million (King, 1982). Boys have been invariably found to represent a much higher proportion of solvent abusers than girls and Watson (1980) found the ratio to be approximately 4:1. Most of the substances enjoying popularity amongst the abusing population contain a mixture of toluene and n-hexane in varying proportions; in many cases it has therefore been difficult to evaluate separately the contributing effects of each substance on its own at least in human subjects. The question of reversibility of neurotoxic effects of solvents became a matter of controversy and some findings will be discussed briefly in the following section.

2.1.1 N-hexane

N-hexane toxicity has been recognised for a number of years. The neurotoxic agent appears to be 2,5-hexanedione, a metabolite of n-hexane and methyl n-butyl ketone, which inhibits glyceraldehyde-3-phosphate dehydrogenase (GAPDH) leading to failure of GADPH dependent axonal transport and axonal degeneration (O'Donahue & Krasavage, 1979; Sabri, Moore & Spencer, 1979). The symptoms described for acute exposure to n-hexane are similar to those for toluene although the limit considered safe for human exposure is higher at 500 ppm. Studies in man found dizziness and giddiness after ten minutes of exposure to 5000 ppm of n-hexane but none of these symptoms after a similar exposure to 2000 ppm. Nausea headache and irritation of eyes and throat have been reported at 1400 to 1500 ppm but no irritation was reported at 500 ppm in subjects unaccustomed to exposure. In the US a 500 ppm limit was set to provide freedom from these acute, reversible central nervous effects (American Conference of Governmental Industrial Hygienists, 1971). A study by Schaumburg and Spencer (1976) demonstrated that n-hexane acts as a neurotoxin producing nerve fibre degeneration in both the peripheral nervous system but also in the central nervous system (CNS). Schaumburg and Spencer intoxicated rats with pure n-hexane, either by repetitive subcutaneous injection or by continuous inhalation. Rats were found to develop clinical and/or pathological evidence of peripheral neuropathy. Animals intoxicated by inhalation of 400 to 600 ppm for periods of up to 162 days displayed giant axonal swellings and nerve fibre degeneration both in the central and peripheral nervous systems. The first detectable abnormality in both systems was local axonal dilatation accompanied by localised fibre swelling. The myelin sheath overlying the axonal swellings was found to be abnormally thin. Nerve

fibres from animals displaying signs of neuropathy were in a more advanced stage of degeneration and were often composed of a chain of myelin ovoids. Perivascular oedema was present in the most heavily affected peripheral nerve fascicles. Inspection of the central nervous system revealed degeneration of myelinated fibres in the ventromedial and peripheral ventrolateral tracts of the lumbosacral spinal cord, the gracile nuclei, the ventromedial medulla adjacent to the hypoglossal nerve, the perimeter of the ventrolateral quadrants of the medulla, the inferior peduncles and in the white matter of the cerebellar vermis. Schaumburg and Spencer stressed the relevance of the central nervous system changes and the need for a reduction in the legal Threshold Limit Value for human exposure. Prior to their ultrastructural studies of the dying back process concerning the evolution of giant axonal degeneration (Spencer & Schaumburg, 1977), it was widely believed that retrograde axonal degeneration resulted from toxic damage to the anabolic machinery of the neuronal perikaryon. Their studies of the spatial-temporal pattern of nerve fibre damage revealed the patterns of degeneration to be more compatible with an axonal locus of toxic damage.

Sabri, Moore & Spencer (1979) demonstrated that neurotoxic compounds such as n-hexane do interfere directly with the metabolism of the nerve fibre. Herskowitz, Ishn & Schaumburg (1971) described three cases of industrial exposure to n-hexane with average concentrations of 650 ppm and peaks at 1300 ppm. All three patients had developed weakness and sensory loss, and reduction in nerve conduction times. Muscle biopsies showed an angulation of fibres and target fibres indicating denervation of muscle. Severity of symptoms was reported to be directly proportional to duration and intensity of exposure. Goto et al. (1974) investigated four cases of

severe toxic polyneuropathy due to glue sniffing. Examination of their patients revealed a predominant motor polyneuropathy but of mixed type. The authors considered the cause of the polyneuropathies to be inhalation of vaporised elements of adhesive agents which contained mainly n-hexane and toluene. They regarded n-hexane as being chiefly responsible for the polyneuropathy but considered toluene as possibly having an influence on the course of the illness. An important observation in their study was that symptoms in their patients were slowly progressive up to three months **after** ceasing inhalation; thereafter they showed gradual improvement. Another interesting finding in the Goto et al. study was that their cases presented mainly with a motor polyneuropathy whereas n-hexane had previously been considered to produce mainly sensory or mixed polyneuropathy.

Towfighi, Gonata, Pleasure, Cooper & McCree (1976) published a study on two cases of progressive sensorimotor neuropathy who had prolonged voluntary exposure to n-hexane. Both patients appeared to have initially inhaled substances not containing n-hexane but a mixture of toluene and other substances. No significant abnormalities were observed during this period. After their patients had changed to n-hexane containing substances a significant deterioration took place within a matter of months resulting in weight loss and a number of neurological abnormalities. Nerve biopsies showed loss of axons, accumulation of filaments, widening of nodes of Ranvier, and focal enlargements confirming the presence of progressive sensorimotor neuropathy and a dying back neuropathy i.e. gradual degeneration of nerve fibres starting at the distal site. After the onset of neuropathy one patient changed to a non n-hexane containing brand and made a complete recovery. The authors therefore concluded that the agent responsible for producing the neuropathy was n-hexane rather than toluene.

Seppalainen, Raitta and Huuskonen (1979) conducted a study employing visual evoked potentials (VEPs) and electroretinograms (ERGs) on fifteen workers who had been occupationally exposed to n-hexane for 5-21 years and on ten healthy volunteers. The amplitude of the VEP components was clearly smaller among the exposed subjects. In addition, the latencies of P1 and N1 where longer among the exposed workers. The peak-to-peak amplitude of the ERGs was also diminished among the exposed subjects. Chang (1987) reported the results of his investigations on 28 print workers following an outbreak of polyneuropathy. Workers had been exposed extensively to n-hexane vapours for a period of three months. Patients presented with progressive weakness and muscle atrophy symmetrically involving the distal part of the lower extremities. Patterned visual evoked potentials (pVEPs) showed significantly longer latencies and decreased amplitudes in subclinical and polyneuropathy cases than in 22 normal controls. Findings for brainstem auditory evoked potentials (AEPs) and somatosensory evoked potentials (SEPs) were similarly abnormal showing an increase in latencies and reductions in amplitudes compared to the control group. In the absence of optic nerve atrophy and retrobulbar neuritis, Chang refuted the possibility of pVEP abnormalities being due to toxic effects of n-hexane on the retina or visual pathways peripheral to the geniculate bodies. He concluded that his findings were due to the chronic neurotoxic effects of n-hexane on the central nervous system, including the cerebrum, the brainstem, and the spinal chord.

2.1.2 Toluene

Toluene's effects upon the nervous system are not fully understood and some workers believe these effects to be temporary. One of the earliest experimental studies on the effects of toluene exposure to human performance was conducted by von Oettingen, Neal & Donahue (1942). They exposed three human subjects and three dogs to various concentrations of toluene vapour of 'a high degree of purity' ranging from 50 to 800 ppm for an average of eight hours on a number of days under work conditions. They found that single exposures of human subjects for eight hours daily did not cause definite changes in white blood cells, circulation or respiration. However, inhalation for eight hours of 200 ppm caused slight but definite impairment of coordination and reaction time. With higher concentrations these effects became increasingly severe, and with concentrations of 600 and 800 ppm effects were observed after a few hours exposure. Wilson (1943) reported his findings of industrial exposure to toluene on a work force of a large factory who had been exposed to concentrations ranging from 50 to 1500 ppm. A gradual increase of symptoms was observed depending on concentration and duration of exposure. Patients exposed to more than 500 ppm complained of nausea, headache, dizziness, anorexia, palpitation and extreme weakness with pronounced loss of coordination and 'definitely impaired reaction time'. These patients received medical treatment and after several weeks of rest, symptoms attributable to depression of the CNS began to clear up. Weakness was reported to be the most persistent symptom and slight exertion caused fatigue in one case of aplastic anemia several months after all other symptoms had disappeared. In 1951 Baker and Tichy published a comprehensive report on the effects of organic solvents on the CNS. Because of a high affinity for fatty tissues, all organic solvents

are relatively toxic to the CNS but Baker and Tichy believed that little attention had been paid to the 'injurious action upon the nervous system where these solvents probably exert their most disastrous effects' (p. 475). In animal studies of chronic toluene intoxication they established that changes in the CNS were of 'a more chronic nature (in contrast to single exposures; comment added) with marked shrinkage and hyperchromaticity of many cortical neurons, although many also showed acute swelling and tigrolysis. (...) The appearance of the cerebellar folia suggested a decrease and degeneration in Purkinje cells.' (p. 483).

It is believed that toluene's main toxic impact on the CNS is due to high cerebral perfusion and its affinity for lipid rich tissues such as cerebral white matter from which it is slowly released. Experiments in animals after toluene exposure have shown toluene concentrations in fatty tissues to be eighty times higher than in blood (Carlsson & Lindquist, 1977). Toluene assay on post mortem blood and brain specimens in animals (Bruckner & Peterson, 1981) and humans (King, Day, Oliver, Lush & Watson, 1981) support these findings. Bruckner and Peterson (1981) consistently found higher concentrations of toluene in the liver than in the brain, as did Carlsson and Lindquist (1977). This particular result was surprising since uptake in well perfused tissues was believed to be dependent largely upon the tissues' lipid content. Despite lower perfusion ratios fatty tissue has been demonstrated to serve as the most extensive reservoir for toluene, although it only slowly accumulates the chemical due to its relatively poor blood supply (Carlsson & Lindquist, 1977). Bruckner and Peterson (1981) found that concentrations of toluene initially fell somewhat more rapidly in the liver than in the brain. This was thought to be due to the higher lipid content of the brain and more extensive metabolism in the liver. Their study also

suggested that blood concentrations may be biphasic with an initial peak followed by a trough reflecting lipid binding by the central nervous system and a subsequent peak as toluene is slowly re-released into the bloodstream. At atmospheric concentrations of approximately 200 ppm (which in some countries is considered the legal maximum exposure limit for industrial environments) headache, dizziness, irritability, insomnia, and slowing of reaction time are reported. Interestingly, paralysis of olfaction tends to appear even at this relatively low level. As concentrations increase above 800 ppm, victims become delirious, uncoordinated, and ataxic. Higher concentrations cause depression of consciousness and, ultimately, coma. The limit in Britain has been set at 100 ppm toluene vapour for industrial environments (Utidjian & Weaver, 1974).

Glue sniffers inhale toluene vapors in high concentrations to experience euphoria and perceptual distortions but it has been difficult to derive at exact estimates of the amount of actual exposure. Some investigators believe that chronic abusers may routinely exceed concentrations of 1000 ppm (King, 1982). This figure may be a rather crude estimate and lack relevance since solvent abusers are often found to be unreliable witnesses concerning the particular preparations used, duration and intensity of exposure and concomitant abuse of other drugs which may have potentiating effects. This opinion is shared by Bruckner and Peterson (1981) who observed that animals exposed to 12000 ppm of toluene vapour for 2-3 minutes exhibited signs of ataxia characteristic of inebriation in humans. They thought it likely that solvent abusers on occasion may subject themselves to even greater concentrations of the solvent. Hayden, Peterson and Bruckner (1977) in a review article on the toxicology of toluene quoted evidence to support the view that toluene has the potential to alter the toxicity of numerous chemical agents. It is known that toluene changes the metabolism

of other solvents eg. suppressing the biotransformation of benzene and styrene, and reciprocal inhibition of toluene and trichloroethylene. On the other hand toluene and n-hexane do not seem to modify one another's metabolism.

Blood level toluene assays had been rather rare in the past but became a more routine hospital investigation in the eighties for patients with suspected solvent abuse. This was aided by a more rapid and reliable method for measuring toluene in biological specimens developed by Peterson and Bruckner (1978). Nomiyama and Nomiyama (1978) found 50 ug/ml of toluene in the blood of one of three adolescents who were discovered dead after abusing toluene in a car. However, it was felt that levels had decreased during the interval between death and specimen recovery.

Although there had been isolated reports on the voluntary inhalation of solvents in the fifties, the first paper to attract widespread attention to the fact that this habit was spreading in the United States was published by Glaser and Massengale (1962). The authors found that the mean age was thirteen amongst 130 glue-sniffers arrested in Denver in a two year period. Glaser and Massengale found few physical abnormalities in their examination of six cases and problems were mainly seen as being of psychiatric and/or social nature often predating the onset of the habit. They concluded their report by stating that 'there has been thus far no documented evidence of serious physical side effects of this practice'. In a follow-up paper Massengale, Glaser, LeLievre, Dodds and Kook (1963) arrived at a similar conclusion after examining further cases of young solvent abusers. This conclusion appears somewhat surprising given the fact that there was already some strong evidence both in the clinical and experimental literature suggesting lasting CNS and peripheral nervous system (PNS)

damage. In fact their paper was still quoted by Biggs, Bender and Foreman (1983) as evidence against significant effects of solvent abuse on physical health.

From a case report by Satran and Dodson (1963) it appears that knowledge about possible physical side effects was clearly accessible. Satran and Dodson reported the case of a 30 year old man who admitted to having voluntarily inhaled toluene for ten years. Despite his long contact with toluene, none of the clinical or laboratory investigations indicated systemic pathological abnormalities. EEG recordings were interpreted as being abnormal, with excessive episodic slow activity, and occasional sharp, nonfocal discharges. The findings were regarded as consistent with diffuse encephalopathy but the features of the record were nonspecific and their significance as a single recording was felt to be difficult to determine. Grabski (1961) reported the case of a young man in his late twenties who had deliberately exposed himself to - as it would appear - an almost pure form of toluene over a period of seven years. His consumption consisted of one gallon of toluene which lasted him for four to six weeks with apparently continuous inhalation throughout the day. The patient's resulting neurological abnormalities consisted of slight but persistent nystagmoid movements on lateral gaze, equivocal Babinski signs bilaterally, titubating gait and rebound phenomena. From this symptomatology Grabski concluded that the patient's chronic use of toluene might have led to cerebellar atrophy. In a follow-up report on the same patient, Knox and Nelson (1966) disputed Grabski's anatomical localisation of toluene's effect and concluded that the process was primarily a corticobulbar and corticospinal disorder and not a cerebellar syndrome. Following Grabski's evaluation in 1958 the patient appeared to have continued in his habit of excessive toluene abuse resulting in a total duration of fourteen years of exposure to toluene. A

pneumoencephalogram showed cerebral atrophy but normal cerebellar folia. Knox and Nelson's refutation of Grabski's diagnosis is somewhat surprising for at least three reasons: 1) at the time of their study there was sufficient evidence available to support the diagnosis of cerebellar degeneration resulting from toluene inhalation; 2) neurological symptoms of ataxia, rapid tremor, limb incoordination, brisk snout reflex and Babinski's signs appeared to be even more pronounced during their examination; these symptoms are generally regarded as suggestive of cerebellar dysfunction; 3) pneumoencephalography is a rather crude neuroimaging technique lacking the sophistication and resolution of today's standards and it appears feasible that evidence of cerebellar degeneration might have escaped image analysis. In addition, Knox and Nelson's interpretation of the images may have been somewhat naive, not allowing for a sufficiently large error margin.

Dodds and Santostefano (1964) failed to find any differences on a number of psychological tests measuring the ability to maintain continuous attention and concentration, problem solving and visual-motor coordination between a group of 12 boys (mean age 13.8 years) who had been apprehended while intoxicated from sniffing glue, and a group of 21 controls (mean age 12.6 years). The authors conceded that exposure to solvents may not have been long enough to exceed a possible threshold for the development of permanent impairment although they maintain that all their subjects were considered to be chronic inhalers. Secondly, they considered the possibility of cerebellar damage based in the light of Grabski's (1961) findings but admitted that such impairment might have escaped their evaluation given the range of tests employed. Their paper was given much weight in the debate whether chronic abuse of solvents might lead to persistent psychological and/or neurological

damage. Press and Done (1967) found that susceptible persons may develop hallucinations and become psychotic as a result of toluene abuse. Heuser (1968) was one of the first to report a case of polyneuropathy due to voluntary toluene sniffing although there has been some earlier experimental evidence from animal studies. Kelly (1975) described the case of a 19 year old girl who had for one and a half years become habituated to almost daily sessions of paint sniffing. The paint was thought to contain toluene as its main constituent. She complained of increasing clumsiness, incoordination, and unsteadiness of gait prior to the neurological investigation. Her complaints were felt to be indicative of cerebellar dysfunction secondary to a toxic factor in the paint. EEG, radionuclear brain scan, carotid and vertebral arteriography, and pneumoencephalopgraphy were within normal limits. Neurological examination five months after discontinuing paint sniffing indicated objective improvement.

Boor and Hurtig (1977) studied two patients who had been almost exclusively exposed to pure toluene. One patient was an optician who due to anosmia exposed himself accidentally to toluene vapors over a prolonged period using the substance commercially in his business. He complained of disturbances in concentration and memory, excessive sleep and exhaustion. On examination some minor neurological abnormalities were discovered with gait ataxia being the most prominent feature. He made a complete recovery within a few months after withdrawal from toluene. Their second patient was a 25 year old man who had voluntarily inhaled an almost exclusively toluene containing cleaning agent for over ten years. On examination he was said to be alert but lethargic, presenting as intellectually dull and performing poorly on serial sevens. Recent memory was said to be fair and there were no signs of aphasia although speech was mildly slurred. His main problems were a very

pronounced ataxia with difficulties in maintaining a standing posture and showing poor coordination of limb movements. A CT scan revealed widening of the cortical and cerebellar sulci over both hemispheres suggesting diffuse cerebral and cerebellar atrophy. There were no obvious signs of peripheral neuropathy; electromyographic and nerve conduction studies were in the normal range giving rise to the conclusion that the toluene induced neurological syndrome is exclusively central, sparing peripheral nerves. Boor and Hurtig interpreted their findings as contradicting Heuser's (1968) and Goto's et al. (1974) claims that toluene might play a role in producing peripheral neuropathy.

Tsushima and Towne (1977) compared twenty paint sniffers (mean age 18.5 years; range 11-24 years) and twenty non-sniffers (mean age 18.0 years) on thirteen neuropsychological measures sensitive to brain dysfunction. Average consumption in the sniffers was 2.3 cans of paint per day with a mean duration of 5.9 years (range 1-13 years). There was no accurate breakdown of substances contained in the paints but the authors thought that toluene might have been a common element. Sniffers showed statistically significant impairment on 11 of the 13 measures. Differences were most striking for measures involving visuomotor coordination such as the Grooved Pegboard Test and Coding B from the Wechsler Intelligence Scales for Children but also on tests with a strong cognitive component requiring inhibition of response such as the Stroop Test. However, non-sniffers were significantly superior in IQ which produced some difficulty in interpreting findings. A relationship was found between duration of paint sniffing and neuropsychological test performance indicating a decrease in performance for subjects with a longer history of abuse. Tsushima and Towne interpreted this finding as possible evidence that paint sniffing rather than

premorbid intellectual ability was a major cause of the neuropsychological differences found in their study. There was a significantly higher daily consumption for subjects with a longer history of sniffing with a correlation of $r=0.65$ ($p<0.001$) between years of sniffing and number of cans consumed. Tsushima and Towne interpreted this finding as possibly implying an increased tolerance to paint sniffing. Given the wide age range of their sample and their failure to correlate consumption and duration with age commands some caution with respect to this interpretation. A short coming in this study lies the fact that no assays were obtained allowing identification of substances and recency of abuse. All sniffers admitted to inhaling the day before testing and thus results may reflect subacute effects to some degree.

Comstock (1977) in a review of psychological measures relevant to CNS toxicity with specific reference to solvent inhalation came to the conclusion that the Halstead-Reitan neuropsychological test battery would probably be best suited for this purpose. However, only two of her 22 cases were assessed on this test: 'one scored within the normal range after an abuse free interval. The other scored well into pathological ranges on many subtests, reflecting diffuse impairment' (p. 321). Unfortunately no information was given about the duration of the abuse free interval in the former case nor about the second case or whether he might have suffered from the acute effects of intoxication. Bigler (1979) used the Halstead-Reitan battery and the WAIS on ten 16 to 20 year old chronic inhalant abusers screened out of 198 solvent abusers admitted to his unit over a period of ten months. He found that chronic inhalant abusers as a group could not be differentiated on the basis of these neuropsychological measures from patients with confirmed cerebral pathology. However, the inhalant group could be differentiated from the non-brain damaged/non-psychotic control group. Bigler

attributed the deficits in the inhalant group to both direct neurotoxic effects and to anoxic encephalopathy resulting from repeated bouts of subclinical hypoxia associated with inhalant abuse.

Escobar and Aruffo (1980) reported the case of a 27 year old Mexican male who had been addicted to glue sniffing and thinner inhalation for twelve years. The patient developed neurological and behavioural disturbances which led to hospital admission and death. The patients was said to have inhaled different compounds containing 'thinner' (sic!), toluene and n-hexane. CT scan showed cerebral and cerebellar atrophy with prominence of the sulci at the level of the cerebral convexity and dilated lateral ventricles. At autopsy coronal sectioning showed thinning of the cerebral cortex and the corpus callosum. Examination revealed that the change in the corpus callosum was most evident at the level of the interparietal connections and was due to the loss of interhemispheric fibres which originate primarily from the third and sixth layers. The cerebral cortex, basal ganglia, and cerebellum proved to be the most affected parts with diminished neuron density. The cerebellar cortex was affected severely and most of the Purkinje cells were replaced by diffuse gliosis. The parietal cortex in the association areas was severely damaged, mainly the second, third and sixth layers. This case represents one of the best illustrated examples of a chronic solvent abuser coming to autopsy.

Allister, Oliver, Lush and Watson (1981) reported the case of a 15 year old boy who presented after a grand mal seizure followed by uncontrolled status epilepticus. The cause for his condition was initially obscure but analysis of a brain specimen obtained to rule out an infectious condition revealed a toluene concentration of 14 ug/g

tissue. The patient recovered gradually and on follow-up two years later showed no focal neurological deficit. Psychometric tests indicated no definite impairment but he continued to have one or two seizures a month and exhibited major behavioural problems. Will and McLaren (1981) published their findings of renal damage in a 14 year old boy who had abused solvents for two years. During the previous eight months he had used one pint of adhesive daily. Laboratory findings and symptomatology were compatible with renal failure but after some four weeks of abstinence his symptoms had disappeared and laboratory findings had returned to normal. This case is remarkable with respect to the widespread belief that toluene has low or no hepatorenal toxicity, particularly when considering the absence of any evidence of renal or hepatic damage in a sample of 132 cases studied by Watson (1978). However, O'Brien, Yeoman and Hobby (1971) had previously reported the case of a 19 year old boy who had been inhaling a proprietary brand of liquid cleaner over three years. Gas chromatography identified its main constituent to be toluene. Symptoms and laboratory findings were indicative of hepatic and renal dysfunction. On follow-up six months later the patient was asymptomatic having abstained from solvents for the same period of time.

Korman, Matthews and Lovitt (1981) conducted a study on 68 inhalant abusing and 41 other-drug-abusing adolescent subjects. No information was provided regarding their subjects' mean age or age range or sex nor about substances abused by either group apart from the global distinction into inhalers being 'very heavily involved with inhalants' compared to 'almost no use of inhalants' by controls. Information on recency and frequency or quantity of inhalants abused was also missing. Subjects were assessed on a battery alleged to consist of 68 measures. However, measures

were counted repeatedly including summary measures. This also applied to the twenty measures reported to show statistically significant differences between inhalers and controls. Differences were found to be highly significant for WAIS VIQ with inhalers scoring ten scale points lower than controls. The authors fail to appreciate the possible influence this presumably premorbid difference might exert on other test results. It is therefore difficult to accept the authors' conclusion that 'the effect of inhalant abuse may be severe and widespread' without.

King, Day, Oliver, Lush and Watson (1981) published a report on nineteen patients (age range 8 -14 years) who had been admitted to hospital with neurological impairment following glue sniffing. Tests of renal and hepatic function were normal in all patients. Electroencephalograms (EEGs) were carried out in ten patients and were found abnormal in three, showing diffuse slow wave activity in two and unilateral slowing in the other patient. Repeat EEGs three weeks later in these patients were normal. Five patients were noted to show psychological and personality change on discharge from hospital. Thirteen patients made a complete recovery. Unfortunately no information was provided about frequency and recency of inhalant abuse nor was there a breakdown of substances contained in the adhesives used by this group although they were said to contain toluene. The nature of the neurological impairment was not specified nor was any information given about the measures employed to judge psychological and personality change. This information is also missing in a paper by King (1982) on apparently the same group of patients but including one additional case. Shikler, Seitz, Rice & Strader (1982) performed CT investigations on eleven out of 42 solvent abusers with histories of inhaling the fumes of pure toluene. Patients selected were in the age range of 15-31 years and showed neurological

abnormalities including tremor, slow speech, impaired thought processes, paresthesia, dystonia or amnesia. Six of the eleven patients with a history of 10-16 years of solvent abuse displayed changes compatible with diffuse brain damage. Four of them were judged to suffer from mild atrophy including enlargement of the ventricular system, basal cisterns and convexity sulci. Two patients also had cerebellar atrophy with prominence of the fourth ventricle, the pontine and cerebello-pontine angle cisterns and/or shrinkage of the cerebellar folia. The authors expressed their uncertainty as to whether the pathophysiological process responsible for cortical atrophy identified in their patients was due to recurrent hypoxia or a direct neurotoxic effect of toluene or one of its metabolites.

Iregren (1982) compared the effects on psychological test performance of 34 retrogravure printers exposed to toluene with the effects of exposure to a mixture of organic solvents in spray painters and a group of industrial workers not exposed to any solvents. There were no differences between the printers and the control group in most of the functions assessed except for a significantly poorer simple RT in the printers. However, spray painters were significantly impaired on four of the eleven measures. This study suggests that either some of the solvents to which spray painters had been exposed were more neurotoxic than toluene, or that the interactive effects of these mixtures produced more serious side effects. Anshelm-Olson (1982) conducted a study on 47 workers who had been exposed daily to a mixture of solvents for more than ten years or were exposed to concentrations clearly above the legal limits at the time of the investigation. Her aim was to assess the effects of chronic industrial solvent exposure on CNS function. Workers were examined before and after a work day on a battery of tests including simple RT, perceptual speed, short -term memory,

and critical flicker fusion. Exposed workers performed less well than the non-exposed group on the tests. Differences were most pronounced for the group exposed to higher solvent concentrations. Anshelm-Olson interpreted her findings as being primarily due to acute effects.

Channer & Stanley (1983) reported a case of a sixteen year old boy with persistent visual hallucinations secondary to chronic solvent encephalopathy. Apparently exposure to agents containing a mixture of toluene and n-hexane was limited to three months. However, VEPs to checker board pattern reversal were delayed by 2.5 SD on the right and 3 SD on the left. A CT scan showed no abnormalities. Repeated EEGs over a three months period disclosed widespread generalised slow wave activity and irregular posterior alpha waves on eye opening. On follow-up four months later the EEG was unchanged and VEPs were delayed 2 SDs from normal. Another study attributing abnormalities in four solvent abusers to the exclusive use of toluene containing substances was conducted by Lazar, Ho, Melen & Daghestani (1983) who claimed that toluene abuse is a cause of slowly progressive multifocal CNS dysfunction. They interpreted their findings of impairment in cognitive, cerebellar, brainstem, auditory, and pyramidal tract function in their subjects as evidence of severe multifocal central nervous system damage. All four subjects were assessed intensively on a battery of neurological and neuropsychological measures and on CT scan. Two patients had CT evidence of cerebral cortical, cerebellar and brainstem atrophy. Brainstem dysfunction was confirmed by abnormal auditory evoked potentials. The authors claimed that the cerebellar disorder in two of their patients was unusually severe. They felt that the presence of head and truncal titubation, gait ataxia, scanning speech, and limb ataxia indicated vermian and hemispheric toxicity of

toluene. Both patients were found to have evidence of cerebellar degeneration. Lazar et al. stressed that none of their patients had clinical signs of peripheral neuropathy, and that nerve conduction studies were normal in all their patients. One patient had objective signs of audiological dysfunction assessed by audiometry and dichotic listening tests; another patient reported subjective hearing loss but unilateral impairment on the dichotic listening test. Sensorineural hearing loss as a result of chronic solvent abuse was also described in a single case study by Ehyai and Freemon (1983). Their 27 year old patient developed cerebral and cerebellar atrophy over a period of five years of extensive solvent abuse; in addition the patient developed bilateral optic atrophy with blindness. The authors were able to chart deterioration in their patient over a period of five years. EEG, CT and nuclide brain scan were all normal at first presentation but five years later CT revealed cortical and cerebellar atrophy with slightly enlarged ventricles. Psychological evaluation using the WAIS and WMS showed a dull normal range but indicated a slight decline in overall scores from previous assessment. The patient's intellectual decline and mild encephalopathic features were felt to correlate well with the anatomical evidence of cerebral cortical atrophy as revealed by CT. The process of visual loss in this patient was gradual and in the earlier stages seemed to be due to retrobulbar optic neuritis. Evidence for this argument is gained from the fact that marked reduction of visual acuity occurred when the optic discs were of normal appearance; later mild bilateral optic atrophy was seen. The sensorineural hearing loss in this patient was described as 'quite dramatic', progressing to an almost total deafness within a period of three years. Since the patient had been repeatedly negatively screened for any other possible causes for his symptoms the authors concluded that symptoms could be attributed to intensive solvent abuse. Unfortunately no breakdown is given of the substance(s) involved in

this case. However, the patient was said to have shown evidence of subclinical sensory neuropathy.

Fornazzari, Wilkinson, Kapur & Carlen (1983) published an exceptionally detailed study on 24 chronic solvent abusers with a mean age of 23 years and a mean duration of 6.3 years of solvent abuse. Inclusion criteria for their study were daily use of solvents for at least one year and evidence of intoxication on the day of admission. Substances involved were said to contain toluene but the authors failed to provide sufficient information as to whether other solvents might have played some part. Assessment procedures included physical examination, extensive neuropsychological testing, cerebrospinal fluid collection, and CT scan. Indices of brain atrophy were derived by planimetric calculations rather than clinical inspection rendering separate scores for cortical, ventricular and cerebellar measures which were compared to a control group. The most profound differences discovered between solvent abusers and controls was the prominence of cerebellar sulci. Differences were also found to be significant for measures of cortical and ventricular abnormalities. Marked neurological abnormalities were found in just under 50% of their sample; abnormalities included gait ataxia and intention tremor, cranial nerve abnormalities, and two patients showed evidence of peripheral neuropathy. On the basis of these results patients were categorised as either 'impaired' or 'unimpaired' for the purpose of further analysis. The unimpaired group performed normally on all psychological measures except verbal IQ possibly indicating low premorbid IQ. In contrast the impaired group performed abnormally on every component of the test battery. The authors found complete (sic!) concordance with their neurological classification and neuropsychological abnormalities. Performance IQ showed the strongest correlation

with neurological findings and Rail Walking test scores but also with "neurological short term memory" assessment. The pattern of results was interpreted as indicating a syndrome of functional impairment resulting from profound disturbance of fine motor control, with some concomitant impairment of short term memory. Scores on tests containing motor elements were all significantly correlated with the cerebellar scores. Tests assessing neuropsychological impairment and memory tended to be correlated with all the morphological scores with the exception of the Memory Quotient of the WMS which was significantly correlated with the cerebellar but not the ventricular and cortical scores. The latter finding is interpreted as possibly being due to cerebellar morphology representing the most sensitive index of brain damage associated with toluene abuse. The authors concluded that the principal findings of their study were the discovery of an association between long term chronic inhalation of products containing toluene and a behavioural syndrome showing profound impairment of motor control and associated impairment of some intellectual and memory capacity. Behavioural deficits were accompanied by marked brain atrophy, particularly in the cerebellum but also in the ventricles and cortical sulci.

Biggs, Bender and Foreman (1983) investigated 22 solvent abusing and 22 non-solvent abusing delinquents with a mean age of 15.5 years to establish whether groups differed psychologically on a number of self report questionnaires. They used the Jesness Inventory, the Rosenzweig Picture-Frustration, the Semantic Differential and the Internal-External Locus of Control scales but failed to find significant differences on any of these scales. This is in contrast to Woolfson's (1982) findings in a study of solvent abusers who were described as being more "outgoing, heedless, cheerful, adventurous, alert and extrovert" (p.66). Allison and Jerrom (1984) administered a

psychological test battery assessing memory, intelligence and attention to ten delinquent solvent abusers and ten matched controls with a mean age of 15 years. Solvent abusers showed significant impairment on memory, nonverbal IQ, and in attention and concentration. Clisser (1987) conducted a survey on illicit drug abuse in 152 young offenders and 113 university students. He found that 21% of the offenders had used solvents at least once with a majority of 77% having used solvents for more than six months. In contrast only 3 of the university students or 2.7% had ever used solvents. Evans and Raistrick (1987a) compared a group of 31 young toluene inhalers with a group of 12 butane gas inhalers. The authors were interested in phenomenological differences between the two types of inhalants rather than in psychometric differences or physical indices. In the toluene group thoughts were found more likely to be slowed, time appeared to pass more quickly and tactile hallucinations were more commonly reported than in the butane group. In a second paper (Evans & Raistrick, 1987b) the authors analysed patterns of use and solvent related harm in the same two groups. Although the two groups were found to give similar reports in terms of patterns of use and solvent related harm, toluene users were more likely to sniff only in a group setting. This habit was thought to be related to the relatively longer duration of intoxication resulting from toluene.

The literature reviewed above presents somewhat overlapping clinical pictures but it seems that the two major substances involved in solvent abuse produce differential clinical symptoms: n-hexane appears to act predominantly on the peripheral nervous system resulting in both sensory and motor polyneuropathies whereas toluene has been found to exert its toxicity and subsequent degenerative effects more exclusively on the central nervous system. This distinction is based on laboratory and industrial

studies of exposure to a single toxic agent rather than on studies of solvent abuse since the latter rarely provides a clear picture of the number and amount of substances involved.

A number of the studies discussed above have failed to avoid methodological complications commonly arising with this particular group. The first problem in any study of substance abuse is that of avoiding measurement of acute or withdrawal effects. There is no precise information on the duration of acute effects in humans and in particular not for the quantities consumed by chronic inhalers. Likewise, reliable information on withdrawal effects is generally lacking; one of the few sources revealing anything about the duration of such effects is the study by Goto et al. (1974) who found progressive neurological deterioration of up to three months after cessation of use. Except for a few single case studies, many investigators have failed to provide adequate details on recency, frequency and duration of solvent use. Ron (1986) in a comprehensive review article of the literature has further argued that confounding aspects such as poly-drug abuse or psychiatric or neurological abnormalities such as head injury are often not sufficiently controlled for. When cases of cortical atrophy and other cerebral abnormalities have been reported it is not entirely clear whether solvents could be blamed as the sole or even as the major determinant causing atrophy. Follow-up studies investigating recovery of functions after withdrawal and a period of abstinence are still few to date and often suffer from lack of adequate control.

2.2 STUDY OF CHRONIC SOLVENT ABUSERS.

Between January 1985 and July 1986 I had a chance to study the effects of chronic long-term solvent abuse and possible recovery following a request by the prison services to investigate some individuals in a local young offenders institution. The individuals were known to the prison authorities to be chronic solvent abusers who complained about feelings of drowsiness, nausea and mental slowness. A prison in general and the institution where this study was conducted in particular seemed to be a good environment for addiction/substance abuse research for the following reasons: (1) security was tight and access to any drugs during the period of the study was almost impossible; it was virtually excluded that subjects might have had recent use of solvents and a sufficient period of detoxification could therefore be established. (2) A prison provides a relatively homogeneous environment with a recurrent rhythm for all inmates and controlled nutritional intake. (3) Subjects are available for follow-up investigation provided their sentences are long enough to cover the period of the study.

Given the nature of neuronal and central nervous system (CNS) abnormalities associated with solvent abuse described in the studies discussed in section 2.1 it was hoped that this study would provide a particularly useful background to assess the clinical utility for the Event Perception tasks outlined in chapter 1. If solvents do produce optic nerve fibre and other neuropathies (eg. Schaumburg & Spencer, 1976) and result in increased latencies or latency variations and noise, and decreased amplitudes in nerve fibre conduction as reported eg. by Chang (1987) then solvent abusers might be particularly impaired on the Event Perception Threshold and Event Perception Movement tasks. According to one possible interpretation outlined in

chapter 1 Event Perception Threshold requires efficient temporal separation and processing of transient signals to retinal ON and OFF responses and Event Perception Movement needs strong, clear amplitudes to allow processing of a relatively small increase in the sustained response signalling movement of the target. Since most subjects had used a mixture of toluene and n-hexane containing substances it was suspected that neuropsychological and neurological abnormalities - if any - would be due to either central or peripheral effects or both. In an attempt to separate effects, a neuropsychological test battery which was seen as differentially sensitive to both central and peripheral functioning was felt to be the most appropriate form of assessment.

2.3 SINGLE CASE STUDY[1]

Inmate AB (fictitious initials) who was 18 years of age at the time of the initial interview was brought to our attention when he reported at the prison's medical centre complaining of drowsiness, insomnia, lack of concentration, and memory problems. He also suffered from poor coordination, unsteadiness of gait and general apathy. He was described by prison staff and fellow inmates as clumsy and uncooperative and considered to be mildly mentally impaired. AB stated that he had started inhaling solvents at the age of 13 years and continued its use until the day he was arrested for attempted rape - a crime he had committed under the influence of solvents. At the age of 16 he habitually consumed 250-500 ml of glue per day for 3 to 4 days a week. He

[1] This case study has been published as a "Letter to the Editor' by Wiedmann, Power, Wilson & Hadley (1987). Recovery from chronic solvent abuse. **Journal of Neurology, Neurosurgery & Psychiatry, 50,** 1712-1713.

almost exclusively used 'Evostik' an adhesive which contains 48.5% toluene and 5.3% n-hexane (information obtained from the manufacturer). During the year before he was arrested his consumption had increased to 500-750 ml per day. His experience with other drugs was restricted to isolated experiments with alcohol and cannabis.

On initial presentation AB had been in custody for four months: a time assumed to be well beyond the acute effects of intoxication and immediate withdrawal from solvents and possibly also beyond the period of further deterioration observed by Goto et al. (1974). AB was assessed neuropsychologically on both traditional measures and a battery of novel computerised tests described in detail later. He was followed up at 3 monthly intervals over a period of 18 months resulting in a total of six assessments. Only computerised measures and the State Anxiety questionnaires were used in follow-up assessments.

2.3.1 Results.

AB's score of 43 on the Ravens Progressive Matrices (Raven, 1960) placed him at the lower end of the "intellectually average" group: assessment on the Matrices was performed 12 months after the initial referral. All scores on the WAIS subtests were significantly lower when compared with standard norms but also in comparison to the control group of fellow prisoners from the main study (see table 2.1).

AB gradually recovered to normal functioning on seven tasks, but after 18 months he was still impaired on two tasks (see table 2.1). Scores on Word Recognition had improved considerably but he still showed a sizable difference from the control group.

After 18 months AB was given a standard neurological examination, performed by a visiting neurologist. The examination showed no signs of any residual focal or peripheral abnormalities. At this time a brain scan performed on a Magnetic Resonance Imaging (MRI) device was also obtained. The neuroradiological investigation showed bilateral atrophy of the occipital cortex and the cerebellar vermis with a cistern of Galen being visible. The ventricular system was judged normal for the patient's age and no discrete focal lesions were observed. Unfortunately neither neurological examination nor brain scan were available on initial presentation for comparison.

2.3.2 Discussion.

This case suggests that neuropsychological deficits can be present and documented in chronic solvent abusers after a period well beyond the acute effects of solvent use or withdrawal. However, even after extensive solvent abuse recovery appears to be possible to a considerable degree, although after a period of 18 months of abstinence normal functioning was still not fully reinstated in the present case. This is consistent with previous studies discussed earlier reporting permanent neurological and neuropsychological damage in solvent abusers. Abnormalities found on MRI are also in line with previous studies using CT reporting cerebellar and generalised atrophy. The nature of the recovery process and the extent of permanent damage as a consequence of solvent abuse found in the present case were generally in line with previous findings.

2.4 GROUP STUDY.[2]

2.4.1 Methods.

Subjects. Subjects were 12 young offenders with a mean age of 18.1 years (SD=1.3 years) and an average of 5.9 (SD=2.5) years of solvent abuse, and a control group of 12 prisoners who had not been using solvents. Average consumption of solvents was 630 ml (SD=280 ml) per day during their peak periods of solvent abuse which lasted for a minimum of one year. Most of their sentences were either in connection with burglary or other crimes against property to provide them with money for solvents, or for crimes of violence carried out under the influence of solvents. The control group consisted of 12 prisoners serving longer term sentences with a mean age of 20.0 (SD=0.7) years with no significant drug or alcohol abuse. Subjects of both groups came from a similar socioeconomic background and the majority had grown up in the West of Scotland. Participation of the control subjects was voluntary but solvent abusers were seen through routine referrals. However, solvent abusers were allowed to withdraw if they did not want to participate in the study which was the case for two individuals (see Table 2.2).

Assessment procedures.[3] The theoretical framework for the visual Event Perception tasks used in this study has been outlined in chapter 1. A brief description of other tasks employed will be given in the following section.

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[2] Part of this study was presented at the INS IXth European Meeting in Veldhoven, Netherlands, July 1986.

[3] Procedures were described in: Wilson JTL, Wiedmann KD, Phillips WA & Brooks DN. (1988). Visual event perception in alcoholics. **J. Clinical & Experimental Neuropsychology, 10:3,** 222-234.

Simple and Choice Reaction Time. Reaction times were measured using a procedure based on work by Van Zomeren (1981) which allows a decision time and a movement time to be distinguished. On the basis of work with head injured patients Van Zomeren argues that this task is sensitive to attentional deficits indicated by particularly slow choice decision times. Responses were recorded using a purpose built keyboard. Decision time is equivalent to conventional reaction time and is the time taken to lift the index finger from a centrally located button in response to the illumination of a light emitting diode. Simple and choice reaction times were measured using one and four response buttons, respectively. Subjects were given eight practice trials and 40 experimental trials under both simple and choice conditions. Median reaction times were computed for each subject.

Visual Search. This task involved searching for a target symbol in an array of non-targets. Symbols were abstract, unfamiliar shapes, and each symbol measured approximately 10 mm by 10 mm. There were 25 symbols in a 170 mm by 130 mm array. The symbol at the centre of the array was the target and was displayed within a box. The subject's task was to search the rest of the display for a symbol corresponding to the target, but not necessarily at the same orientation. The target was randomly assigned an orientation of 0, 90, 180, or 270 degrees. Subjects were instructed to point to the corresponding symbol as quickly as possible using a light pen. There were 8 practice trials and 32 test trails. For the test trials there were eight target stimuli; each was presented four times, once in each quadrant. The order of target stimuli was randomised. For each subject the median response time for the 32 test trials was computed.

Word Recognition Threshold. A measure of the patient's ability to recognise briefly presented words. Any difficulties encountered on the event perception tasks might be due to a general disability in processing rapidly changing stimuli. This test was therefore included to determine whether there was an impairment in the ability to identify rapidly presented words. Words were common nouns presented in a large display format. Each word comprised of four letters and measured 45 mm by 12 mm. Before the display commenced subjects fixated a point in the centre of the display. The word was displayed for a short time, and preceded and followed by masking stimuli. The masks comprised of parts of letters randomly arranged and they were each displayed for 100 ms. The subject made a verbal response and was then given feedback. The duration of the target word was changed using the tracking procedure described above for the Detection Threshold task. The procedure yielded a threshold in milliseconds for word recognition. The threshold is an estimate of the target display duration needed in order for 50% of targets to be correctly identified.

Visual Span. This was a measure of short term visual memory (Wilson, Scott & Power, 1987) analogous to digit span. It provides a measure of short term visual memory that is distinct from both sensory storage and verbal memory (Phillips, 1983). Subjects were presented with a pattern constructed by randomly filling half the cells in a matrix. The pattern was displayed for 2 secs; after a retention interval of a further 2 secs the pattern was redisplayed with one previously filled block missing. The subject's task was to point to the place where the block was missing. The initial pattern consisted of two cells, one of which was filled. After each correct response pattern complexity was increased by two cells and one additional filled block. After an incorrect response subjects were tested with a second pattern of the same complexity.

Testing terminated when subjects failed to remember two consecutive patterns of the same complexity. Span was taken to be the number of blocks in the last pattern remembered correctly. Two determinations of span were made for each subject.

Microcomputer Apparatus. Stimulus control and timing for all of the above tests were accomplished using an Apple IIe microcomputer. The visual display unit had a viewable area of 290 mm by 215 mm and was equipped with a very short persistence P49 phosphor. The VDU was positioned at a convenient distance for subjects to point to the screen, giving a viewing distance of approximately 60 cm. Free binocular viewing was employed, corrected when necessary. Timing of stimulus displays was by reference to the 50 Hz refresh rate of the VDU and was in 20 ms intervals. All other timings were accomplished using a millisecond clock. The luminance of the display was 34 cd/m^2 as measured using a photometer. A Symtec lightpen was used by the subjects to respond to visual displays.

Ataxiameter. A Wright-Codoc Ataxiameter was used as a measure of ataxia. The patient stood erect with eyes open and attempted to maintain this position with as little movement as possible for one min. The meter measured body sways in units of 20 minutes of arc. The test was administered twice.

Traditional Tests. All control subjects but only a subsample of solvent abusers were also assessed on the following subtests of the Wechsler Adult Intelligence Scales (WAIS; Wechsler, 1955) (the number of solvent abusers is indicated in parenthesis): Vocabulary (7), Digit Symbol (12), Block Design (9), and Digit Forward and Backward (9). The National Adult Reading Test (NART; Nelson, 1981) was used to

obtain a quick estimate of premorbid IQ for all controls and nine solvent abusers. In addition subjects were assessed on the State-Trait Anxiety Questionnaire by Spielberger, Gorsuch & Lushene (1970) except for two of the solvent abusers who were dyslexic.

2.4.2 Results.

The results in Tables 2.3 and 2.4 show that solvent abusers were significantly impairmed on 17 out of the 18 measures employed. There was a statistically significant difference on t-tests between solvent abusers and controls for age ($t= 4.4$ $p<0.001$) and for NART errors ($t=-3.6$ $p<0.002$). Since groups differed significantly on both age and NART errors indicating a possible premorbid IQ difference, an Analysis of Covariance (ANCOVA) was conducted controlling for age and NART. Since NART results were missing for three of the solvent abusers a method of median substitution recommended by Tabachnik & Fidell (1989) was used to prevent exclusion of their scores in subsequent calculations. The median for the nine solvent abusers assessed on the NART was 35.0 which was the value assigned to the three missing cases. This value appeared to be a good estimate of their cognitive abilities when comparing the estimated Full Scale IQ equivalent of 100 derived from this scale (Nelson, 1981) with other WAIS scores from the same subjects. With these adjustments eight of the seventeen measures continued to show statistically significant differences.

The most striking differences between solvent abusers and controls after correction for age and NART errors were found on Event Perception Threshold, Event

Perception Movement, and Digit Symbol. Thus all three Event Perception tasks continued to show a statistically significant difference after correction but Visual Span, Visual Search, Word Recognition, and Body Sway did not. The movement scores on simple and choice Reaction Time were both significantly related to NART error score; RT choice movement was also related to age. After correction simple RT movement just fell outside the range of conventional levels of significance ($p=0.06$) but choice RT movement was now significant at $p<0.03$ indicating longer RTs for solvent abusers.

Only seven solvent abusers were assessed on the Vocabulary subtest of the WAIS. Their raw score was about half that obtained by controls rendering a highly significant difference. As might be expected these scores were strongly affected by the NART error score but differences remained highly significant at $p<0.001$ after correction. The three remaining WAIS subtests (Digit Span Backward & Forward and Block Design) ceased to show statistically significant differences after correction.

Although solvent abusers scored on average fifteen points higher on State Anxiety, t-tests failed to show a statistically significant difference, but there was a significant age effect on the ANCOVA. When correcting for age and NART error differences the higher score obtained by solvent abusers was now statistically significant from controls. The opposite was true for Trait Anxiety scores which - although affected by age - ceased to show a significant difference after correction despite an absolute score difference of 10 points.

Partial correlations were obtained for each group independently between all

measures controlling for age and NART errors. Table 2.5 shows the results for solvent abusers. Event Perception showed a significantly relationship at r= -0.61 ($p<0.05$) with its equivalent Event Perception Threshold, at r= 0.75 ($p<0.01$) with Event Perception movement, with Visual Search at r= -0.67 ($p<0.05$), Simple RT movement at r= -0.61 ($p<0.05$), and Body Sway at r= -.076 ($p<0.01$). Body Sway showed significant relationships with six other measures (all computerised), and yielded also the highest correlation values in numerical terms. Neither State nor Trait Anxiety measures appeared to influence performance to any significant degree. The only WAIS subtests which were significantly correlated with any other measures were Digit Span Forward and Backward with Word Recognition Threshold (r= -0.87 $p<0.01$; r= -0.77 $p<0.05$).

For controls there were equally many correlations in the predicted direction as there were correlations counter to the predicted direction (see Table 2.6). Visual Search was the only measure showing consistent relationships with Event Perception Movement, Block Design and Digit Span Backward whereas Body Sway yielded only one correlation in the predicted direction with Word Recognition and three correlations were counter to prediction.

2.4.3 Discussion.

This study established clear neuropsychological deficits in a group of 12 solvent abusers compared with a control group of 12 non-solvent abusing volunteers. However, comparisons were somewhat problematic with groups differing

significantly on demographic variables such as age and estimated IQ. It must be stressed that the NART was not originally designed for the assessment of such a young age group and IQ estimates may therefore not be completely reliable especially since solvent abusers were significantly younger than controls and may therefore have been at a further disadvantage. It is well known that this particular part of the population is often found to be educationally disadvantaged resulting in lower VIQs. This view is shared eg. by Press and Done (1967) who stated that 'most customary measures of IQ often fail to completely reflect intellectual potential of underpriviledged children or children with educational or language handicaps' (p.456). On the other hand performance on the neuropsychological tasks within this study combined with the overall clinical impression seemed to confirm the possibility of a general IQ difference between the two groups. These differences were also strongly reflected in a highly significant difference on Vocabulary raw scores with the mean score for the seven solvent abusers assessed amounting to only half the score for controls. Since controls volunteered for this study some self selection with a trend towards brighter and less timid individuals may have occurred. This possibility gains further support from the fact that all control subjects came from the ranks of the best behaved prisoners according to an internal behavioural grading system. It also proved difficult to avoid a significant age difference since selection of controls was aimed at prisoners serving longer sentences to secure reliable follow-up. Such longer sentences are only rarely found amongst younger offenders; on the other hand younger prisoners were more likely to be referred for problems relating to solvent abuse. It was therefore felt appropriate to employ statistical procedures such as ANCOVAs (SPSSX, 1986) and partial correlations attempting to correct for these differences.

Statistically significant differences on Visual Memory Span disappeared when controlling for age and NART although neither of the covariates on its own nor their combined effects reached statistical significance. Differences on this test can therefore not be considered very pronounced and reliable, and there is thus little reason to believe that visual memory is specifically affected by solvent abuse.

Results on the Reaction Time (RT) tasks undergo some capricious changes when subjected to the ANCOVA. All four measures were affected by the estimated IQ measure (NART errors) although only movement times were affected to a statistically significant degree. In the present study movement time was a measure of the time taken to execute a precise, visually guided movement from one position to another. Performance on RT tasks could be affected by either sensorimotor impairment as a result of peripheral neuropathy or by central impairment representing a higher level disorder of motor control. Taking into account the strong effect of the IQ estimate and the fact that solvent abusers were also impaired on simple decision time - the cognitive component of this task - it appears plausible to assume that results are due to a central motor control disorder. Nevertheless given the fact that solvent abusers commonly used mixtures of toluene and n-hexane a degree of sensorimotor neuropathy may have been present in at least some subjects and may have influenced performance.

Solvent abusers were significantly impaired on Digit Symbol, a task which involves a component of speeded, visually guided movement, and which is frequently found to be highly sensitive to the effects of diffuse brain damage. Surprisingly though results were not related to estimated premorbid IQ but to some (not statistically significant) degree to age ie. older subjects showed better performance. When

performance on Digit Symbol was compared with performance on other measures scores were only significantly related to Digit Span Forward ($r=0.84$ $p<0.001$) and Backward ($r=0.74$ $p<0.001$) after controlling for age and NART. This would suggest that the strongest component in the Digit Symbol task is the efficient use of short-term memory which in turn was shown to be significantly impaired as reflected in significantly lower scores on Digit Span Forward and Backward (without using corrections) in solvent abusers in the current study. Impairment of short-term memory was also reported by Fornazzari et al. (1983). The argument for a sensorimotor impairment as a component in impaired performance is weakened by the fact that the Block Design task also carries a strong sensorimotor component; yet there was no significant impairment on this task nor did Block Design correlate with any other measure. Scores for both Digit Span Forward and Backward were significantly lower for solvent abusers on t-tests. With correction Digit Span Forward was affected by NART errors and Digit Span Backward to a significant degree by age ($p<0.01$) rendering differences for both tasks non significant on the ANCOVA. It appears plausible that these tasks should be influenced by IQ differences. However, it appears less plausible that age should affect Digit Span Backwards given that the age range for the current sample was only 18-21 years. The question arises whether this result should be taken as one of the potential traps/pitfalls of inferential statistics. Although test results for the variables concerned (age, NART errors, Digit Span Backward) may have been consistent, the theoretical framework pertaining to these well established and widely used tests would contradict such a finding. It may therefore be assumed that differences found on t-tests genuinely reflected poorer short-term memory in solvent abusers. Further evidence that the partial correlation programme might not have been completely reliable to partial out age and IQ estimate effects can be gained

from the finding for Digit Symbol where better performance was associated with higher age rather than the fact that the older subjects also represented brighter individuals.

Differences on both Visual Search and Word Recognition Threshold were statistically significant using t-tests with poorer performance for solvent abusers but both tests ceased to show reliable differences after correction. The implications for statistically significant differences on all three Event Perception tasks will be discussed in more detail in the general discussion.

2.5 FOLLOW-UP STUDY.

Eleven control subjects and four of the solvent abusers were assessed on another two occasions on the computer tests and on the Wright-Codoc ataxiameter. Randomisation of individual trials on test procedures was used to ensure minimisation of practice effects. Additional measures of State Anxiety were obtained during each session. Although both age (solvent abusers: 19.0; controls: 20.0 $p<0.05$) and NART errors (solvent abusers: 35.8; controls: 26.3 $p<0.01$) were significantly different for the two groups, no corrective measures were employed for the following reasons: (1) the actual age difference was only one year and although consistent this difference was considered negliable; (2) although groups differed significantly on NART errors they were also assessed on Ravens Progressive Matrices (Raven, 1960) where they failed to show any significant differences (solvent abusers: 43.5 SD= 7.2; controls: 47.0 SD=5.1 n.s.); the RPM were considered a more appropriate and reliable form of

assessment than purely verbal procedures like the NART for reasons discussed in the introduction to this chapter.

2.5.1 Results

Table 2.7 gives the test results for solvent abusers and controls on all three occasions. To allow better comparison the initial scores for the four solvent abusers were tested independently from the group study against the initial scores of the control group. Initial scores were generally in line with those in table 2.3 and 2.4. Controls showed some practice effects between the initial and the second assessment but little further gains during the third session. The four solvent abusers showed far fewer gains during the second assessment but improved in the third session. Table 2.7 also shows that controls achieved better scores on six tasks when scores from the final assessment were compared with scores from the initial assessment. Solvent abusers only showed significant gains for four measures.

2.5.2 Discussion

With any study using the same test procedures repeatedly some unavoidable practice effects tend to occur. In the current study an attempt was made to keep practice effects to a minimum by presenting novel stimulus configurations from trial to trial and from one session to another. Table 2.7 shows that this attempt was only partly successful when comparing scores from initial and final assessments for controls on t-tests. Six of the measures showed a statistically significant improvement through practice. However, three of the tasks showing significant improvement contained an

element of guided movement (Visual Search, simple and choice RT movement) which has been found more susceptible to practice effects than the cognitive component (Van Zomeren, 1981). On the other hand it is interesting to note that decision times for both RT tasks have hardly changed from the first to the final assessment. Gains in Event Perception Appearance although statistically significant are very small (0.5 points) and not of much clinical relevance; they may simply represent fuller alertness to the task. It should be noted that both controls and solvent abusers became increasingly cooperative and motivated during the course of the study, and particularly the controls had entered into some kind of competition amongst themselves, trying to achieve the best possible scores. Visual Span improved by 1.5 blocks and may indicate an improvement in strategy rather than in visual memory capacity. Improvement in Body Sway by 4.4 units is of much greater concern, introducing a degree of doubt concerning the sensitivity and reliability of this task.

T-test results comparing initial and final scores for solvent abusers were clearly depressed by the small number of subjects. This fact is most evident when comparing the much larger absolute differences between initial and final scores with control absolute scores. On Event Perception Appearance and Visual Memory Span the absolute differences were 2.2 units, and on Body Sway 6 units - yet none of these differences reached statistical significance. The most impressive improvement was observed on Event Perception Threshold where final scores were almost identical with final control scores. It seems plausible to assume that genuine recovery of function had taken place leading to much improved performance on this task. The prolonged period of abstinence from solvent abuse may have led to remission of any possible neuropathy and/or transient cerebellar dysfunction. This explanation would also apply

to improved scores on Body Sway. However, scores for Event Perception Movement - although significantly improved - were still significantly lower than control scores. This may be taken as either indicating incomplete recovery or as a sign of permanent CNS damage. Similar arguments might be used in the case of choice RT movement which showed significant improvement but at the same time values remained significantly above those for controls. Definite improvement appears to have occurred for choice RT decision. It may therefore be assumed that improvements of test scores for solvent abusers are due to recovery of some neuropsychological functions. Solvent abusers had better scores on all tests from initial to final assessment except for simple RT decision where scores remained identical to the initial values.

In summary it can be said that there was unequivocal improvement in performance on some tasks for solvent abusers beyond that of mere training effects. On the other hand the test battery proved not to be entirely free from training effects and some results must be interpreted with caution. The study showed that recovery of function is possible even after prolonged solvent abuse but with sufficiently long periods of abstinence. However, the study also showed that some impairment may be permanent or, employing a more optimistic prognosis, would require a very prolonged period of recovery.

2.6 GENERAL DISCUSSION.

A study of 12 chronic solvent abusers and 12 non-solvent abusing controls was conducted which showed significant differences on 17 out of 18 measures on a neuropsychological test battery. Because of significant differences in age and estimated premorbid IQ, corrective statisitical measures were indicated which reduced the number of statistically significant test score differences to eight. The most striking differences between solvent abusers and the control group were found in noticing and locating rapid visual change and in psychomotor speed tasks. Impairment on the Event Perception tasks could be taken as being in line with the theoretical framework outlined in chapter 1 and with the neurological, neuroradiological and histological evidence outlined in the introduction to the current chapter. The observed changes in myelinated nerve fibres (Schaumburg & Spencer, 1976) and optic neuropathy (Ehyai & Freemon, 1983) caused by toluene intoxication may be responsible for the poor performance on the visual Event Perception tasks. However, like in other conditions of confirmed (optic neuritis, chapter 4) or suspected (alcoholics next chapter) optic nerve fibre pathology, it is not possible to state unequivocally whether the impairment is due to increased latencies, increased background noise as a result of increased spontaneous firing, or a combination of both. Solvent abusers performed significantly worse on Event Perception Appearance which had a fixed Stimulus Onset Asynchrony (SOA) of 2 secs. The absolute difference was relatively small (difference=2.4 units) which means that in general solvent abusers were attending to the task. Only three individuals had scores lower than 20. Their low scores might be explained by a general attention deficit considering that their decision times on simple RT were also significantly slower compared to controls as well as for the solvent abuser group as a

whole. Decision times were not significantly longer for the choice RT condition. This could be taken as further evidence for the argument that solvent abusers suffer from a more specific attentional deficit relating to perceptual processes involving rapid change. The finding of occipital and cerebellar atrophy in AB does lend support to the idea that deficits on the Event Perception tasks are of central origin. Chang's (1987) findings indicated that patients suffering from n-hexane polyneuropathy showed both increased latencies and decreased amplitudes on pattern reversal VEPs. These findings combined with the model of neuronal coding for the Event Perception tasks proposed in chapter 1 would allow at least three possible interpretations:

(1) if the deficit produced by solvent toxicity results in decreased amplitudes then this should affect all three Event Perception tasks but since the majority of subjects performed within the normal range on the Event Perception Appearance task this explanation may only be true for the worst affected subjects. On the other hand individual performance on Event Perception Threshold seems to demonstrate graded impairment ranging from average SOAs of 292 ms to 42 ms. These values are much shorter than the SOA of 2 secs used in the Event Perception Appearance task. Thus the reason for impaired performance on Event Perception Appearance may be due to occasional complete lapses of attention or they may be due to an inability of proper fixation for reasons discussed later. Impaired performance on Event Perception Movement could be explained by a decrease in amplitude if the model of neural representation outlined in chapter 1 is assumed to be correct, arguing that the mechanism required to detect short range apparent movement is based on an increase in absolute spike frequency rather than requiring a transient neuronal signal to attract attention.

(2) if the deficit involved leads to increased variability of latencies in nerve fibre conductance this could explain poor performance on the Event Perception Threshold task which as a consequence would require longer than average temporal separation of background and stimulus in affected subjects, and relatively preserved performance on the Event Perception Appearance task which has a long, fixed SOA of 2 secs.

(3) Movement sensitive channels activated by Event Perception Movement possibly operate on higher spatial frequencies than the channels involved in signalling appearances. Initially, there may be equal impairment to the channels mediating signals to appearances, and the channels involved in Event Perception Movement. The fact that solvent abusers continue to show impairment on Event Perception Movement after 12 months of abstinence suggests that high frequency movement channels are more severely affected than those involved in signalling appearance of a stimulus. In addition, if high frequency channels use smaller diameter nerve fibres, these smaller fibres could be more seriously affected by the toxic effects of solvents than larger diameter fibres. This differential sensitivity to disease processes has been found in optic neuritis where smaller fibres can be affected earlier and more severely by the demyelination process than larger fibres. This possibility will be discussed in further detail in chapter 4 where more evidence for this possibility will be provided.

The question as to where in the CNS these changes might occur is difficult to answer. It could be argued that changes are already present in the retinal cells or the optic nerves up to the Lateral Geniculate Nucleus (LGN) as in patients suffering from optic neuritis (see chapter 4). However, Seppalainen, Raitta & Huuskonen (1979) found abnormal amplitudes and latencies of flash visual evoked potentials in industrial

workers exposed to n-hexane and interpreted these changes as being the result of cerebral dysfunction, possibly due to a conduction block in intracerebral axons. Likewise, Chang (1987) interpreted his findings of patterned VEP abnormalities as not attributable to toxic effects on the retina or visual pathways peripheral to the LGN since he failed to find any optic nerve atrophy or retrobulbar neuritis in his patients. He argued that since P1 of patterned VEP is generated in the primary visual cortex but does probably not reflect the first cortical component, the latency abnormalities in his patients would therefore result from cerebral dysfunction. He believed that cerebral dysfunction could also be responsible for the amplitude attenuation in his polyneuropathy patients. No detailed neuro-ophthalmological assessments were carried out on the solvent abusers in the present study but all prisoners underwent a general health screening programme including assessment of visual acuity. No abnormalities were reported for any of the subjects. It appears therefore likely that the effects observed in this study represent a summation of all of these effects.

The pattern of intercorrelations in Table 2.5 suggests yet another possible interpretation of findings in this study. In solvent abusers Body Sway was significantly correlated with six of the computerised measures. Body Sway is considered to represent some aspects of cerebellar functioning. The cerebellum's role in movement, posture and gait control has long been recognised. Sherrington in 1898 was able to conclude that the cerebellum coordinates movements but that it does not initiate them. There is now no longer any doubt that the cerebellum is a central control point for the organisation of movement. It modulates or reorganises motor commands, and by coordinating diverse signals it obtains the maximum efficiency for these commands. The cerebellum is therefore seen as an organ of regulation in the highest

sense. Lundberg & Oscarsson (1962) found that some cerebellar activity is connected with the internal state of the central nervous system. One of the main afferent tracts leading to the cerebellum, the ventral spinocerebellar tract, conveys information about the activity of inhibitory interneurons in the spinal chord. This kind of internal monitoring mechanism might be necessary in a system intended to refine or revise motor commands before they reach the muscles like eg. in the cerebellar control of eye movement. Cerebellar dysfunction has been found to disrupt precise tracking movements of the eyes (Lisberger, 1982; Ito, 1982). Two regions of the cerebellum are known to participate in these functions. One is the floccular-nodular area which regulates the position of the eyes with respect to orientation of the head and body. The other is the cerebellar vermis, which is believed to control rapid or saccadic eye movements and which is of importance in visual tracking. Llinas & Wolfe (1977) showed that activation of Purkinje cells by mossy fibers increases about 25 ms before the initiation of eye movements. This implies that cerebellar regulation through the mossy fibre system is capable of correcting mistakes before they have reached the muscles and have been expressed in actual movement. This correction process by the cerebellum appears to be inhibitory. Although it is not yet clear why organic solvents appear to some extent to selectively impair and destroy neurons in the cerebellum, damage to this area is one of the most frequently reported form of brain abnormality in solvent abusers. Atrophy of the cerebellar vermis was also reported for single case AB. The ability to maintain a constant gaze at a fixation point is essential in all three Event Perception tasks. It is therefore plausible to assume that cerebellar integrity is essential for successful performance on the Event Perception tasks. If the inhibitory regulation of eye movements is weakened or lost fixation may become difficult. Without proper fixation successful performance on the Event Perception tasks would

appear to be compromised due to a continually changing retinal disparity of the background pattern resulting in the production of transient neural signals indicating "novel" background stimuli and thus masking for the target event. The argument for cerebellar involvement gains further support from the finding that Body Sway was also correlated with both simple and choice RT movement and Visual Search, all of which being tasks which have a strong component of a visually guided, precise motor response. As argued previously, the actual motor response would not be initiated but moderated by the cerebellum, and - if losing its inhibitory effect - precision in pointing response will be lost.

There was a marked reduction in Body Sway in the four solvent abusers on repeat examinations dropping from an initial 21.9 unit/min to 14.9 unit/min on their third assessment but there was also some reduction in Body Sway in controls from an initial 14.9 unit/min to a final 10.5 unit/min. The statistically significant change in controls commands some caution concerning the reliability of the Body Sway measure. However, reduction in Body Sway was parallelled by improvement on other measures in the solvent abusers and in some cases it exceeded by far the training effects observed in controls. Gains were found to be most marked for Event Perception Threshold and Event Perception Movement although performance on the latter was still significantly worse than for controls. It might therefore be concluded that cerebellar impairment was either not permanent, or where such impairment was confirmed neuroradiologically like in case AB - that some readjustment and reinstatement of the internal equilibrium of functional units had taken place. In either case parallel recovery of Body Sway and performance on the neuropsychological tasks further strengthens the argument of cerebellar involvement in these tasks.

Nevertheless, the argument cannot be completely dismissed that Body Sway as a physical measure might merely reflect general impairment of the CNS which is parallelled in impairment on the neuropsychological measures.

2.7 CONCLUSIONS

The present study has shown that visual Event Perception tasks were highly sensitive to the effects of solvent abuse. Individuals with prolonged histories of chronic solvent abuse performed significantly worse on Event Perception Threshold and Event Perception Movement than matched controls. Reports of increased latencies and noise, and decreased amplitudes in nerve fibres exposed to solvent intoxication from both experimental and clinical studies in the literature suggested that solvent abuse provides an ideal background for testing the hypothetical models of Event Perception processing outlined in chapter 1. The results in the current study seemed to confirm to some extent the hypothesis that performance on the Event Perception tasks depends on the capacity of both individual and groups of neurons to efficiently separate and process transient signals arising from ON and OFF retinal activity. If this capacity is compromised by - as in this instance - toxic agents causing neuropathy, the resulting variability in latencies and increase in background noise in neuronal channels will prevent temporal separation of transient signals produced by background stimuli and target stimuli in the case of Event Perception Threshold. Longer temporal separation is therefore required between background and target onset resulting in higher (impaired) scores on the Event Perception Threshold task. However, increased noise and decreased amplitudes may have resulted in significantly lower (impaired)

scores in the Event Perception Movement task which was thought not to require transient signals to attract attention. The assumed small increase in sustained firing caused by the target in this task could easily be lost in an environment producing abundant spontaneous firing as a result of nerve fibre damage. An already weakened increase in amplitude in response to the target may therefore easily go unnoticed.

A problem with this interpretation arises because of suspected impairment of proper fixation caused by cerebellar dysfunction. Although subjects had been instructed to maintain fixation no formal assessment of eye movements was attempted. It must be stressed that it is not argued here that solvent abusers have voluntary control in when and whether they want to fixate: the inability to maintain fixation is a result of the pathological process of cerebellar degeneration in itself. The point is rather that without guaranteed proper fixation the basis of the above model explaining impairment would be compromised due to a continuous shift in neural representation of the background pattern. The importance of cerebellar involvement was further indicated by the relationship of Body Sway with simple and choice RT movement and Visual Search.

A further possibility of explaining deficits in performance on Event Perception tasks is that signals in response to movement are mediated by channels which are different from those mediating signals arising from appearances of stimuli. If signals to movement are relayed by smaller nerve fibres, impairment might result from higher susceptibility of these smaller fibres to the toxic effects of solvents.

In conclusion Event Perception tasks were specific in assessing deficits in an area of functioning, namely visual processing, which is known to be affected by solvent toxicity but which has previously been rather difficult to assess in humans when using traditional measures. Findings in this study confirmed that the Event Perception tasks were sensitive to the effects of solvent toxicity and that they were differentially sensitive in showing persisting deficits with detection of movement onset but not with detection of appearances. It is also of importance to note that the tests were reliable in repeated assessments and showed relatively small training effects.

TABLES

Table 2.1 Initial and follow-up results for AB and controls.

	INITIAL ASSESSMENT		FOLLOW-UP	
TEST	AB mean	CONTROLS mean (SD)	AB mean	CONTROLS mean (SD)
VISUAL SPAN (no. of blocks)	13.5	14. (3.5)	13.0	16.2 (3.6)
THRESHOLD (ms)	241**	32 (8)	22.5	33 (14)
MOVEMENT (correct out of 25)	4**	20 (3.4)	19	21.3 (2.8)
VISUAL SEARCH (ms)	3772**	2693 (282)	2513	2293 (420)
WORD RECOGNITION (ms)	245**	60 (14)	110**	56 (14)
RT SIMPLE DECISION (ms)	319*	255 (30)	305	260 (30)
RT SIMPLE MOVEMENT (ms)	297**	195 (21)	237*	157 (30)
RT CHOICE DECISION (ms)	344	295 (28)	308	294 (27)
RT CHOICE MOVEMENT (ms)	341**	199 (24)	217*	159 (29)
BODYSWAY (deg/min)	53.2	14.9 (4.8)	13.8	10.5 (4.4)

Difference between controls and AB: * > two Standard Deviations ** > three Standard Deviations

TABLE 2.2 COMPARISONS BETWEEN SOLVENT ABUSERS AND CONTROLS: DEMOGRAPHICS

	SOLVENT N=12 mean (SD)	CONTROLS N=12 mean (SD)	T-TEST t-value	p
AGE (years)	18.7 (0.8)	20.0 (0.7)	4.41***	.001
NART (errors) 9/12$	35.0 (5.2)	26.3 (5.0)	-3.6***	.002
DURATION OF USE (years)	5.9 (2.5)			
QUANTITY (ml)	624 (284)			
DETOXIFICATION (weeks)	9.0 (5.2)			

* = p< 0.05 ** = p< 0.01 *** = p< 0.001 $ = Only 9 solvent abusers were assessed

Table 2.3 COMPARISONS BETWEEN SOLVENT ABUSERS AND CONTROLS ON T-TESTS AND ANCOVA

TEST	SOLVENT	CONTROLS	T-TEST		ANCOVA			
	mean (SD)	mean (SD)	t-value	p	F	AGE	NART	AGE+NART
VISUAL SPAN (no. of blocks)	11.0 (3.4)	14.7 (3.5)	2.6*	.02	3.2	3.0	0.0	2.2
EP APPEARANCE (correct out of 25)	22.1 (3.1)	24.5 (0.7)	2.7*	.02	5.0*	3.9	0.3	2.2
EP THRESHOLD (ms)	162 (88)	32 (8)	-5.1***	.002	12.5***	2.8	1.5	5.6**
EP MOVEMENT (correct out of 25)	12.8 (4.8)	20.0 (3.4)	4.2***	.001	9.9**	0.1	4.8*	4.8*
VISUAL SEARCH (ms)	3381 (829)	2693 (282)	-2.6*	.02	2.6	0.7	0.9	2.1
WORD RECOGNITION (ms)	114 (58)	60 (14)	-2.5*	.04	3.7	0.3	1.9	2.7
RT SIMPLE DECISION (ms)	291 (37)	255 (30)	-2.7**	.01	6.1*	0.3	3.6	2.1
RT SIMPLE MOVEMENT (ms)	226 (50)	195 (21)	-2.0	.07	3.8	2.5	7.8**	3.9*
RT CHOICE DECISION (ms)	326 (37)	295 (28)	-2.3*	.03	1.6	0.0	2.5	2.3
RT CHOICE MOVEMENT (ms)	231 (58)	199 (24)	-1.8	ns	5.8*	8.5*	16.2***	8.2**

Significant difference between controls and solvent abusers (2-tailed): * = $p < 0.05$ ** = $p < 0.01$ *** = $p < 0.001$ EP = Event Perception

Table 2.4 COMPARISONS BETWEEN SOLVENT ABUSERS AND CONTROLS ON T-TESTS AND ANCOVA

TEST	SOLVENT mean (SD)	CONTROLS mean (SD)	T-TEST t-value	p	ANCOVA F	AGE	NART	AGE+NART
VOCABULARY (raw score) 7$	23.7 (8.4)	45.6 (9.1)	5.2***	.001	12.1***	0.1	13.8**	11.2***
DIGIT SYMBOL (raw score) 12$	44.1 (11.4)	59.0 (8.2)	3.7***	.001	10.9***	2.9	0.0	2.2
BLOCK DESIGN (raw score) 9$	30.9 (6.6)	38.6 (7.5)	2.4*	.03	2.5	1.8	0.1	1.1
DIGIT SPAN FORWARD (raw score) 9$	6.3 (0.9)	7.3 (0.9)	2.6*	.02	1.5	0.0	4.0	3.9*
DIGIT SPAN BACK (raw score) 9$	4.2 (0.7)	5.7 (1.3)	3.0**	.01	3.6	8.4**	0.7	5.0*
BODYSWAY (deg/min)	21.9 (10.5)	14.9 (4.8)	-2.1*	.05	2.6	0.2	0.4	0.8
STATE ANXIETY (out of 80) 10$	49.7 (9.7)	34.1 (6.0)	-4.7	.001	7.9**	4.9*	0.5	6.0**
TRAIT ANXIETY (out of 80) 10$	49.8 (10.4)	39.2 (10.3)	-2.4*	.03	0.4	3.1	0.2	3.5*

* = p< 0.05 ** = p< 0.01 *** = p< 0.001 $ = number of subjects

TABLE 2.5 PARTIAL CORRELATIONS CONTROLLING FOR AGE AND NART: SOLVENT ABUSERS

TEST	SPAN	EVENT	THRESH	MOVE	SEARCH	WORD	SWAY
VISUAL SPAN							
EP APPEARANCE			-.61*	.75**	-.67*		-.76**
EP THRESHOLD				-.73**	.57*		.93***
EP MOVEMENT					-.79**		-.82**
SEARCH							.70*
WORD RECOGNITION							
RT SIMPLE DECISION							
RT SIMPLE MOVEMENT		-.61*	.55*	-.71**			.71**
RT CHOICE DECISION					.57*		
RT CHOICE MOVEMENT			.66*	-.74**			.72**
DIGIT SYMBOL							
BLOCK DESIGN							
DIGIT SPAN FOR						-.87**	
DIGIT SPAN BACK						-.77*	

* = p< 0.05 ** = p< 0.01 *** = p< 0.001 Counter to prediction: $ = p< 0.05 $$ = p< 0.01 EP = Event Perception

TABLE 2.6 PARTIAL CORRELATIONS CONTROLLING FOR AGE AND NART: CONTROLS

TEST	SPAN	EVENT	THRESH	MOVE	SEARCH	WORD	SWAY
VISUAL SPAN							
EP APPEARANCE							
EP THRESHOLD							
EP MOVEMENT					-.62*	.58$	
SEARCH							
WORD RECOGNITION							.55*
RT SIMPLE DECISION							-.59$
RT SIMPLE MOVEMENT							
RT CHOICE DECISION							-.64$
RT CHOICE MOVEMENT							
DIGIT SYMBOL							.79$$
BLOCK DESIGN					-.91***		
DIGIT SPAN FOR							
DIGIT SPAN BACK					-.66*		

* = p< 0.05 ** = p< 0.01 *** = p< 0.001 Counter to prediction: $ = p< 0.05 $$ = p< 0.01 EP = Event Perception

TABLE 2.7 FOLLOW-UP STUDY: COMPARISONS BETWEEN SOLVENT ABUSERS AND CONTROLS ON T-TESTS

TEST	1. SOLVENT mean (SD)	1. CONTROLS mean (SD)	2. SOLVENT mean (SD)	2. CONTROLS mean (SD)	3. SOLVENT mean (SD)	3. CONTROL mean (SD)
VISUAL SPAN (no. of blocks)	12.9 (2.9)	14.7 (3.5)	13.3 (1.6)	14.8 (4.3)	15.1 (0.6)	16.2 $ (3.6)
EP APPEARANCE (correct out of 25)	22.3 (3.0)	24.5* (0.7)	24.8 (0.2)	24.9 (0.5)	24.5 (1.0)	25.0 $$ (0.0)
EP THRESHOLD (ms)	155 (82)	32*** (8)	64 (14)	30*** (10)	36 $ (10)	33 (14)
EP MOVEMENT (correct out of 25)	10.8 (5.7)	20.0*** (3.4)	11.5 (5.5)	20.3*** (2.4)	17.0 $ (4.7)	21.3* (2.8)
VISUAL SEARCH (ms)	3336 (911)	2693* (282)	3019 (504)	2417** (313)	2929 (293)	2293**$$ (420)
WORD RECOGNITION (ms)	134 (77)	60** (14)	124 (90)	62* (15)	99 (55)	56* (14)
RT SIMPLE DECISION (ms)	287 (33)	255 (30)	296 (42)	268 (37)	287 (35)	260 (30)
RT SIMPLE MOVEMENT (ms)	234 (56)	195* (21)	234 (54)	164*** (20)	227 (56)	157**$$$ (30)
RT CHOICE DECISION (ms)	325 (17)	295* (28)	328 (36)	293 (31)	302 $$ (23)	294 (27)
RT CHOICE MOVEMENT (ms)	253 (65)	199* (24)	233 (37)	169*** (25)	211 $$ (50)	159*$$$ (29)
BODYSWAY (units/min)	20.9 (9.5)	14.9 (4.8)	17.8 (4.3)	11.7** (3.0)	14.9 (2.3)	10.5*$$$ (4.4)
STATE ANXIETY maximum 80	45.5 (3.5)	34.1*** (6.0)	48.3 (10.7)	31.4** (7.9)	41.8 (9.3)	32.0 (8.8)

Significant difference between controls and solvent abusers (2-tailed): * = p< 0.05 ** = p< 0.01 *** = p< 0.001 EP = Event Perception

Significant difference between 1. and 3. assessment (1-tailed): $ = p<0.05 S$ = p<0.01 $$$ = p<0.001

3.0 EVENT PERCEPTION IN ALCOHOLICS.[1]

3.1 INTRODUCTION.

Immediately after withdrawal of alcohol many alcoholics exhibit obvious signs of disturbed concentration and coordination. After this transient phase there is a period during which there is gradual recovery of intellectual functions. Some alcoholics appear to recover functions completely while others show persisting deficits of intellect and memory (Acker, 1982a; Kleinknecht & Goldstein, 1972; Tarter, 1975, 1980). It is possible that a proportion of alcoholics may have, at least during the recovery phase, disorders of attention. The kinds of complaint made by patients which may be indicative of deficits of attention are: poor concentration, forgetfulness, and mental slowness. Many alcoholics exhibit a distinct slowing (Goldstein & Chotlos, 1965; Kleinknecht & Goldstein, 1972). For example, alcoholics often perform poorly on timed tasks such as the Digit Symbol, Block Design, and Object Assembly subtests of the Wechsler Adult Intelligence Scales (Long & MacLachlan, 1974; Parsons & Farr, 1981). It has also been demonstrated that alcoholics have slower reaction times than controls (Talland, 1963; Vivian, Goldstein & Shelly, 1973). Electrophysiological evidence of deficits of attention in the visual modality has also been presented (Porjesz & Begleiter, 1979; Porjesz, Begleiter & Samuelly, 1980). Chan, McLeod, Tuck, Walsh & Feary (1986) studied 52 alcoholics without and 8 with Wernicke-Korsakoff syndrome and 42 controls using visual evoked potentials. Abnormal VERs were

[1] A version of this chapter has been published in: Wilson JTL, Wiedmann KD, Phillips WA & Brooks DN. (1988). Visual event perception in alcoholics. **J. Clinical & Experimental Neuropsychology, 10:3,** 222-234.

found in 23% of patients without and 37% with Wernicke-Korsakoff syndrome. The main VER abnormalities found in both groups were prolonged latency and reduced amplitude of the P100 component.

A number of hypotheses have been advanced concerning the relationship between alcohol abuse and brain pathology. Jones and Parsons (1971) proposed the view that psychological functions in alcoholics are relatively more disrupted in the right than the left hemisphere. Support for their claim was derived from the finding that the majority of deficits in alcoholics appear to involve non-verbal tasks. A majority of studies (cf. Tarter, 1975) reported a small but consistent inferiority of performance IQ relative to verbal IQ on the Wechsler Adult Intelligence Scales (WAIS; Wechsler, 1955) in alcoholics. Traditionally, performance tasks including assessment of spatial capacities were believed to reflect functioning of the right hemisphere (cf. McFie, 1975). O'Leary, Donovan, Chaney, Walker & Schau (1979) found the Block Design subtest to be the most powerful discriminator between alcoholics and non-alcoholics. Miglioli, Buchtel, Campanini & DeRisio (1979) administered a battery of verbal and non-verbal tests to a group of alcoholics and controls, and found that non verbal measures discriminated alcoholics more reliably from controls than verbal tasks. They interpreted their results as evidence for right hemisphere dysfunction. Ryan and Butters (1979) found the largest deficits when alcoholics were presented with unfamiliar non verbal information. The important aspect in this study seemed to be that alcoholics proved to be inferior under circumstances requiring adaptation to a novel situation. This was confirmed in a study by Parsons, Tarter and Edelberg (1972) where alcoholics were found to be less able in using their non preferred hand compared to controls. Goodglass and Peck (1972) using a dichotic listening paradigm

found that only items presented to the left ear were recalled less well by alcoholics when compared to normals. Tarter (1980) in summarising the psychological evidence for lateralised impairment in alcoholics felt that it was not clear whether these impairments were due to lateralisation of cerebral pathology or whether the threshold for the observed impairment was lower for visual spatial than for verbal tasks. He continued that because verbal processes are highly automatic and overlearned in the habits of everyday living, they may be less susceptible to the effects of cerebral pathology induced by alcohol abuse. Hypothetically equal atrophy in each hemisphere might therefore reveal psychological deficits in only the visual spatial modality. The idea of verbal superiority which is a rather popular view may be somewhat misleading considering the range of psychological assessment procedures employed in neuropsychological research which does not normally include procedures exclusively assessing visual or visuo-spatial capacities. Thus there are no exact estimates of the extent to which our everyday lives depend on purely visual information processing without any verbal components and it is therefore inappropriate to assume verbal superiority without having adequate comparisons. Secondly, the evidence for lateralisation of performance tasks as representing right hemisphere functioning has been weakened by a number of studies employing neuroradiological procedures (eg. Ron, Acker, Shaw & Lishman, 1982). The hypothesis of differential hemispheric impairment in alcoholics is based entirely on psychological findings since there is no pathological evidence supporting this suggestion. In the absence of such evidence the hypothesis suggesting lateralisation of deficits in alcoholics must be regarded with a degree of caution.

Kleinknecht and Goldstein (1972) proposed the idea that chronic excessive

consumption of alcohol would cause an acceleration of the aging process. Their assumption was based on a number of studies including a report by Jones and Parsons (1971) in which the authors observed that young alcoholics performed as well as young controls on a battery of neuropsychological tests, but that older alcoholics performed much more poorly than their age matched controls. Kleinknecht and Goldstein concluded that alcohol interacts with the aging process with immunity from deficit during the early years of abusive drinking but with an accelerated rate of deterioration as drinking and aging conjointly proceed. Williams, Ray & Overall (1973) analysed the WAIS profiles of 158 alcoholics and reported independent dual processes of accelerated mental aging and organicity. Schau and O'Leary (1977) using the Halstead-Reitan battery found that the brain-age quotient of alcoholics was significantly lower than that of a group of normal subjects. Ryan and Butters (1980) reported that alcoholics who had been sober for several months still exhibited cognitive impairment on a number of experimental tasks which were more demanding than standard clinical tests. They found that alcoholics between the age of 34-49 years performed almost identically with a normal control group aged 50-59 years. Similar results were reported for a higher age group. The findings by Ryan and Butters illustrate that even young alcoholics may be impaired relative to their age matched controls, suggesting an insidious adverse effect from drinking even at an early stage. The study also showed that more specific tests may elicit deficits at specific stages of the drinking history. The idea of interpreting relative impairment on standardised neuropsychological test batteries as evidence of premature aging may appear somewhat peculiar. Most neuropsychological assessment procedures are not categorical measures which would allow one to dichotomise patients into categories such as can/cannot perform a specific task but they give a continuum of performance from

childhood to old age. This approach at interpreting test results is common practice in developmental psychology where mental age in children is estimated according to their performance relative to other children's performance of the same age group. To some extent this idea is borne out in neuroradiological assessments of brain atrophy which is usually measured relative to an age matched control group. Thus appearances interpreted as brain atrophy in a fifty year old alcoholic may be equivalent to normal values in an eighty year old non alcoholic control. These examples may be in support of an interpretation of neuropsychological deficits in alcoholics as premature aging but its heuristic and clinical value remains equivocal.

The most widespread view concerning the effect of alcohol on the central nervous system is that chronic alcohol abuse leads to diffuse brain damage. Definitions of diffuse brain damage are sometimes equivocal and opinions vary considerably concerning the exact limits but the term implies that damage from any causal agent is not localised in any specific brain site or system. The symptoms of generalised cerebral atrophy are usually taken to involve memory impairment, poor judgment, reduced intellectual competence, reduced clarity of consciousness, and disorientation. Although memory impairment and reduction in intellectual competence has been reported in many studies, alcoholics are usually oriented to time, space and person and are often not seriously impaired in their judgment. Ron, Acker, Shaw & Lishman (1982) in a study investigating 100 alcoholics and 50 controls on CT found significant differences between the two groups with alcoholics showing a high incidence of cortical shrinkage and ventricular dilatation. Alcoholics were without clinically overt signs of brain damage but all CT scan measurements differed significantly between alcoholics and controls. The degree of widening of cortical sulci, Sylvian fissures, and

interhemispheric fissure, and the size of the ventricular system were all greater in the alcoholic group with two thirds showing unequivocal sulcal widening. Ten per cent of the alcoholics also showed signs of cerebellar atrophy. Asymmetrical involvement of the hemispheres was found to be rare. The left hemisphere showed a greater degree of abnormality than the right in 12 alcoholics and the reverse was true in 2 cases. The latter finding would be in stark contrast to the hypothesis of greater right hemisphere impairment in alcoholics. Some of the clinical variables such as age, years and amount of drinking, and social decline showed significant but relatively weak relationships. However, it is clear from this study that diffuse brain damage can be present in alcoholics without any obvious clinical signs and appears to be the most common sequel in chronic alcoholism.

A more specific attempt at localising alcoholic brain damage was made by Tarter (1976; 1980) who proposed that alcoholics suffer from fronto-limbic-diencephalic pathology. Tarter suggested that lesions in various locations within this system have been shown to produce similar behavioural deficits both in humans with naturally occurring lesions and in animal experiments. Among the similarities between the alcoholics and other patients with diencephalic pathology were qualitatively comparable performance on cognitive tasks which require shifting of cognitive set, utilising an error response, and inability to persist with a cognitive set to sustain a correct mode of responding (Tarter, 1973). Another common characteristic found in humans and animals with anterior basal lesions is spatial perseveration or a tendency to respond to a particular physical location during a task, regardless of stimulus characteristics or task demands. Goldstein and Chotlos (1965) found that spatial scanning, as measured by maze tests, was deficient in alcoholics. Bertera and Parsons

(1978) argued that the spatial deficit may be related to a more fundamental deficit in visual searching abilities. It is well known that demented or Korsakoff alcoholics suffer from neurological pathology in the limbic and diencephalic regions with atrophy of the mammillary bodies which is usually considered to be the hallmark of Korsakoff's syndrome. Tarter (1976) argued that it would be conceivable that alcoholics have similar disturbances as Korsakoff patients but in a less advanced stage which would nonetheless be detectable upon psychological measurement. There is ample evidence demonstrating structural and functional connections between the frontal and the basal regions of the brain. When considering the basal area one has to conceive this area as an integrated functional system rather than merely representing a discrete brain region or structure. This means that although the disease process in Korsakoff patients may manifest itself most clearly in atrophy of the mammillary bodies they can by no means be taken as the solely responsible site for the cognitive-behavioural deficits observed in these patients but as an indicator of severe disruption of the functional unit. Segal, Kushnarev, Urakov and Misionzhnik (1970) studied the effects of alcohol on the activity of cerebral deep structures and found that alcoholics during detoxification displayed symptoms similar to non alcoholics suffering from diencephalic lesions. Berglund and Ingvar (1976) found differences in regional cerebral blood flow in alcoholics that were most pronounced in the anterior regions of the brain. However, this is also the case for patients suffering from dementia and a general, nonspecific bloodflow deficit in the anterior regions is usually associated with atrophy. Some support for the hypothesis of a fronto-limbic deficit may be gained from a study by Samson, Baron, Feline, Bories & Crouzel (1986) who investigated local cerebral glucose utilisation using PET technology in a group of 6 alcoholics. Cerebral metabolic rate was not significantly modified in the selected cortical,

subcortical and cerebellar regions of interest but the metabolic distribution index, which reflects the distribution pattern of glucose utilisation, was selectively and significantly decreased in the medio-frontal area, suggesting a limbic metabolic dysfunction apparently linked to chronic alcoholism. Although the hypothesis suggesting fronto-limbic-diencephalic pathology in alcoholism is supported by a number of studies from clinical human and experimental animal research it should be kept in mind that the structures involved comprise more than 50 per cent of the entire brain mass and should therefore present a reasonable bet in guessing the site responsible for many of the abnormalities observed in alcoholics as well as other patients suffering from neurological conditions.

In an unpublished pilot study Wilson & Phillips observed that alcoholics failed to notice some targets on a visual event perception task under conditions in which controls normally perform perfectly. This task is easy because the appearing target cell stands out against the background and attention is automatically drawn to it (the task is identical with the Visual Change Perception task in the previous chapter).

The present study had the following aims: (1) to find out how common deficits in event detection are in alcoholics; (2) to investigate whether alcoholics had deficits in other aspects of visual processing; (3) to compare the sensitivity of three versions of the Event Perception tasks to alcoholic impairment, and (4) to compare performance on the Event Perception tasks with performance on conventional neuropsychological measures, particularly those of visuo-spatial functions.

3.2 METHODS.

3.2.1 Subjects.

Alcoholics. One hundred and eighty six in-patients from two alcohol treatment units in the West of Scotland were screened initially. Excluded from the study were: (1) patients who had been hospitalised with a head injury, (2) patients with a history of major psychiatric illness, (3) patients diagnosed as suffering from alcoholic dementia on clinical psychiatric examination, (4) patients with major physical complaints, (5) patients reporting any current visual disorder, excepting the need for correcting lenses, and (6) patients over the age of 60. Forty patients (38 male) fulfilled the criteria and were included in the study. Initial testing was carried out shortly before patients were discharged from in-patient care. At initial testing all patients had been abstinent for at least 7 days (mean=9.2 days). Tranquillisers and other drugs or vitamin supplements taken during detoxification were noted, and patients were not tested until at least 48 hours after their last drug intake. The results of liver function tests were recorded; no patient included in the sample had a diagnosis of hepatitis or cirrhosis of the liver at the time of testing. Patients were asked to return after 2 weeks to undergo repeat neuropsychological testing. Patients were breathalyzed at the time of retesting, and any patient with a positive result was excluded. Twenty-four patients who reported that they had not resumed drinking in the interval were retested; the mean period of detoxification was 26.7 days.

Controls. Forty controls were recruited by advertising in a local newspaper and at a Job Centre. Controls were paid £8.00 for participation. Anyone with a history of problem drinking, or psychiatric illness was rejected at initial interview. Controls were

matched with alcoholics for age and IQ as estimated by the National Adult Reading Test (NART; Nelson, 1981) and with respect to social class, education, and employment history, all of which were very closely related (see table 3.1). Care was taken to test controls and alcoholics at similar times of day. Twelve controls returned for retest.

3.2.2 Assessment procedures.

Measures and assessment procedures were identical to those used in the previous study and a repeated description will be omitted here. In addition to these tasks two more questionnaires were administered: the Beck Depression Inventory (Beck, Ward, Mendelson, Mock & Erbaugh, 1961) and the research version (30 items) of the General Health Questionnaire (Goldberg, 1978).

3.3 RESULTS.

3.3.1 Initial assessment.

Matched variables. The mean age of alcoholic (40.4) and control (38.4) groups did not differ significantly. The error scores on the NART were not significantly different (19.0 and 17.0 respectively). The full scale WAIS IQ predicted from these scores is 112 and 114 respectively. There were no significant differences on the measures taken of educational attainment, profession, or employment history. Nineteen alcoholics were unemployed at the time of testing (mean number of years unemployed = 3.8), and 16 controls (unemployed = 4.1 years) (Table 3.1).

A similar analysis was conducted comparing the 24 alcoholics who returned for retest with the 12 retested controls. There were no significant differences between the two groups either in age (alcoholics = 42.6 years; controls = 40.3 years, t= 0.74 ns) or in the number of errors on the NART (alcoholics = 17.6; controls = 14.9, t= 0.97 ns). Retested alcoholics were compared with alcoholics not retested to determine if there were any biases in sampling of alcoholics for retest. There was a difference in the number of years of problem drinking with 11.3 years for those not returning and 9.3 years for those retested but this difference was not statistically significant. A difference was found for the number of units drunk on a typical drinking day with 47.0 units for those not retested and 32.3 units for those retested which was statistically significant at t= 2.3 $p<0.05$. This suggests that alcoholics with lower consumption and fewer years of problem drinking were more likely to return for retest. However, none of the neuropsychological measures showed any significant differences between the two groups and for the majority of measures performance was virtually identical. A similar analysis was conducted for the control group and a comparable trend was observed. The difference in number of units consumed on a typical drinking day between controls not retested (3.7 units) and those coming for retest (2.2 units) was statistically significant at t= 1.8 $p<0.05$ (one-tailed). The only neuropsychological procedure showing a significant difference between groups on initial assessment was Event Perception Movement where those not retested performed better with a score of 18.6 compared to 14.4 for retested controls (t= 2.9 $p<0.01$).

Questionnaires. Alcoholics were significantly more likely than controls to report feelings of anxiety, both immediate and long-term, as measured by the State-Trait Anxiety Questionnaire. The alcoholics made significantly more negative

responses than controls on the General Health Questionnaire. A major feature of the alcoholics was the prevalence of signs of depression as estimated by the Beck Depression Inventory (alcoholics = 20.5). The controls as a group gave only a very moderate number of responses indicative of depression (mean = 4.6), despite the poor employment history of many subjects in this group (Table 3.1).

Neuropsychological assessment. Table 3.2 gives a summary of the results of the initial assessment comparing alcoholics and controls. Alcoholics showed statistically significant impairment on 11 of the 19 assessment procedures. Alcoholics performed more poorly than controls on all three Event Perception tasks. However, the absolute differences between the means for alcoholics and controls on Event Perception Appearance and Event Perception Movement were small. There was a clear ceiling effect on performance in the Event Perception Appearance task, however, there was no such effect in the Event Perception Movement task. There were consistent differences between alcoholics and controls on Event Perception Threshold. Two alcoholics performed very poorly on this test; for the purpose of data analysis a cut-off was arbitrarily set at 200 ms and any threshold larger than this was treated as equal to 200 ms. Other computer based measures on which alcoholics were impaired were the movement times from the Reaction Time tasks, and Visual Search. No significant differences were found on Body Sway although alcoholics were slightly more ataxic than controls as measured by Body Sway amplitude. On the traditional neuropsychological measures alcoholics were impaired on the Digit Symbol and Block Design tests, and on all subtests of the Rey Figure. There were no significant differences between alcoholics and controls on any of the verbal measures Associate Learning, Digit Span, or Vocabulary.

Patients were split into a low score group with a score of 14 or less and a high score group with scores of more than 14 on Event Perception Movement to investigate whether there were any systematic differences between alcoholics performing poorly on this test and those whose performance was within control limits. The cut-off point of 14 was chosen as being the closest to one standard deviation below the control mean which gave an approximately equal distribution in numbers and resulting in an almost perfect match on demographic variables. Table 3.3 shows that there were no significant differences between groups for age, NART errors, amount of alcohol consumed, and years of problem drinking. On the other hand this division seemed to split groups also with respect to performance on many other tasks. The low score group performed significantly worse than the high score group on 8 of the 19 measures. For traditional neuropsychological measures performance by the low score group was inferior on Block Design, Rey Figure Copy and Associate Learning. Differences between groups were most pronounced on Event Perception Threshold and Event Perception Movement. Low scorers also had longer Choice Reaction times on both components. The division of alcoholic subjects into a low score and high score group also means that about half of the alcoholics showed no impairment on the Event Perception tasks.

Table 3.4 shows how performance on Event Perception Threshold and Event Perception Movement was related to other tasks. There were no significant relationships for alcoholics between age, NART errors, amount of alcohol consumed and years of problem drinking, and performance on the Event Perception tasks. Event Perception Movement showed a significant relationship with 14 of the 18 measures, the strongest being with Event Perception Threshold followed by Block Design and

Rey Figure immediate and delayed recall. Event Perception Threshold was significantly related with 8 measures but these relationships were found to be rather weak. For the control group there was a significant relationship between Event Perception Movement and age and the amount of alcohol consumed. Performance on Event Perception Movement was not significantly related with performance on Event Perception Threshold but to some degree with the Event Perception Appearance task and more strongly with Visual Search. The only other significant relationship found was with Digit Symbol. Event Perception Threshold was related with performance on the Event Perception Appearance task but also, rather peculiarly, there was a relationship with Digit Span. A significant relationship was also found with performance on Visual Span.

Years of problem drinking was not related with any of the neuropsychological test procedures. Amount of alcohol consumed was significantly related with Event Perception Movement in controls but counter to the expected direction, indicating better performance for subjects with a higher alcohol consumption. Amount of alcohol consumed was not related with any of the measures in the alcoholic group.

Folate and vitamin B12 levels which are considered to reflect nutritional status were only available from alcoholics and obtained from blood samples taken on admission. Neither of these measures was significantly related with performance on any of the neuropsychological tests.

3.3.2 Follow-up assessment.

The results of the follow-up assessment for alcoholics and controls on the computer based measures are summarised in table 3.5. There were significant differences between alcoholics and controls on Event Perception Threshold and Visual Span. Differences on other measures did not reach statistical significance.

Table 3.6 presents the results from a test-retest analysis on the 12 controls retested. There were significant training effects for Event Perception Movement, Word Recognition, and Visual Span. Test-retest reliability expressed as correlation coefficients was reasonably strong for Event Perception Appearance, Event Perception Movement, Word Recognition, and Choice Reaction Time Decision but poorer for other measures. However, the sample was rather small for a proper analysis of test-retest reliabilty.

Table 3.7 shows a similar comparison between initial and follow-up scores of the 24 alcoholics retested. Scores were significantly improved on 9 of the 12 measures including repeat administration of the State Anxiety questionnaire. However, caution must be exercised with respect to the three tasks showing significant training effects in the control group (Event Perception Movement, Word Recognition, and Visual Span) as to whether to interpret these changes as improvement. Correlation coefficients showed that test - retest reliability was in general acceptable for most tasks but slightly low for Event Perception Threshold and Body Sway.

3.4 DISCUSSION.

Results in the current study showed that alcoholics were impaired at noticing and locating rapid visual changes on initial testing and at retest. It could be argued that the results on initial testing were associated with withdrawal (Gross, Lewis & Hastey, 1974). However, the immediate symptoms of withdrawal would almost certainly have abated by the time of retest. Of the three measures of event perception only Event Perception Threshold was impaired at retest.

A possible explanation of the poor performance of alcoholics is that it is due to a generally depressed and anxious state. This might appear plausible since alcoholics had significantly higher scores on both the Depression Scales and the State-Trait Anxiety Questionnaire. However, only Event Perception Threshold was significantly related with scores on both the Beck Depression Inventory ($r= 0.30$ $p< 0.05$) and the GHQ ($r= 0.43$ $p<0.01$). An analysis of covariance controlling for state and trait anxiety showed that the differences between alcoholics and controls on all three Event Perception tasks remained significant, suggesting that anxiety does not account for poor performance on these tests. Similar results were obtained when controlling for Depression and GHQ scores. The impression based on reports of subjects was that the computer-based measures provoked less anxiety than conventional procedures. The computer-based procedures were more impersonal, and seemed to give less of a sense of failure than conventional tests. These positive effects of computerised assessments were also found in a study by Acker (1982b) and Acker, Acker & Shaw (1984) who devised a battery of computerised tests consisting of a mixture of novel and traditional tasks adapted for computer use.

For Reaction Time tasks alcoholics showed no difference in decision times compared to controls, and, in particular, the choice decision times of the groups were very similar. Because of its additional mental load alcoholics might have been expected to show differences on this task especially if they were suffering from general brain atrophy or ventricular enlargement (cf. Van Zomeren, 1981). However, the alcoholics did have slower movement times than controls on both RT tasks. This suggests that previous reports of slowed reaction times in alcoholics (Smith & Layden, 1972; Talland, 1963; Vivian, Goldstein & Shelly, 1973) reflect impaired sensorimotor performance rather than attentional deficit. In the present study movement time was a measure of the time taken to execute a precise, visually guided movement from one position to another. High level disorders of motor control have been reported previously in alcoholics (eg. Parsons, Tarter & Edelberg, 1972). A sensorimotor impairment is also consistent with the finding that alcoholics were significantly more ataxic than controls on initial testing. Another task which involved a precise movement was Visual Search, and it is not clear to what extent the deficit shown by alcoholics on this task was due to a sensorimotor disorder. On the other hand the suggestion of functional or structural impairment in the frontal lobes including the visual eye fields as proposed by Bertera & Parsons (1978) cannot be dismissed in the absence of structural or functional brain scans. Impairment in this area would interrupt mechanisms of visual attention and might provide an alternative or additional explanation of the deficits observed in alcoholics on the Event Perception tasks. Although preserved performance on decision time seems to contradict a general attention deficit, more than one mechanism of attention may be involved in the tasks used in this study.

The results on the traditional measures employed in the present study were consistent with previous findings. Digit Symbol and Block Design have been found among the most sensitive of the WAIS subtests to alcoholic deficits (Parsons & Farr, 1981; O'Leary et al., 1979). Impairment on the Rey Figure has also been reported previously (Miglioli et al., 1979). An important issue is the extent to which sensorimotor impairment underlies poor performance on the traditional neuropsychological measures. It is immediately obvious that Digit Symbol and Block Design involve a component of speeded, visually guided movement and therefore would be sensitive to such an impairment. It is less obvious that the performance of alcoholics on the Rey Figure can be explained in this way, however, the task does include a component of precise, visually guided movement. The extent to which sensorimotor disorders underlie poor performance on these conventional procedures remains unresolved. The above results show that sensorimotor deficits must be controlled for in studies of higher visuo-spatial deficits.

The absence of reliable relationships with measures such as number of years of problem drinking and amount of alcohol consumed with performance on neuropsychological measures is also consistent with the alcohol research literature. The lack of such relationships is believed to stem from an inherent lack of reliability of alcoholics as an informant with respect to their consumption and denial as to when drinking started to be considered a problem. Rather more surprising was the absence of any relationships with vitamin levels. However, sometimes alcoholics had been started on a vitamin supplement treatment before the blood samples were taken which would have contaminated values.

Alcoholics were not impaired on initial testing or at retest on the Word Recognition task. Thus there is no evidence of a general decrease in the ability to process briefly presented visual targets in alcoholics. There was no impairment of Visual Memory span on initial testing, however, surprisingly there was a significant difference between alcoholics and controls on retest. A possible explanation of this finding is that controls benefited from practice on this task while alcoholics did not. This would imply a learning deficit in alcoholics rather than a short-term memory deficit. The results of the Rey Figure recall tasks also suggest that alcoholics show a learning deficit related to visual material. A specific deficit for visual learning has been described previously in alcoholics (Ellenberg, Rosenbaum, Goldman & Whitman, 1980). Deficits of adaptational learning have also been found in a study by Ryan and Butters (1979) who showed that alcoholics were inferior in conditions requiring adaptation to a novel situation which would also be applicable in the visual memory tasks.

When alcoholics were split into two groups according to performance on Event Perception Movement it emerged that this test could be used as a discriminator between alcoholics who were generally more impaired and those who showed little or no impairment. The low score group performed significantly worse than the high score group on 8 of the 19 measures. The means on all three Event Perception tasks were approximately 2 SDs lower compared to the control group. This would initially suggest equal impairment on all three tasks but although tasks were significantly interrelated the size of the squared correlation coefficients suggested that only one third of the variance was shared between Event Perception Threshold and Event Perception Movement leaving two thirds of the variance to be explained by other factors. It is

therefore suggested that despite apparently equal impairment in terms of deviation from the control mean, performance on Event Perception Threshold and Event Perception Movement reflects impairment of distinct processes. Relationships with other neuropsychological tests and Event Perception Movement were more consistent for the low score group than for the high score group probably indicating generally impaired performance rather than intrinsic task relatedness. When performance of individual alcoholics on Event Perception Movement and Event Perception Threshold was compared it emerged that the two tasks doubly dissociated in 2 patients. The criteria applied for dissociations were the same used by Warrington (1982) requiring the unimpaired test score to fall within 1 SD of the control mean and the impaired score to be at least 3 SDs below the control mean (see table 3.8).

The results of retesting on the computerised measures demonstrated considerable short-term recovery in alcoholics. The present study supports the view that many alcoholic deficits show short-term reversibility (Goldman, 1983; Page & Linden, 1974). Previous studies have reported short-term recovery of motor function (Goldman, Whitman, Rosenbaum & Vandevusse, 1980), and of visual search (Goldman, Williams & Klisz, 1983). Areas in which persisting deficits have been reported are visuo-spatial learning (Ellenberg et al., 1980) and detection of cutaneous stimulus (Goldman et al., 1980). The pattern of results in the present study is consistent with these findings and, in addition, suggests that alcoholics have persistent deficits in noticing and locating visual events. Correlation coefficients in table 3.6 also indicated that retest reliability was fairly high. The fact that controls scored significantly better on Event Perception Movement at retest may initially be of some concern with respect to reliability of this procedure. However, for some peculiar

reason this was the only measure on which retested and not retested controls differed significantly in their initial test scores. Even at follow-up retested controls did not reach the mean of 18.6 representing the initial score for not retested controls. A better control sample would have to be recruited to allow sound judgment upon the retest reliability of this task.

The results in this study do not support the idea that the deficit on the Event Perception tasks is due to general disruption of visual attention. It remains quite possible that the deficit reflects a specific failure of the processes whereby rapid changes attract attention. Porjesz and Begleiter (1979) reported that alcoholics in their study had abnormal P300 amplitudes in a task requiring discrimination of double and single flashes and clicks. Alcoholics may therefore have a specific attentional impairment, the precise nature of which remains to be elucidated. It is possible, however, that a deficit occurs in the processes which generate ON and OFF responses in the visual system. Electrophysiological studies have demonstrated that pattern reversal evoked potentials are abnormal in up to a quarter of chronic alcoholics (Ahmed & Hines, 1983; Chan et al., 1986; Posthuma & Visser, 1982); among the abnormalities reported are decreased amplitude and increased latency of the early components. In normal subjects systematic variations in the early components of the evoked potential can be related to performance on the Event Perception tasks (Wilson, 1983). In the present study impairment at the sensory level on the Event Perception Threshold measure could arise from several sources. It could arise from a decrease in the amplitude of the responses to the target, from an increase in the amount of noise in the system, or from variations in latency which resulted in greater overlap between the responses to target and background. These possibilities are not mutually exclusive,

and indeed both the Event Perception Movement and Event Perception Threshold test may be particularly sensitive because they are affected by changes in both response amplitude and response latency. The characteristic, but rarely diagnosed, visual disorder, associated with alcoholism is alcohol amblyopia (Dreyfus, 1974), and abnormal visual evoked responses have been described in alcoholics with this condition (Kupersmith, Weiss & Carl, 1983). Frequently this type of amblyopia is also associated with tobacco smoking. Although a majority of alcoholics were heavy smokers the number of cigarettes smoked per day was not related to performance on any of the neuropsychological measures. If the present results reflect alcohol amblyopia, then they imply that this condition is common in alcoholics in a subclinical form.

3.5 CONCLUSIONS.

A group of 40 detoxified alcoholics was compared with a group of 40 moderately or non-drinking controls on a number of neuropsychological assessment procedures. Alcoholics performed significantly worse than controls on 11 of the 19 procedures during initial assessment. At follow-up alcoholics were significantly impaired on only 2 measures. Performance on all three Event Perception measures was found to be significantly impaired in alcoholics on initial assessment. Alcoholics continued to show significant impairment on Event Perception Threshold at follow-up.

It was concluded that these deficits did not reflect a general deficit of visual attention because of unimpaired performance on other visual processing tasks but a rather specific failure of the processes involved in attracting attention in response to rapid change. It was thought that this deficit might occur at a level at which ON and OFF responses are generated in the visual system. The possible underlying condition was could be a subclinical form of alcoholic amblyopia which is caused by pathological changes of nerve fibres in the visual system in response to the toxic effects of alcohol and its metabolites. These changes were found to affect performance on the Event Perception tasks differentially. Although alcoholics seemed to be equally impaired on all three tasks on initial assessment when comparing performance with the control mean, the correlations between these tasks suggested that they were measuring different processes. Double dissociations found in individual alcoholics further strengthen the argument that the perception of movement can be impaired independently from the perception of appearances and vice versa. At follow-up these differences were even more distinct when alcoholics were only significantly impaired

on Event Perception Threshold. The study therefore shows clearly that the processes by which signals attract attention in the appearance tasks and those in the movement task must be distinct and that these processes can dissociate across a group of alcoholic patients. A dissociation in performance on these tasks was also found between different patient groups when the findings from the previous study are taken into consideration where solvent abusers showed persistent deficits on Event Perception Movement but not on Event Perception Threshold. In fact, alcoholics were unique amongst all the patient groups studied in this project in showing more persistent impairment on the Event Perception Threshold task and not on the Event Perception Movement task as found in other patient groups.

The dissociation between different patient groups further strengthens the proposal that detection of appearances is neurally distinct from detection of movement and provides validation for the tests as being differentially sensitive to different neurological conditions.

TABLES

Table 3.1 Demographic background for alcoholics and controls.

	Alcoholics N=40	Controls N=40	t-value	p
Age (years)	40.4 / 8.6	38.4 / 9.6	-0.9	ns
NART errors (max=50)	19.0 / 10.2	17.0 / 7.6	-1.0	ns
Amount of alcohol drunk in typical day (units)	37.9 / 19.0	3.3 / 2.7	-11.3	0.001
Years of problem drinking	10.0 / 6.1	- - / - -		
STATE Anxiety (max=80)	53.0 / 15.7	32.8 / 7.2	-7.4	0.001
TRAIT Anxiety (max=80)	53.2 / 12.4	36.1 / 9.9	-6.8	0.001
BECK Depression Inventory	20.5 / 9.8	4.6 / 5.3	-9.0	0.001
General Health Questionnaire	52.1 / 19.1	25.6 / 8.9	-7.9	0.001

TABLE 3.2. T-tests comparing all alcoholics with the control group.

TEST	Alcoholics N=40 Score/SD	Controls N=40 Score/SD	t-value	p
Digit Span+	12.9 / 1.3	13.3 / 0.8	1.1	ns
Vocabulary+	55.0 / 13.7	59.9 / 12.3	1.7	ns
Digit Symbol+	49.6 / 11.5	60.4 / 10.8	4.4	0.001
Block Design+	32.1 / 7.0	37.2 / 6.2	3.4	0.001
Rey Copy (max=36)	35.3 / 1.2	35.9 / 0.5	2.9	0.01
Rey Imm. (max=36)	20.0 / 6.7	24.8 / 5.1	3.6	0.001
Rey Del. (max=36)	20.7 / 6.8	24.0 / 4.9	2.5	0.05
Assoc. Learn. (max=21)	16.0 / 2.9	16.4 / 2.8	0.9	ns
EP Appearance (max=25)	22.9 / 2.9	24.0 / 1.2	2.2	0.05
EP Threshold (ms)	80 / 51	46 / 26	-3.8	0.001
EP Movement (max=25)	14.0 / 4.9	17.4 / 4.6	3.2	0.001
Visual Search (ms)	3362 / 872	2911 / 477	-2.9	0.01
Word Recognition (ms)	57 / 19	53 / 17	-0.9	ns
SRT Decision (ms)	281 / 47	271 / 36	-1.1	ns
SRT Movement (ms)	245 / 60	220 / 39	-2.2	0.05
CRT Decision (ms)	304 / 46	305 / 39	0.1	ns
CRT Movement (ms)	257 / 74	223 / 44	-2.5	0.05
Visual Span (blocks)	11.6 / 3.5	11.8 / 3.7	0.3	ns
Body Sway (units)	14.7 / 10.2	13.2 / 10.2	0.6	ns

+ = Raw Scores EP = Event Perception SRT = Simple Reaction Times CRT = Choice Reaction Times Rey Imm. = Rey immediate recall Rey Del. = Rey delayed recall Assoc. Learn. = Associate Learning

TABLE 3.3. T-tests comparing alcoholics with low and high scores on EP movement.

TEST	Low Move N=22	High Move N=18	t-value	p
Age (years)	40.5	40.2	-0.1	ns
Nart errors (max=50)	19.0	19.0	0.0	ns
Amount of Drink (units)	36.7	39.4	0.4	ns
Years of problem drinking	9.1	11.1	1.0	ns
Digit Span+	12.8	13.1	0.9	ns
Vocabulary+	53.7	56.5	0.6	ns
Digit Symbol+	47.7	51.8	1.2	ns
Block Design+	30.0	34.5	2.0	0.05
Rey Copy (max=36)	35.0	35.6	1.7	0.05$
Rey Imm. (max=36)	18.9	21.4	1.2	ns
Rey Del. (max=36)	19.2	22.4	1.5	ns
Assoc. Learning (max=21)	16.3	17.8	1.8	0.05$
EP Appearance (max=25)	22.1	23.8	2.0	0.05$
EP Threshold (ms)	102	52	-3.7	0.001
EP Movement (max=25)	10.5	18.3	8.6	0.001
Visual Search (ms)	3515	3175	-1.2	ns
Word Recognition (ms)	60	55	-0.6	ns
SRT Decision (ms)	289	272	-1.2	ns
SRT Movement (ms)	257	229	-1.5	ns
CRT Decision (ms)	316	288	-2.1	0.05
CRT Movement (ms)	273	237	-1.7	0.05$
Visual Span (blocks)	11.0	12.3	1.1	ns
Body Sway (units)	15.9	13.2	-0.8	ns

$ = one-tailed tests
+ = Raw Scores EP = Event Perception SRT = Simple Reaction Times CRT = Choice Reaction Times Rey Imm. = Rey immediate recall Rey Del. = Rey delayed recall Assoc. Learn. = Associate Learning

TABLE 3.4 Pearson correlations between performance on EP tasks and performance on other tasks for alcoholics (N=40) and controls (N=40).

TEST	Alcoholics		Controls	
	EP Move	EP Treshold	EP Move	EP Treshold
Age (years)	-0.13	0.16	-0.42***	0.16
Nart (max=50)	-0.12	0.12	-0.10	0.10
Amount of drink (units)	0.08	-0.02	0.28*	-0.14
Years of drinking	0.03	-0.07	- - -	- - -
Digit Span+	0.19	0.08	0.18	-0.53***
Vocabulary+	0.18	-0.04	0.16	-0.01
Digit Symbol+	0.38**	-0.17	0.27*	-0.19
Block Design+	0.49***	-0.26*	0.03	-0.14
Rey Copy (max=36)	0.29*	-0.04	-0.01	0.05
Rey Imm. (max=36)	0.48***	-0.32*	-0.06	-0.07
Rey Del. (max=36)	0.48***	-0.31*	0.10	-0.21
Assoc. Learn. (max=21)	0.34*	-0.23	0.22	0.03
Event Perception	0.42**	-0.24	0.32*	-0.40**
EP Threshold (ms)	-0.59***	- - -	-0.23	- - -
EP Movement (max=32)	- - -	-0.59***	- - -	-0.23
Visual Search (ms)	-0.37**	0.35*	-0.48***	0.17
Word Recognition (ms)	-0.29	0.12	-0.24	0.09
SRT Decision (ms)	-0.23	-0.05	-0.15	0.08
SRT Movement (ms)	-0.40**	0.37*	-0.17	-0.08
CRT Decision (ms)	-0.41**	0.03	-0.18	0.08
CRT Movement (ms)	-0.46***	0.35*	-0.08	0.02
Visual Span (blocks)	0.39**	-0.24	0.08	-0.37**
Body Sway (units)	-0.29*	0.26*	-0.12	-0.08

+ = Raw Scores EP = Event Perception SRT = Simple Reaction Times CRT = Choice Reaction Times Rey Imm. = Rey immediate recall Rey Del. = Rey delayed recall Assoc. Learn. = Associate Learning ! = $p<0.05$ counter to predicted direction

TABLE 3.5. T-tests comparing follow-up test scores for alcoholics and controls.

TEST	Alcoholics N=24 Score/SD	Controls N=12 Score/SD	t-value	p
EP Appearance (max=25)	24.1 / 1.6	24.0 / 1.0	-0.3	ns
EP Threshold (ms)	60 / 52	36 / 10	-2.2	0.05
EP Movement (max=25)	16.0 / 5.6	17.8 / 4.3	1.0	ns
Visual Search (ms)	3080 / 693	2755 / 578	-1.5	ns
Word Recognition (ms)	63 / 28	59 / 13	-0.7	ns
SRT Decision (ms)	290 / 52	216 / 43	0.6	ns
SRT Movement (ms)	216 / 43	228 / 26	0.8	ns
CRT Decision (ms)	306 / 47	305 / 50	-0.1	ns
CRT Movement (ms)	216 / 37	223 / 26	0.7	ns
Visual Span (blocks)	12.5 / 4.0	15.5 / 3.4	2.1	0.05
Body Sway (units)	10.2 / 6.0	10.3 / 5.0	0.0	ns
STATE Anxiety	42.2 / 12.8	30.3 / 10.1		

+ = Raw Scores EP = Event Perception SRT = Simple Reaction Times CRT = Choice Reaction Times Rey Imm. = Rey immediate recall Rey Del. = Rey delayed recall Assoc. Learn. = Associate Learning

TABLE 3.6. T-tests comparing initial and follow-up test scores for alcoholics.

TEST	Initial test N=24 Score/SD	Retest N=24 Score/SD	Corr.	t-value	p
EP Appearance (max=25)	23.1 / 3.1	24.1 / 1.6	0.74***	-2.2	0.05
EP Threshold (ms)	80 / 58	60 / 52	0.52**	1.9	0.05$
EP Movement (max=25)	14.1 / 4.9	16.0 / 5.6	0.72***	-2.4	0.05
Visual Search (ms)	3214 / 841	3080 / 693	0.70***	1.1	ns
Word Recognition (ms)	56 / 17	63 / 28	0.74***	-1.8	0.05$
SRT Decision (ms)	277 / 41	277 / 47	0.78***	-0.1	ns
SRT Movement (ms)	240 / 39	216 / 43	0.72***	3.8	0.001
CRT Decision (ms)	301 / 40	306 / 47	0.78***	-0.9	ns
CRT Movement (ms)	248 / 41	216 / 37	0.73***	5.4	0.001
Visual Span (blocks)	11.3 / 3.6	12.5 / 4.0	0.77***	-2.2	0.05
Body Sway (units)	16.9 / 12.6	10.2 / 6.0	0.62**	2.9	0.01
STATE Anxiety (max=80)	51.0 / 17.0	42.2 / 12.8	0.72***	3.4	0.001

Level of significance: * = $p < 0.05$ ** = $p < 0.01$ *** = $p < 0.001$ denotes significantly related with initial test

$ = one-tailed tests EP = Event Perception SRT = Simple Reaction Times CRT = Choice Reaction Times Corr. = Correlation coefficient

TABLE 3.7. T-tests comparing initial and follow-up test scores for controls.

TEST	Initial test N=12 Score/SD	Retest N=12 Score/SD	Corr.	t-value	p
EP Appearance (max=25)	23.8 / 1.6	24.0 / 1.0	0.82***	-0.6	ns
EP Threshold (ms)	45 / 31	36 / 10	0.44	1.0	ns
EP Movement (max=25)	14.4 / 5.5	17.8 / 4.3	0.83***	-3.7	0.001
Visual Search (ms)	2867 / 568	2755 / 578	0.70**	0.9	ns
Word Recognition (ms)	54 / 15	59 / 13	0.74***	-1.8	0.05$
SRT Decision (ms)	288 / 35	290 / 52	0.64*	-0.2	ns
SRT Movement (ms)	228 / 33	228 / 26	0.41	-0.0	ns
CRT Decision (ms)	312 / 41	305 / 50	0.89***	1.0	ns
CRT Movement (ms)	216 / 29	223 / 26	-0.01	-0.6	ns
Visual Span (blocks)	13.4 / 3.4	15.5 / 3.4	0.54	-2.3	0.05
Body Sway (units)	11.6 / 6.0	10.3 / 5.0	0.67*	0.9	ns
STATE Anxiety (max=80)	30.7 / 6.7	30.3 / 10.1	0.60*	0.1	ns

Level of significance: * = p< 0.05 ** = p< 0.01 *** = p< 0.001 denotes significantly related with initial test

$ = one-tailed tests EP = Event Perception SRT = Simple Reaction Times CRT = Choice Reaction Times Corr. = Correlation coefficient

Table 3.8 Individual acloholics showing double dissociations on Event Perception Movement and Event Perception Threshold.

		UNIMPAIRED	
		EP Movement	EP Threshold
IMPAIRED	EP Movement	2	58 ms Patient 1
	EP Threshold	288 ms	14 Patient 2

CONTROL VALUES			
	MEAN	SD	NORMAL RANGE
EP Move (max=25)	17.4	4.6	12.8 - 22.0
EP Thresh (ms)	46	26	20 - 72

EP = Event Perception

4.0 VISUAL EVENT PERCEPTION AND OPTIC NEURITIS.

4.1 INTRODUCTION.

Optic neuritis is the first manifestation of multiple sclerosis (MS) occurring in approximately 20% of cases and about three-quarters of those with optic neuritis will go on to develop definite MS (McDonald, 1983; Francis, Compston, Batchelor & McDonald, 1987). Multiple sclerosis has attracted considerable research interest for being one of the neurological conditions in which causality remains elusive. MS is characteristically marked by recurrent attacks of demyelination of nerve fibres which can be distributed widely in the central nervous system. Generally, MS is a chronic and relapsing disease, and some of the specific disabilities may wax and wane during the patient's life. The usual clinical presentation of MS is that of an intermittent and progressive disorder of ambulation, vision, coordination, or bladder control beginning in young adults. Visual field defects in the form of scotomas are more often unilateral than bilateral and may involve primarily the macular or peripheral vision. The description patients give of their symptoms varies from just dimming of colours to hazy vision and complete inability to see in patchy distribution. Fundoscopy in the acute phase of optic neuritis reveals swollen optic discs and sometimes haemorrhages if the demyelinated and inflamed plaque is adjacent to the eye bulb (Stefoski, 1981). Nystagmus is amongst the most frequent signs and is seen in virtually all patients with MS at some point during the disease.

Epidemiological studies have shown a geographical gradient with progressively higher prevalence of MS in northerly latitudes and for caucasians relative to other races. Prevalence in Southern England has been reported to be 63 per 100,000 but found to be highest in North-East Scotland with 155 per 100,000 and particularly in the Orkneys with 258 per 100,000 (Swingler & Compston, 1986). Hereditary factors have been considered as a possible contributor to the development of MS and an association between the gene responsible for control of immune mechanisms has been found. It has become clear that there is an association between MS and the 6th chromosome particularly with the HLA region which is concerned with the genetic control of immune mechanisms. The strongest associations have been found with the D or DR loci. For most populations of Northern European origin there is a strong association between MS and the gene products Dn2 and DR2 (McDonald, 1986). McDonald (1984) found DR2 in 19% of a control population in London and in 55% of patients with MS. However, Swingler and Compston (1986) found no HLA-DR2 association in parts of Scotland, where the prevalence of MS is highest in the UK, because HLA-DR2 linked genes occur in up to 50% of the normal population from these areas. The number and mode of operation of the genetic factors is still uncertain, but there is evidence for the implication of genetically controlled cellular immune mechanisms in the pathogenesis of the disease (McDonald, 1986). The precise relationship between transient changes in immunological status and the development of new lesions has yet to be defined.

The most frequently found parenchymal changes in MS are periventricular white matter abnormalities and gliosis. Magnetic Resonance Imaging (MRI) has proven superior in the detection of such abnormalities by allowing detection of seemingly

isolated lesions of the type known to occur in MS, namely optic neuritis, brain stem and spinal cord lesions (Ormerod et al., 1986, 1987). MRI is not in itself specific in the detection of abnormalities; it is probable that the similar appearances in multiple sclerosis and cerebral vascular disease both derive at least part from the influence of astrocytic gliosis on proton content and distribution. The significance of gliosis in the disease process remains uncertain. Ormerod et al. (1987) in a large scale investigation studied 401 individuals on MRI of whom 53 were healthy controls. They found periventricular abnormalities in all but 2 patients with MS and discrete white matter lesions in all but 12. Ormerod et al. found the detection of cerebellar and/or brainstem atrophy characteristic of cerebellar degeneration helpful in making a distinction from MS in the absence of white matter abnormalities. More than half the patients with symptoms attributable to isolated focal neurological lesions were found to have additional lesions at presentation. Ormerod et al. provided evidence to support the view that an important source of the abnormal MRI signals in acute lesions were oedema, and in chronic lesions they came from gliosis. They considered demyelination per se unlikely to make an important contribution to the abnormal signal. Honig, Siddharthan, Sheremata, Sheldon & Sazant (1988) studied 41 patients with clinically definite MS and found a strong relationship between CSF and MRI abnormalities in MS patients of longer than 3 years standing. MRI abnormalities were most frequently found in periventricular and supraventricular white matter, often in the atria or genu of the occipital and frontal horns. Other regions with abnormalities included the internal capsule, the centrum semivole, the cerebellum, and the brain stem, notably the pons. MRI and CSF examinations showed approximately equal sensitivity, detecting 76% of patients with definite MS. However, some 20% of their patients had normal examinations by MRI but abnormal CSF findings. The authors

felt that the frequency of negative MRI findings was greatest early in the course of the disease.

Earlier, in an attempt to improve diagnostic reliability in MS Halliday, McDonald and Mushin (1972, 1973) discovered that the visual evoked potential produced by pattern reversal stimulation was often abnormal in patients with optic neuritis or multiple sclerosis. In their study the latency to the peak of the first major positive potential recorded from the affected eye was delayed in 17 of 18 patients with optic neuritis, 16 of whom were studied in the acute phase. In a subsequent study Halliday, McDonald and Mushin (1973) found 49 of 51 patients having a significant delay in the pattern evoked response. The fact that in 8 patients with significant delay full ophthalmological investigation did not detect any ocular abnormalities was interpretated as underlining the technique's strength. Halliday, McDonald and Mushin concluded that the latency of the pattern-evoked response is the single most reliable index of persisting damage to the visual pathways and that patterned VEPs are a valuable test in the early diagnosis of MS. This claim was at least partially confirmed in a study by Asselman, Chadwick & Marsden (1975) who used VEPs in a study comparing 54 control subjects with 51 MS patients and 55 patients with other neurological diseases. The proportion of MS patients with delayed VEPs was lower than in the Halliday et al. studies but the distribution of abnormal VEPs was partly dependend on patients' age, optic status and degree of progression of the disease. However, most later studies have found an incidence of abnormal VEPs closer to the Asselman et al. values (eg. Plant, 1983).

Rushton (1975) introduced a different method of assessing ocular latency

disparities by adapting the Pulfrich pendulum in a way which excluded all depth stimuli except those which stem from retinal disparity. Pulfrich (1922) described an illusion in which a pendulum swinging at right angles to the line of gaze appears to swing in an elliptical path when a dark glass is placed in front of one eye. He suggested that the illusion was caused by a prolongation of the latency of vision of the dimmed eye, causing a disparity between the perceived image of the moving bob from the two eyes and hence an illusion of displacement in depth. Julesz and White (1969) have provided evidence in favour of Pulfrich's explanation in a study of healthy volunteers. Rushton in his study of 41 controls and 58 patients with confirmed or suspected MS used an electronic adaptation of the pendulum to exclude unwanted depth cues. For controls an interocular disparity of 2.4 ms was found while 50% of patients with definite MS had significantly longer disparities. Rushton also found a strong correlation between abnormally large disparities on the Pulfrich pendulum and abnormal VEPs for MS patients. He concluded that Pulfrich's pendulum is an easily performed and potentially useful subjective test for detecting abnormal delay in the visual pathway in MS. However, Regan, Milner & Heron (1976) felt that since the Pulfrich method uses a constant light intensity rather than an abrupt change of light intensity, the dominant stimulus might be motion rather than intensity change. There is a body of evidence suggesting that motion perception and the perception of intensity changes are mediated by different neural mechanisms most likely involving transient and sustained channels (cf. chapter 1 for references). Regan, Milner & Heron (1976) introduced a technique of stimulating different areas in patients of either the same eye or interocularly with two light sources. The onset of one of the lights could be delayed to match an individual's perception of simultaneity ie. the subject could adjust the delay of the second light until simultaneity was perceived. Regan et al. called this form

of assessment "delay campimetry" and found this technique to be more sensitive to demyelinating disease than conventional campimetry. They found that the distribution of delay within the abnormal visual field can be very patchy and that perception may be markedly delayed in retinal regions where visual acuity is normal. They also provided evidence that part of the delay in VEPs in MS patients arises in the retina rather than in conduction along partially demyelinated axons. In addition they found evidence for differential impairment depending whether the response was to an increase or a decrease in light intensity. Regan et al. suggested that the two different visual channels excited by brightening and by dimming are differentially sensitive to derangement by MS.

Another investigation of visual abnormalities in optic neuritis and MS is by measuring patients' contrast sensitivity using sinosoidal gratings. This technique was initially introduced by Schade (1956) and formalised by Campbell & Robson (1968). Measurements of contrast sensitivity were first applied in the investigation of MS patients by Richey, Kooi & Tourtellotte (1971). The justification for this approach was the neurophysiological finding that single cells in the animal visual system respond only over narrow ranges of spatial and temporal frequency (Campbell, 1983). There is psychophysical evidence for discrete spatial and temporal processing mechanisms or channels in human vision. Spatial channels have a bandwidth ranging from less than an octave to one octave (Blakemore & Campbell, 1969) and there are thought to be a minimum of seven (Watson & Robson, 1981). Temporal processing is thought to involve just two broadband channels and Kulikowski & Tolhurst (1973) labelled these channels pattern and movement mechanisms. Investigations of the visual loss resulting from optic nerve demyelination have built upon and benefited from this emerging

framework of normal visual processing. Zimmern, Campbell & Wilkinson (1979) found that a group of low frequency spatial channels can be affected independently of those at high spatial frequencies but individual spatial channels at intermediate spatial frequencies can also be selectively affected (Regan, Silver & Murray, 1977; Regan, Raymond, Ginsburg & Murray, 1981). Hess and Plant (1983) found that visual loss in some cases of optic neuritis depended upon both the spatial and temporal frequency of the stimulus. In their study of 10 patients with optic neuritis low spatial frequency stimuli sensitivity was more severely impaired at low temporal frequencies. When they increased the temporal frequency the threshold anomaly diminished but this was not the case at high spatial frequencies. Hess and Plant concluded that some if not most of their patients suffered from subtle threshold scotoma in different parts of the visual field and that this would be of special relevance to the study of contrast sensitivity. They suggested that small, more localised grating patches should be used to probe different regions of the visual field, an approach which would be a compromise between localisation of abnormalities in space and spatial frequency.

Tourtellotte (1974) reported attempts of restoring conduction by prolonging the action potential through demyelinated nerve fibres by using 4-aminopyridine and a scorpion venom. Gilmore, Kasarskis & McAllister (1985) reported a study in which they had administered the calcium blocker Verapamil in an attempt to decrease response latencies to VEPs, BAEPs and SEPs. It is well known that the electrophysiological characteristics of demyelinated axons are sensitive to changes in plasma calcium concentrations. When calcium influx is inhibited post-synaptic potentials can be prolonged and result in increased amplitudes and decreased latencies of the neuronal signal. Gilmore et al. found that Verapamil shortened pathologically prolonged

latencies in some of their MS patients toward normal.

The current study attempted to relate performance on visual Event Perception tasks developed and described in the previous chapters to findings from patterned VEPs and contrast sensitivity assessments in a number of patients suffering from optic neuritis.

4.2 METHODS.

Patients. Five subjects were recruited from patients participating in trials delivering hyperbaric oxygen to patients with established and suspected MS at the Western Infirmary in Glasgow between October 1985 and March 1986. This form of treatment remains controversial largely because of its lack of specificity. For patients in the current study no firm diagnosis of MS had been placed. No control subjects were assessed for this study but since abnormalities were mostly monocular, values could be compared with the unaffected eyes. As a guideline the values for P1 found by Asselman et al. (1975) are usually accepted as representing reliable control values. Their mean for control subjects under the age of 60 was 90.5 ms and by adding 3 SDs they defined an upper normal limit as 104 ms. Clearly, with a different experimental set-up these values can only be taken as a guide. For Event Perception Threshold values from the controls in the previous study (chapter 3) are given in table 4.1 and for Event Perception Movement control values from chapter 5 are given since subjects in this study were given identical versions of the test.

Procedures. Patients underwent routine ophthalmological examination including assessment of visual acuity and fundoscopy. Contrast sensitivity was assessed by sinosoidal gratings in a standard fashion. Visual evoked potentials (VEPs) were obtained by checkerboard pattern reversal in a standard procedure. In order to minimise sampling error resistance of electrodes was measured for each patient. Three sets of VEP recordings were obtained with patterns being horizontally displaced by 0.5, 0.9 and 1.8 degrees of visual angle.

Psychophysical assessment. Patients were assessed on Event Perception Threshold as described and applied in the two previous chapters and Event Perception Movement in a modified version. It was felt to be methodologically more sound to present all subjects with identical target locations rather than leaving target selection to the random generator function of the computer. Target locations were therefore pre-programmed but presented in a pseudo-randomised fashion without substitution. Furthermore no targets were presented immediately adjacent to fixation. Viewing distance from the display screen was approximately 60 cm. Resulting eccentricities at which a target could appear were therefore half those applied for the laboratory conditions in chapter 1, and measured 3, 4.5, 6 and 7.5 deg/arc horizontally and 2.25, 3.5. 4.75 and 6 deg/arc vertically with 1, 3, 5 and 7 targets displayed respectively. This also ensured that an equal number of (4) targets appeared in each quadrant. Targets were displayed twice in random order resulting in a total number of 32 trials.

4.3 RESULTS.

A summary of findings for all patients is given in table 4.1.

PATIENT 1.

This patient was a 35 year old woman with complaints of pain and blurred vision in her left eye and a diagnosis of optic neuritis. She was the only subject for whom data from three consecutive assessments with two-weekly intervals were available and her results are presented in table 4.2 and figures 4.1, 4.2 and 4.2a.

Visual acuity was 6/9 + 2 for both eyes unaided, and 6/5 - 3 for the right and 6/9 + 4 for the left eye corrected. These values were obtained at first presentation; assessments were repeated during each visit but values were very similar during the other assessments.

Latencies. Latencies in the left eye were increased on all three occasions. On first presentation latencies for the right eye were in the normal range and peaks were clearly identifiable. For the left eye latencies were highly increased and no definite peak could be identified for the 0.9 deg/arc condition. Latencies in the right eye which were initially in the normal range, showed a slight increase during the second assessment but amplitudes were much stronger with clear peaks for the 0.5 and 0.9 degree condition but less so for the 1.8 degree condition. For the left eye it was difficult to find a clear peak for the 0.5 degree condition but the other two conditions showed peaks albeit with reduced amplitudes and increased latencies. Right eye

latencies were lower again at third presentation but left latencies were more or less unchanged. No clear peak could be identified for the 0.5 degree condition and the latency of 118 ms represents a good guess. Latencies for the other two conditions were almost identical at 162 and 167 ms.

Contrast sensitivity. The shape of the sensitivity curves is very similar for the first two assessments with the affected eye showing a clear loss in sensitivity for all spatial frequencies but following by and large the shape of the unaffected eye. During her third assessment the shape of the graph suggested that an observer error might have occurred given the unusual peak reported for the highest spatial frequencies.

Event Perception. Performance on Event Perception Threshold at first presentation was strongly lateralised with the left eye requiring SOAs which were on average three times longer than for the right eye. From her right eye performance of 38 ms and left eye SOAs of 110 ms it may be concluded that binocular performance was affected by the impaired eye averaging at 58 ms. Lateralisation of performance was even stronger on Event Perception Movement with the left eye only detecting 2/32 targets but with a right eye performance (24/32) being almost identical to the detection rate for binocular viewing of 23/32 targets. During the second assessment her right eye detection rate improved to 28/32 but left eye performance increased only marginally to 5/32 with an additional 5 near misses defined as being a response to any of the immediately proximate element to the target. To examine a hypothesis proposed by Regan, Milner & Heron (1976) suggesting that the two different visual channels excited by brightening and by dimming are differentially sensitive to derangement by MS, the patient was presented with a version of the Event Perception programme from

the previous study (cf. chapter 3) with SOAs of 2 secs and with an Appearance condition and a Disappearance condition, each with a maximum number of 16 trials. On binocular testing she reached top score for both appearances and disappearances; when her left eye was tested she detected 15/16 targets in the Disappearance condition and 12/16 in the Appearance condition. The ISI of 2 secs was clearly long enough for her to detect targets but detection rate was indeed lower for appearing targets. However, given the small number of trials it would be wrong to attach much confidence to this finding, although the postulate of differential impairment for differential sensitivity to brightening and to dimming cannot be completely dismissed. Due to a computer storage error all results from the third assessment were lost except for her assessment on Event Perception Threshold for the left eye which showed improvement at 66 ms as compared to her initial values of 110 ms.

PATIENT 2.

This patient was a 39 year old woman who complained of blurring of vision in her right eye. Her results are shown in figure 4.3.

Visual acuity was 6/36 for both eyes unaided, and 6/6 -2 for the right and 6/5 for the left eye corrected.

Latencies. Her latencies for her right eye were somewhat difficult to interpret since peaks did not stand out very clearly and gave rise to three possibilities: the first interpretation would assume latencies between 80 an 92 ms, the second approximately

normal latencies - although peaks were rather unconvincing especially in the 0.9 degree condition - and finally latencies ranging from 137 to 141 ms. However, these last values could also be interpreted as P2s. Latencies and amplitudes were well in the normal range for the left eye except for the 1.8 degree condition were no clear peaks emerged.

Contrast sensitivity. Both eyes were in the normal range for spatial frequencies up to 6 cycles/degree but the right eye took an earlier dip than the left eye suggesting decreased sensitivity for the higher spatial range.

Event Perception. Although SOAs were slightly longer than for controls differences on Event Perception Threshold were within one SD. Differences between binocular (60 ms), left eye (63 ms) and right eye (68 ms) were very small but showed a trend towards right eye impairment. Differences on Event Perception Movement were more clearcut with a binocular detection rate of 23/32, left eye of 20/32 and right eye of 5/32.

PATIENT 3.

This 26 year old male complained of recurrent headaches and blurred distance vision. He also complained about numbness in his hands, legs and stomach. His complaints dated back eight years prior to interview when he was the victim of an assault but with no confirmation of cerebral haematoma or other parenchymal abnormalities. His results are presented in figure 4.4.

Visual acuity was 6/6 for the right and 6/9 for the left eye unaided and corrected.

Latencies. Latencies for the right eye were all within the normal range with clear peaks and strong amplitudes. Latencies were slightly increased for the 1.8 and 0.9 degree conditions for the left eye and considerably longer for the 0.5 degree condition.

Contrast sensitivity. Apart from the 6 cycles/degree condition where the left eye performed slightly worse, performance for both eyes was identical. Neither eye responded to the 22.8 cycles/degree condition.

Event Perception. Binocular performance on Event Perception Threshold was unimpaired and at the top end of age matched control values. Left eye performance was slightly slower at 38 ms and right eye performance was at 50 ms. On Event Perception Movement the binocular score of 19 was rather low as were the right eye score of 17/32 the left eye at 15/32.

PATIENT 4.

This patient was a 37 year old male who complained of blurring and loss of visual acuity and pain in his eyes. He also complained about feelings of exhaustion and memory and concentration problems. He had started working as a spray painter some 5 months before presentation but claimed that his troubles had started during the same month he took up his new job. This case could therefore represent a solvent induced

optic neuritis. The patient denied misusing solvents or a history of alcohol abuse and had in fact discontinued the use of alcohol shortly after onset of his symptoms. There was no history of traumatic brain damage or psychiatric illness. His results are shown in figure 4.5.

Visual acuity was 6/60 for the right and 6/12 for the left eye unaided. Corrected values were 6/24 for the right and 6/12 for the left eye.

Latencies. Latencies in the right eye showed clear peaks and amplitudes but were considerably increased in the left eye with clear peaks for the 1.8 and 0.9 condition but very flat responses for the 0.5 condition.

Contrast sensitivity. Responses were flat over the whole range of spatial frequencies for both eyes and no response was recorded for the 22.8 cycles/degree condition. If these readings are taken to represent reliable measurements the finding of bilateral suppression of contrast sensitivity might enhance the argument of a solvent induced neuropathy.

Event Perception. His binocular score on Event Perception Threshold did not show any evidence of impairment at 38 ms nor did the right eye score of 23 ms. However, the left eye score was slightly increased at 58 ms. His binocular score on Event Perception Movement was somewhat low at 18/32 and 14/32 for right eye presentation. His left eye score was significantly suppressed at 4/32.

PATIENT 5.

This 38 year old patient developed a sensation of pain in the back of his right eye, blurring and clouding of vision some 14 weeks prior to assessment. He lost his sight in the right eye within 7 days of appearance of symptoms. Initially the left eye was also affected but improved spontaneously. He had found some improvement in his right eye over the last 4 weeks prior to examination. His results are shown in figure 4.6.

Visual acuity was 6/6 - 2 for the left eye but could not be assessed for the right eye unaided nor corrected.

Latencies. Latencies in both eyes were increased but more prolonged in the right eye than the left. There were no clear peaks in the right eye response and a peak was completely absent in the 0.5 degree condition.

Contrast sensitivity. No readings could be obtained form the right eye and the left eye showed an abnormal shape for all spatial frequencies except for the 0.5 cycles/degree condition.

Event Perception. His binocular score of 70 ms was in the impaired range but improved somewhat when the left eye was examined alone (53 ms). Examination of the right eye had to be discontinued when the patient still failed to detect targets at SOAs of 3 secs. Event Perception Movement was unimpaired at 26/32 for binocular testing and the patient obtained the same score for left eye examination but could not discern the pattern with his right eye.

4.4 DISCUSSION.

This study showed that the two Event Perception tasks were differentially sensitive to disruption in central nerve conduction. In the case of Event Perception Threshold differences between affected and unaffected eyes were found to be rather subtle and for all but one testable eyes within the normal range compared with control values from chapter 3. However, except for one case SOAs were always higher for the eye showing increased latencies. Event Perception Movement proved to be more easily disrupted and more sensitive to nerve fibre pathology in the patients studied. Except for one patient binocular detection rate was always at least one SD below the control mean. Performance in the affected eye was considerably worse than in the unaffected eye. Binocular presentation seemed to reflect almost entirely performance of the healthy eye as represented in almost identical scores for healthy eye / binocular presentation. In some instances the affected eye seemed to impair binocular performance.

There was a strong relationship between increased latencies and impairment on both Event Perception tasks except for patient 3. His findings were untypical and showed increased latencies only for one condition. His scores were perfectly normal for binocular presentation on Event Perception Threshold and within one SD of the control mean on monocular presentation. His scores on Event Perception Movement were rather low but much more in line with findings for traumatic brain damage described in the next chapter. Since his complaints started following an assault, it is possible that he sustained some brain damage not detected at the time of the injury and that this comprises the source of his difficulties.

Findings for patient 4 were much in line with those for patients with optic neuritis especially with respect to his performance on the sinosoidal gratings and Event Perception Movement. However, the coincidence of his having a job as a spray painter and the onset of his complaints shortly thereafter was more suggestive of a solvent induced neuropathy.

Monocular assessment in all testable patients showed that performance on Event Perception Movement was always at least 3 SDs lower than the control mean. Conversely, apart from one eye, performance on Event Perception Threshold was within the normal range. These differences in performance are taken as providing further evidence that the two procedures involve different processes. Event Perception Threshold, although obviously affected by increased conduction latencies, only showed relatively slight increases in mean SOAs and performance for all but one testable eyes was within the normal range. Although amplitudes were sometimes decreased in the affected eyes, this was far less consistent than the latency changes observed. It appears therefore plausible to suggest that performance on Event Perception Threshold is more affected by variations in conduction latencies. This is in agreement with the model in chapter 1 where it was proposed that the mode of signalling change in this task is dependent upon transient neuronal signals. However, the absence of a clear peak in response to a patterned stimulus from the checkerboard VEPs suggests that the attention mechanism linked to the transient system may have been severely disrupted in some patients for selected spatial frequencies. This would be in agreement with results by Hess & Plant (1983) who found that spatial channels could be differentially impaired. Findings in the current study could be interpret ed along these lines where no or only very vague peaks could be identified for the 0.5

deg/arc condition in the first patient's third assessment and in patients 4 and 5, and for the 0.9 deg/arc condition in the first patient's first assessment. Rather vague peaks were also found in the 1.8 deg/arc condition for patient 1 in her third assessment, and in patients 2, 5 and 6.

Plant (1983) discussed the possibility that the same neural elements might be stimulated by high temporal frequency unpatterned flicker and low spatial frequency gratings, and that these elements might be less susceptible to the effects of demyelination. He assumed "that this may be the case because they are less likely to become demyelinated, or as it seems more likely, demyelination does not impair their function in the same way as other fibres" (pp. 1129-1130). Plant considered the possibility of an interpretation on the basis of the 'X' and 'Y' classification originally proposed by Enroth-Cugell & Robson (1966) in the retinal ganglion cell of the cat. As mentioned in chapter 1, Y cells have larger receptive fields, larger diameter axons and faster axonal conduction velocities than X cells, and exhibit more transient responses to appropriate stimuli. Although Plant expressed his awareness of Lennie's (1980) reservations regarding the functional division of X and Y cells, he continued to speculate that "there is reason to suppose that coarse gratings might predominantly, if not exclusively, activate transient mechanisms" (p. 1130). Spekreijse (1980) has argued that the different temporal frequency components of the flicker evoked potential may reflect activity in the X and Y subsystems independently. Halliday (1981) has proposed a similar argument to explain the differences obtained using uniform-field flash and pattern reversal checkerboard techniques. Clearly, Event Perception Threshold resembles more the flash evoked potential technique than patterned VEPs whereas Event Perception Movement might be seen as resembling more sinosoidal

grating contrast sensitivity assessments. VEPs to unpatterened flash were found to detect abnormalities in optic neuritis and MS patients less frequently than patterned stimulation (Halliday et al., 1972; Richey et al., 1971). Milner, Regan & Heron (1974) found delays in the medium temporal frequency range (13 - 25 Hz) in all their patients but none when high frequency temporal stimulation was used (35 - 60 Hz).

The assumed change in the sustained firing rate signalling short-range apparent movement representing neural events - or target movement - in the Event Perception Movement task is clearly more vulnerable to disruption by demyelinating disease. Since the minimum SOA in this task was 1 sec it appears unlikely that increased latencies could be held responsible for impaired performance as in the case of Event Perception Threshold. Decreased amplitudes or spontaneous firing could account for the failure to perceive small increases in the sustained firing rate as 'change'. Plant's (1983) idea of differential susceptibility to demyelination for X and Y channels provides a further possible explanation in this paradigm. Plant found that delays to pattern onset were greater than to pattern reversal. He thought that pattern onset responses might consist principally of pattern specific mechanisms and that these were conveyed by the X system. He concluded that the reason for longer delays with pattern onset than with pattern reversal stimulation might be because a smaller proportion of the response reflected Y cell activity. When this idea is applied to the current paradigm Event Perception Movement can be taken as a high spatial frequency task which is conveyed by the 'X' system. If the assumption is accepted as being correct that smaller fibres are affected more and earlier than larger fibres by the demyelination process then this would account for the large deficits in optic neuritis patients in this task. Event Perception Threshold on the other hand can be seen as

representing a low frequency task which would consequently be conveyed by the presumably less affected 'Y' system. In addition, the rather weak stimulus produced by the target in the Event Perception Movement task can easily go unnoticed if it falls into a localised or isolated spot of increased latencies as proposed by Regan et al. (1976).

If Rushton's (1975) modified Pulfrich pendulum is taken to represent real movement then the validity of Plant's argument that pattern or X channels might be more impaired than Y or movement channels would depend on the interpretation of what aspects of visual perception checkerboard VEPs measure primarily. In Rushton's study the correlation between the interocular latency difference as measured by the Pulfrich pendulum and the interocular difference as measured by the VEP was not significant at r= -0.032 in MS patients when size and direction of the interocular difference were taken into account. However, when patients were grouped as normal / abnormal on either test a chi square relationship was found to be significant at $p<0.01$ ie. there was a strong correlation between abnormality on the Pulfrich pendulum and on the VEPs for the MS group. If the Pulfrich pendulum does activate motion channels then this would be within the range of short-range movement. The question remains whether the relationship found in Rushton's study arose because the important aspect in checkerboard VEPs is the activation of motion channels created by pattern reversal rather than by the brightness contrast, or because patients were impaired on both aspects of visual perception. DeValois, DeValois & Yund (1979) have demonstrated that whereas visual cortical cells have a narrow response range to gratings of different spatial frequencies, checkerboard stimuli do excite larger populations of cells. This has been taken as evidence that checkerboard stimuli act

predominantly through Y channels. Spatial displacements or periodicity normally used for checkerboard VEPs are far beyond the limits of short-range movement and reciprocal inhibition. Milner, Regan & Heron (1974) in a study of eight cases of optic neuritis found that all patients had abnormal interocular latencies when a check size of 50 min/arc was used but only six were outside the normal range when they used 14 min/arc checks. However, in both instances periodicity was still beyond short-range limits. A reduction in the size of the check pattern with constant periodicity results in an increase in perceived motion and should lead to stronger involvement of transient signals. This might explain why there were fewer patients in the abnormal range if the assumption is correct that patterned VEPs stimulate transient motion channels and if these channels are less vulnerable to disruption. Hennerici, Wenzel & Freund (1977) used foveal small-sized rectangle stimulation to elicit evoked responses which they compared with VEPs elicited by the standard checkerboard pattern. Using foveal stimulation they achieved a significantly better discrimination of optic nerve lesions in the early diagnosis of MS. It would be of interest to record patterned VEPs within a short range of up to 30 min/arc and compare results with detection rates on Event Perception Movement at least for healthy controls.

Conversely, it might be argued that stimuli from sinosoidal gratings are relayed by the X system. In the current study gratings were abnormal in all but patient 3 who showed little abnormality in any of the tests. Hess (1983) found that the contrast perceived by the anomalous eye is a constant ratio below that of normal. This has been confirmed in the current study at least for patient 1 in her first and second assessment, and for patient 2. Hess felt that "the contrast loss in optic neuritis can be thought of as neural blurring because it is quantitatively similar in its effect at any one spatial

frequency to that of optically defocussing the stimulus" (p.1029). This analogy might underline the phenomenological description of some aspects of visual perception in optic neuritis patients and their reports that their vision appears "washed out", "faded", or "blurred".

As an alternative explanation to the X and Y dichotomy, and more in line with Lennie's (1980) arguments, Plant (1983) thought that the smaller axons of cells with smaller receptive fields were more susceptible to demyelination regardless of whether they are X or Y cells since there is a range of fibre diameters and conduction velocities in both classes. This view is strengthened by the Hennerici et al. (1977) study where foveal stimulation achieved better detection of early MS. The fovea is served by a large number of small neurons which might therefore show functional abnormalities as a result of demyelination at a much earlier stage.

4.5 CONCLUSIONS.

The striking differences in performance on Event Perception Threshold and Event Perception Movement in this study provide strong support for the notion that the two Event Perception tasks involve different neuronal processes. Any explanation of the neuronal basis of these differences must remain hypothetical since no direct neurophysiological measures were obtained in response to the Event Perception tasks. However, it appears plausible to assume that appearances of light stimuli in Event Perception Threshold produce transient responses which, although apparently affected by latency variations, are conducted in neurons less affected by demyelination than the weaker signals produced in response to Event Perception Movement which might be conducted by smaller neurons that are more seriously affected by demyelination.

TABLES AND FIGURES

Table 4.1. ***Results for patients with optic neuritis and control data from chapter 3 & 5.***

	Patient 1			Patient 2			Patient 3			Patient 4			Patient 5			Control
EYES	L	R	B	L	R	B	L	R	B	L	R	B	L	R	B	B
Event Perception Treshold (ms)	110	38	58	63	68	60	38	50	25	58	23	38	53	(>3000)	70	46 (26)
Event Perception Movement (max=32)	2	24	23	20	5	23	15	17	19	4	14	18	26	- -	26	29.1 (3.6)
P100 Latencies																
0.5	164	108		102	92/141		123	99		147	109		122	?		
0.9 deg/arc	?	107		104	83/137		104	98		148	103		117	137		
1.8	147	117		101	80/140		107	101		131	105		125	135		
P100 Amplitudes																
0.5	1.4	3.4		3.2	1.6		4.0	4.4		1.4	2.2		1.8	?		
0.9 deg/arc	?	2.4		3.4	1.8		5.4	5.4		3.6	3.6		1.6	0.8		
1.8	3.6	3.4		1.2	2.4		4.2	5.0		3.0	3.6		2.0	0.6		

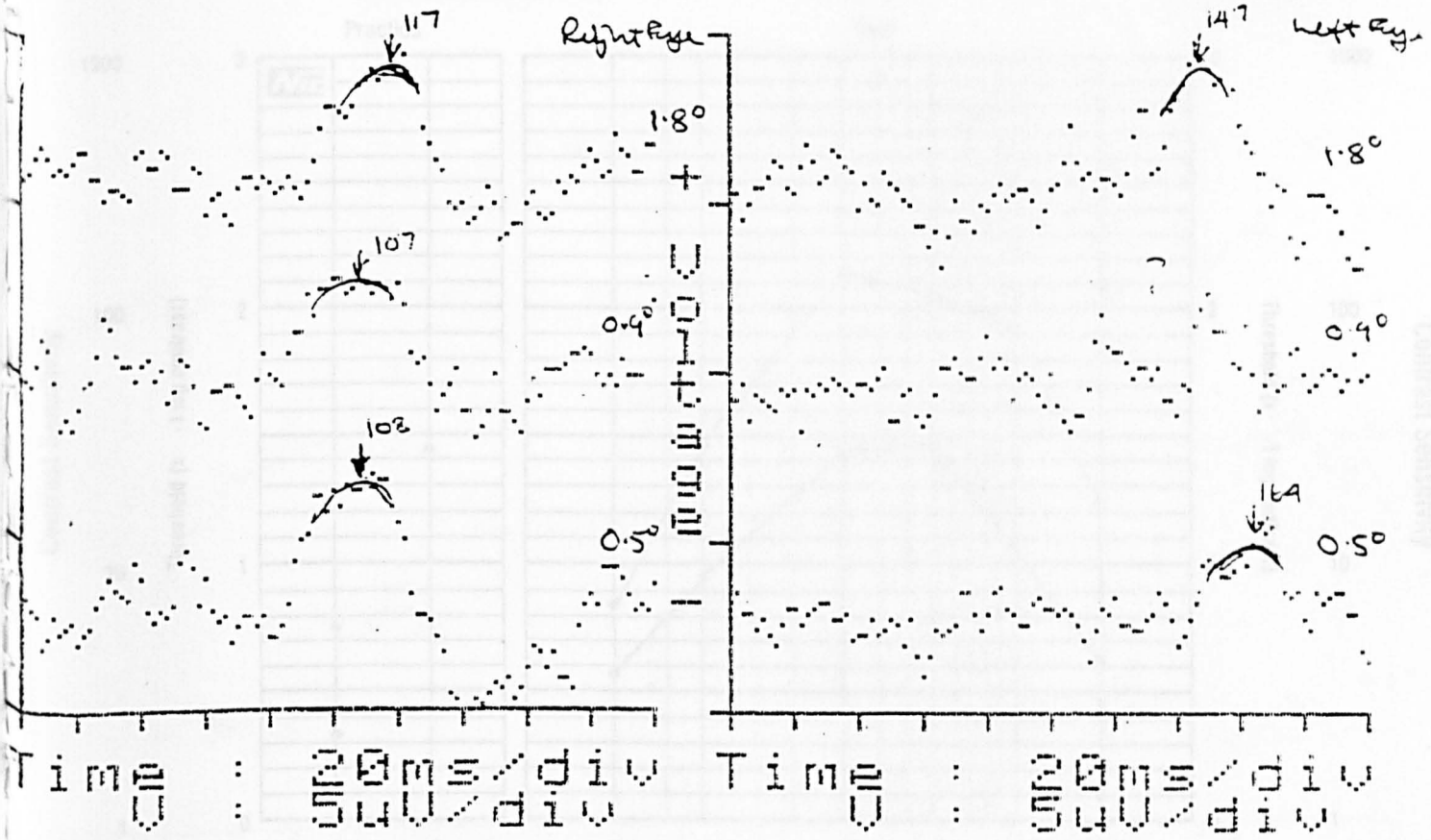
Threshold and Latencies are in ms; amplitudes are in uV; EP Movement scores are correct out of 32.
L= LEFT R= RIGHT B= BINOCULAR ? = no clear peak identifiable

Table 4.2. Results for Patient 1.

Assessment	1			2			3		
EYES	L	B	R	L	B	R	L	B	R
EP THRESHOLD ms	110	58	38	-	-	-	66	-	-
EP MOVEMENT (max=32)	2	23	24	5	-	28	-	-	-
LATENCIES									
0.5	164		108	147		114	118		116
0.9 deg/arc	?		107	162		116	167		103
1.8	147		117	161		120	162		110
AMPLITUDES									
0.5	1.4		3.4	1.6		5.0	0.7		3.6
0.9 deg/arc	?		2.4	2.7		3.4	1.1		1.6
1.8	3.6		3.4	3.6		3.2	2.0		2.3

Threshold and Latencies are in ms; amplitudes are in uV;
EP Movement scores are correct out of 32;
L= LEFT R= RIGHT B= BINOCULAR ? = no clear peak identifiable

Figure 4.1. Visual Evoked Potentials for Patient 1.



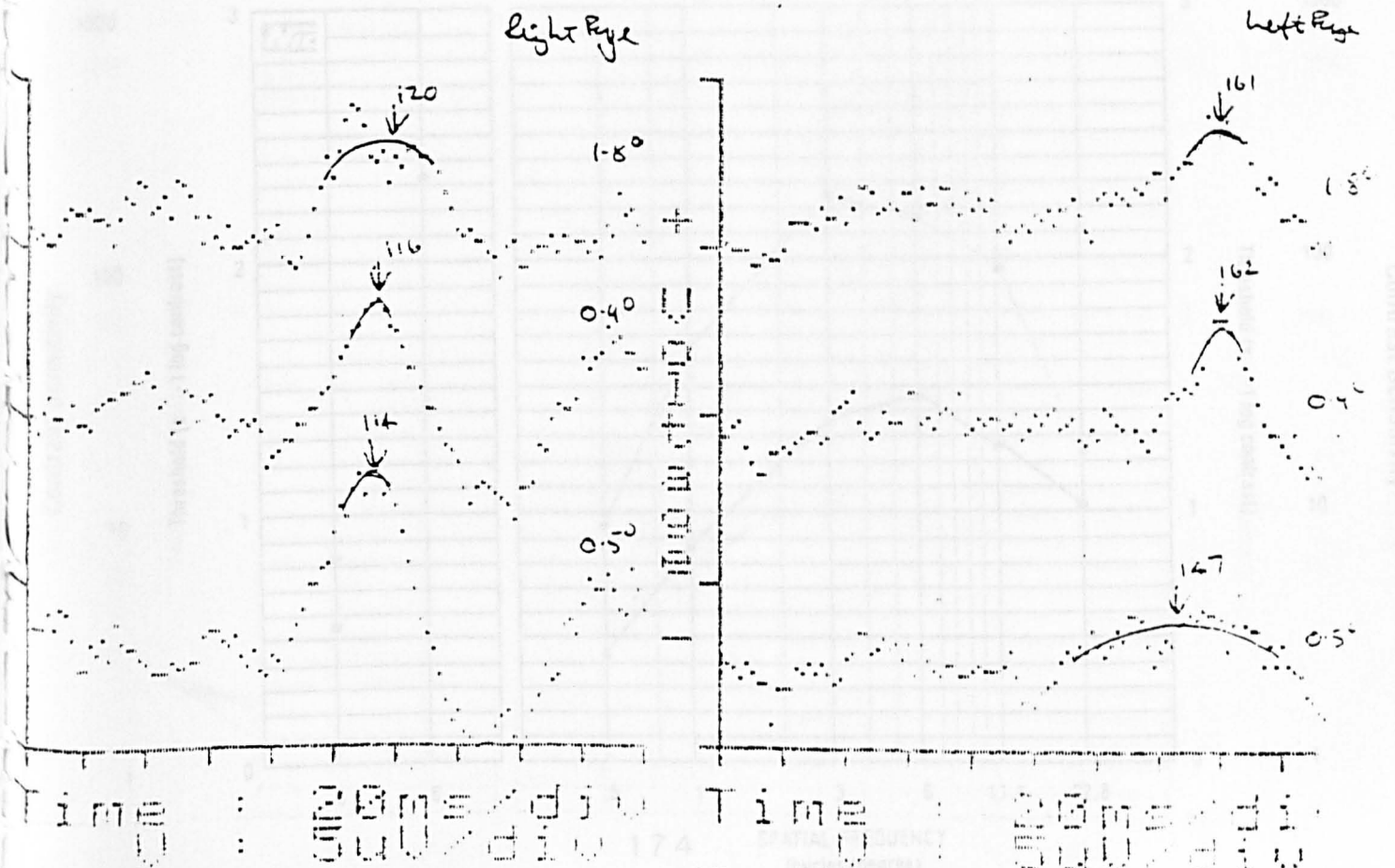
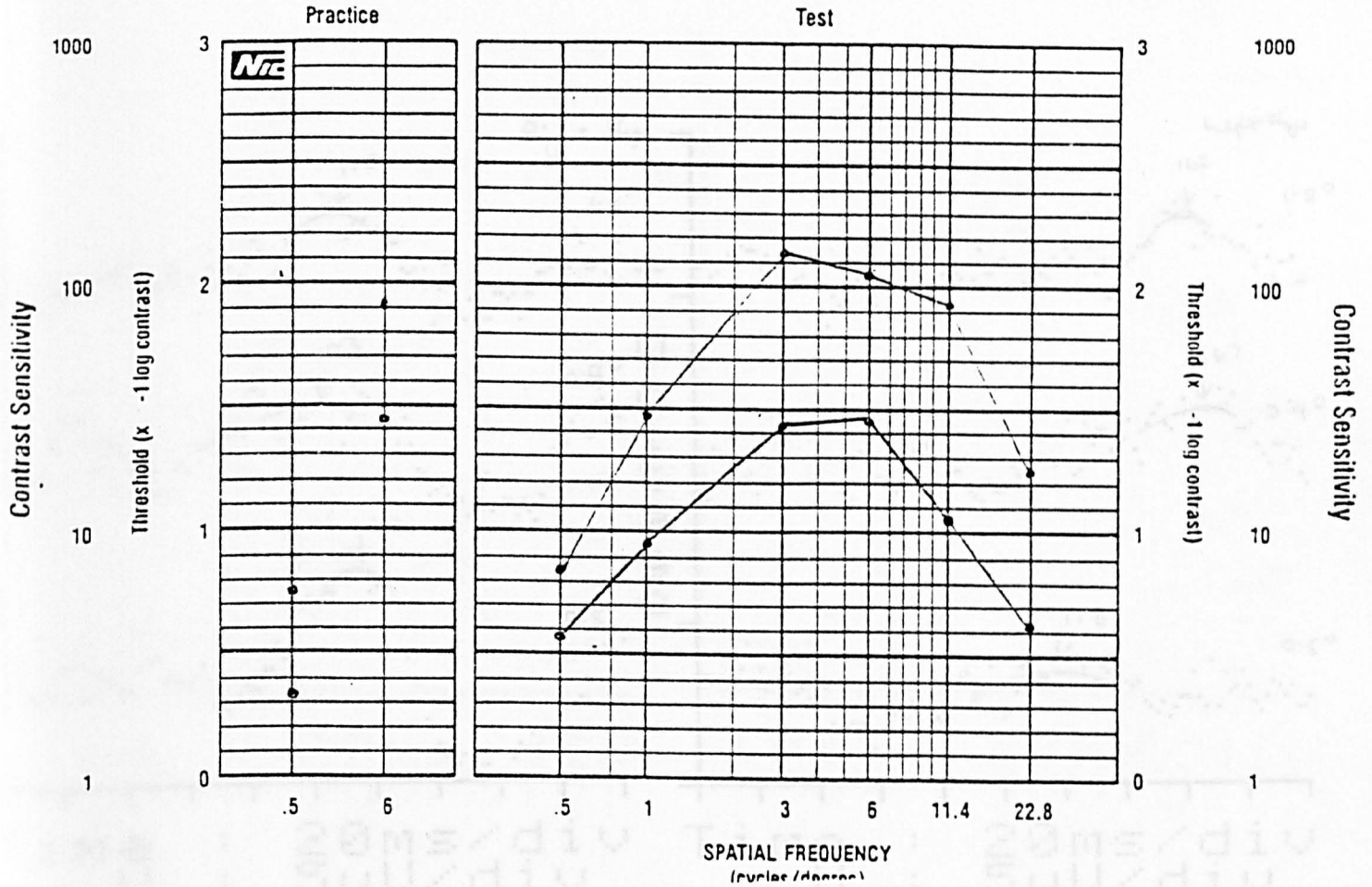


Figure 4.2. Contrast Sensitivity Assessments for Patient 1.



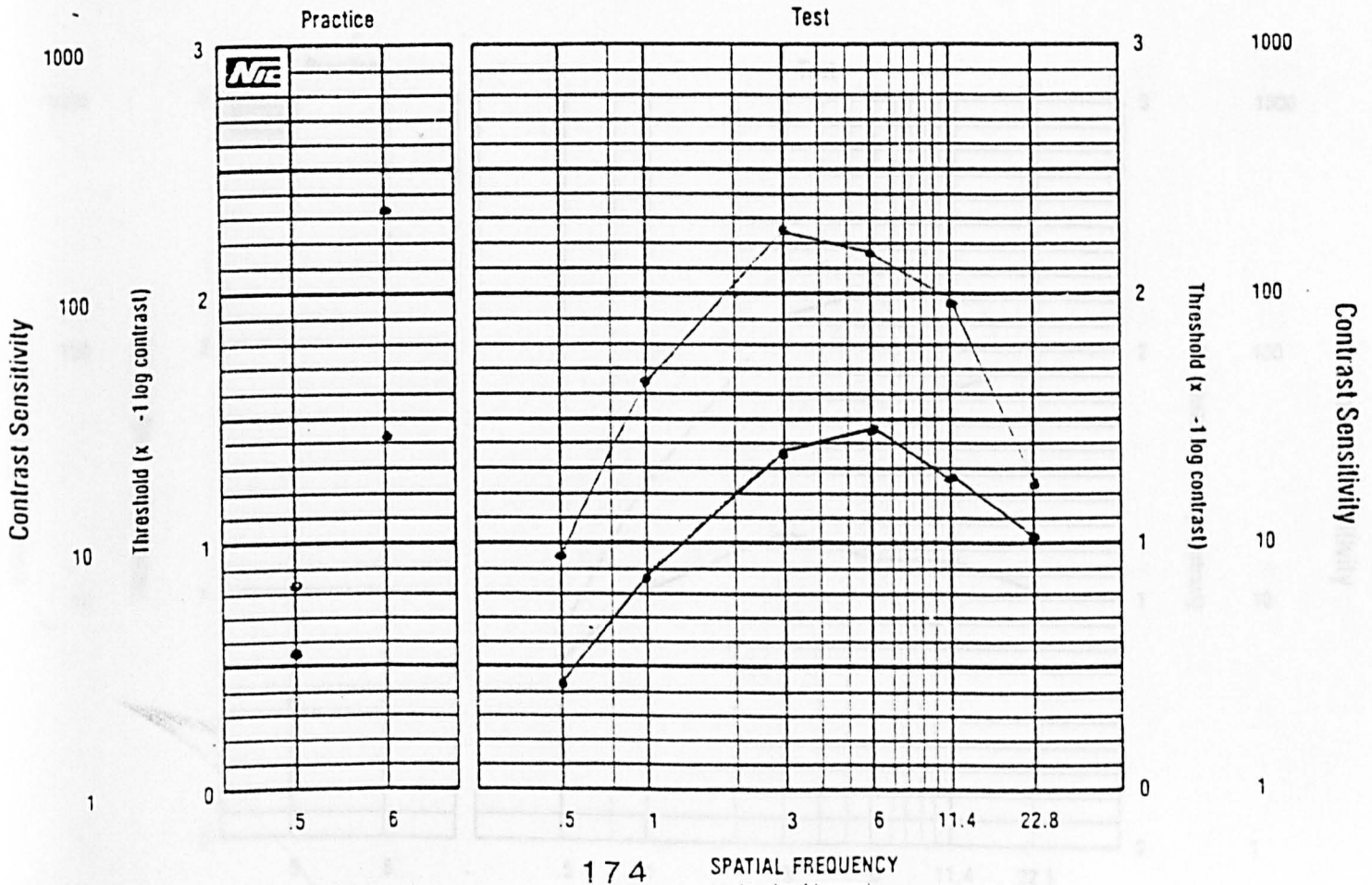
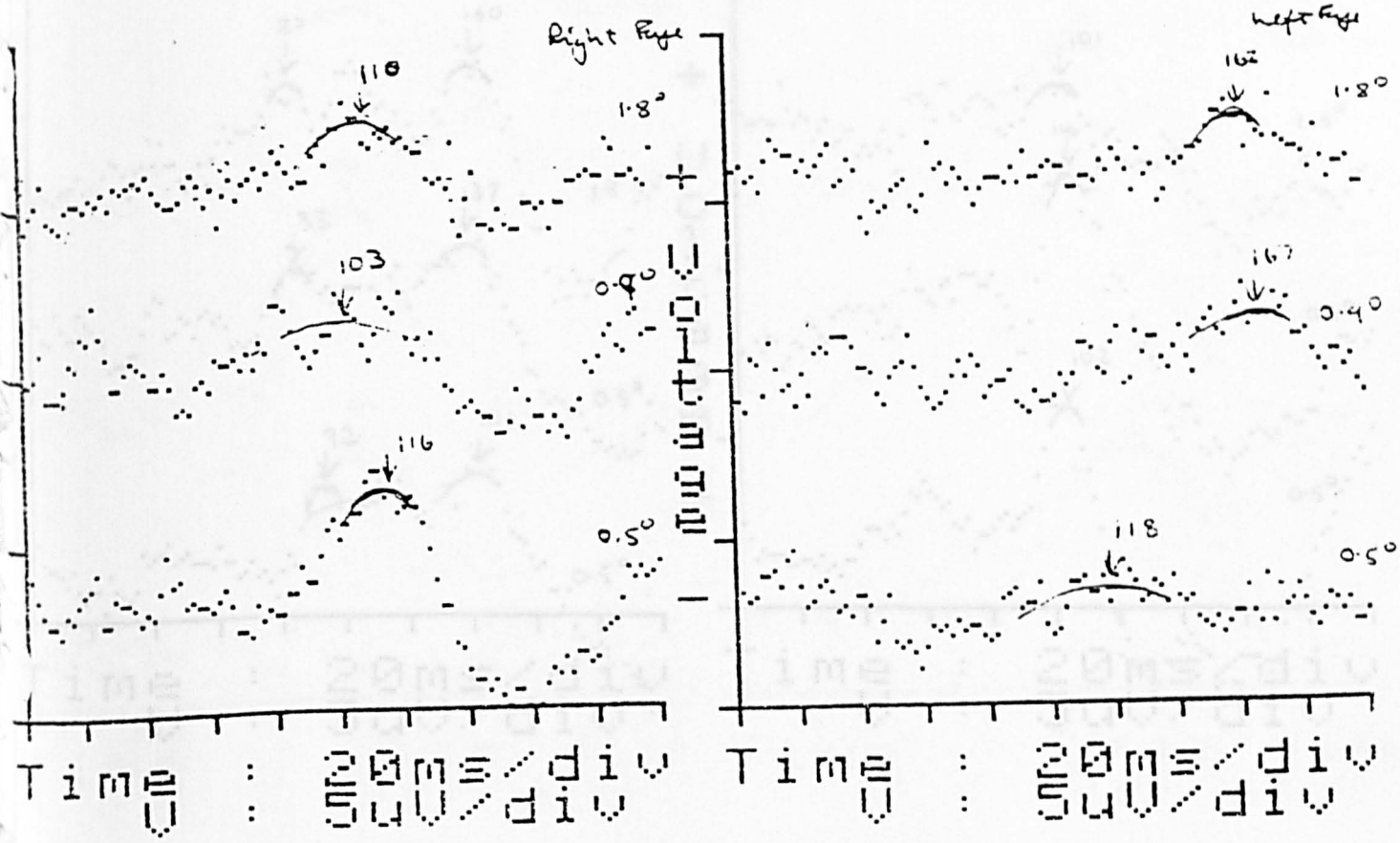


Figure 4.2.a Visual Evoked Potentials and Contrast Sensitivity Assessments for Patient 1: Third visit.



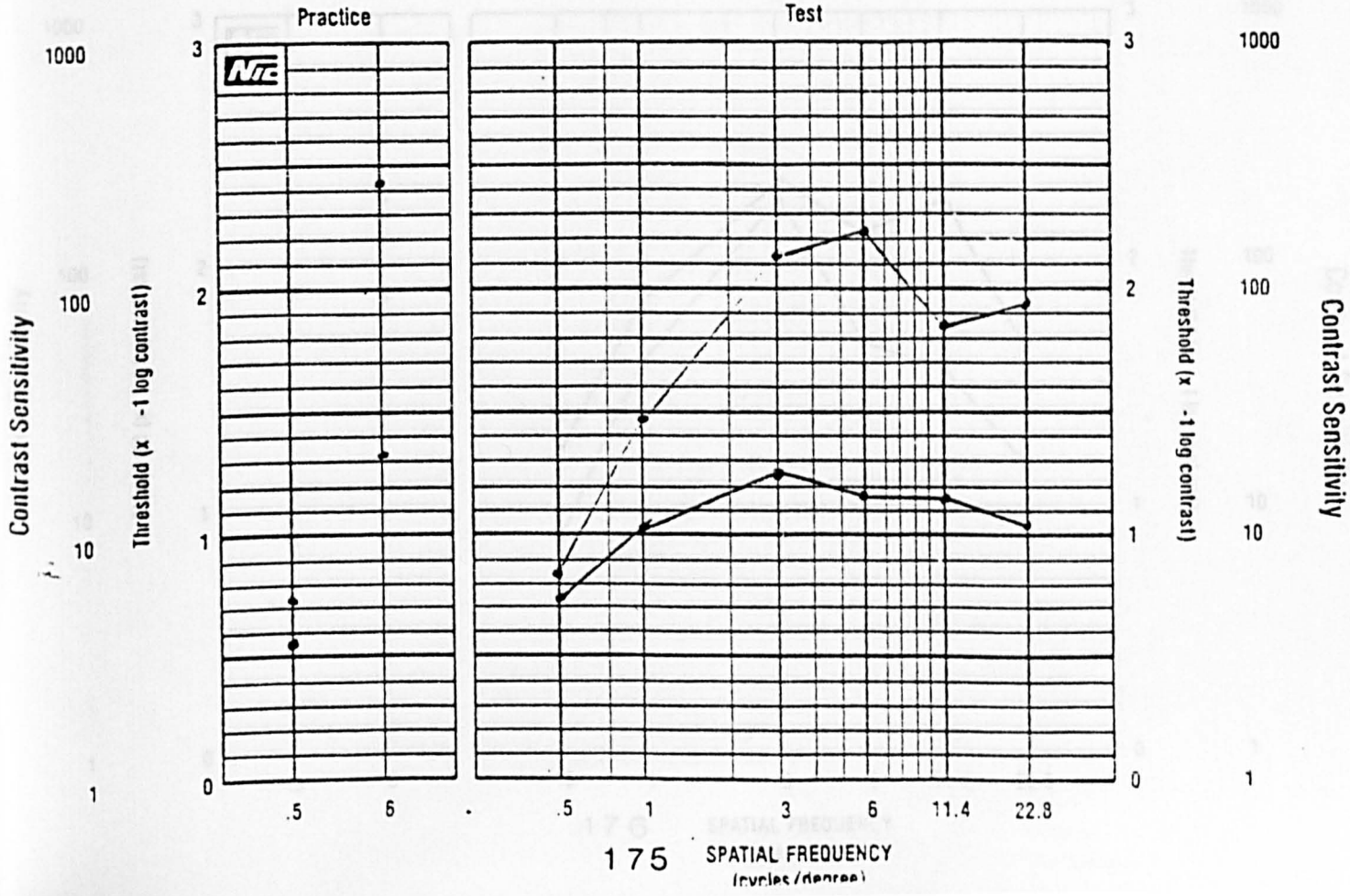
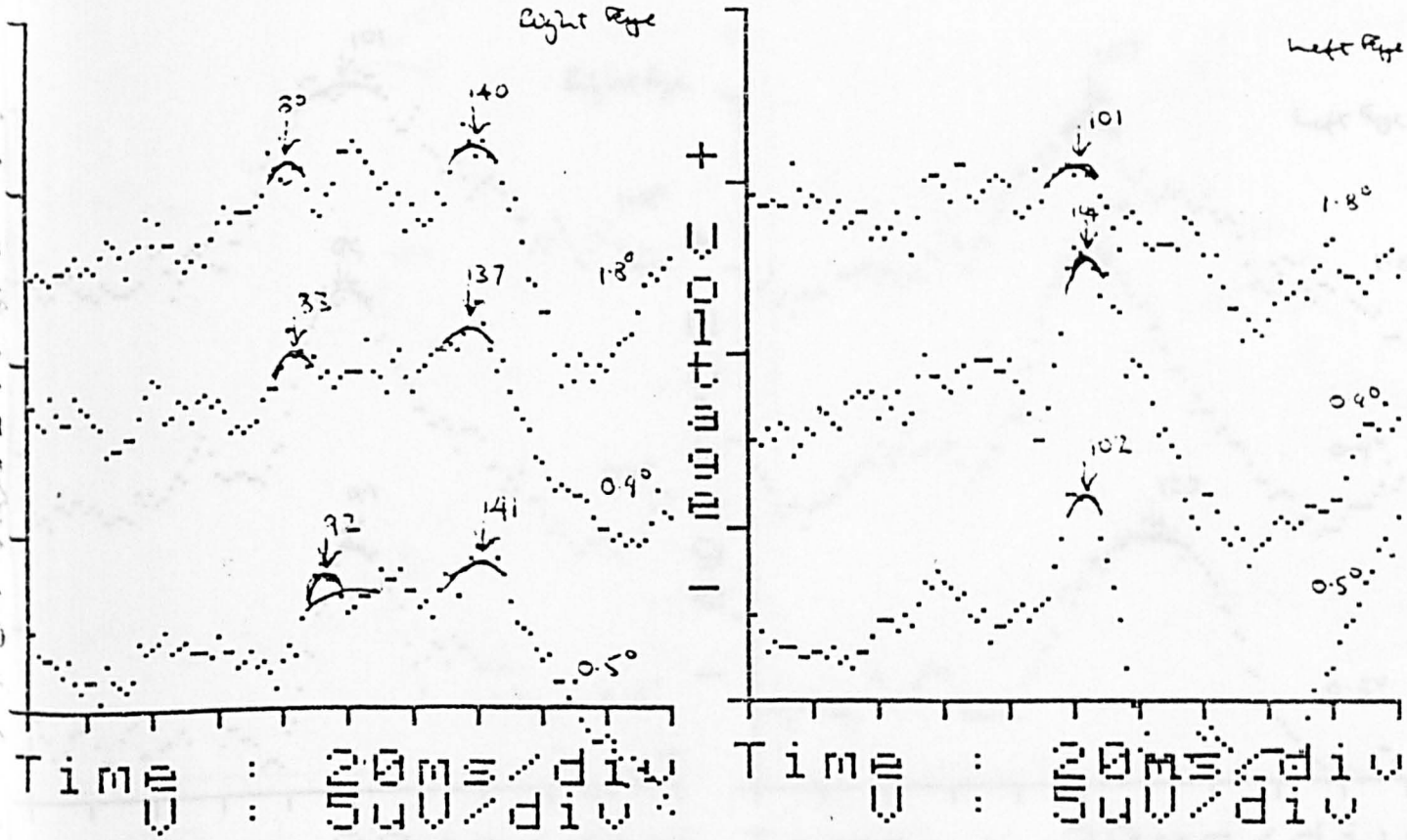


Figure 4.3. Visual Evoked Potentials and Contrast Sensitivity Assessments for Patient 2.



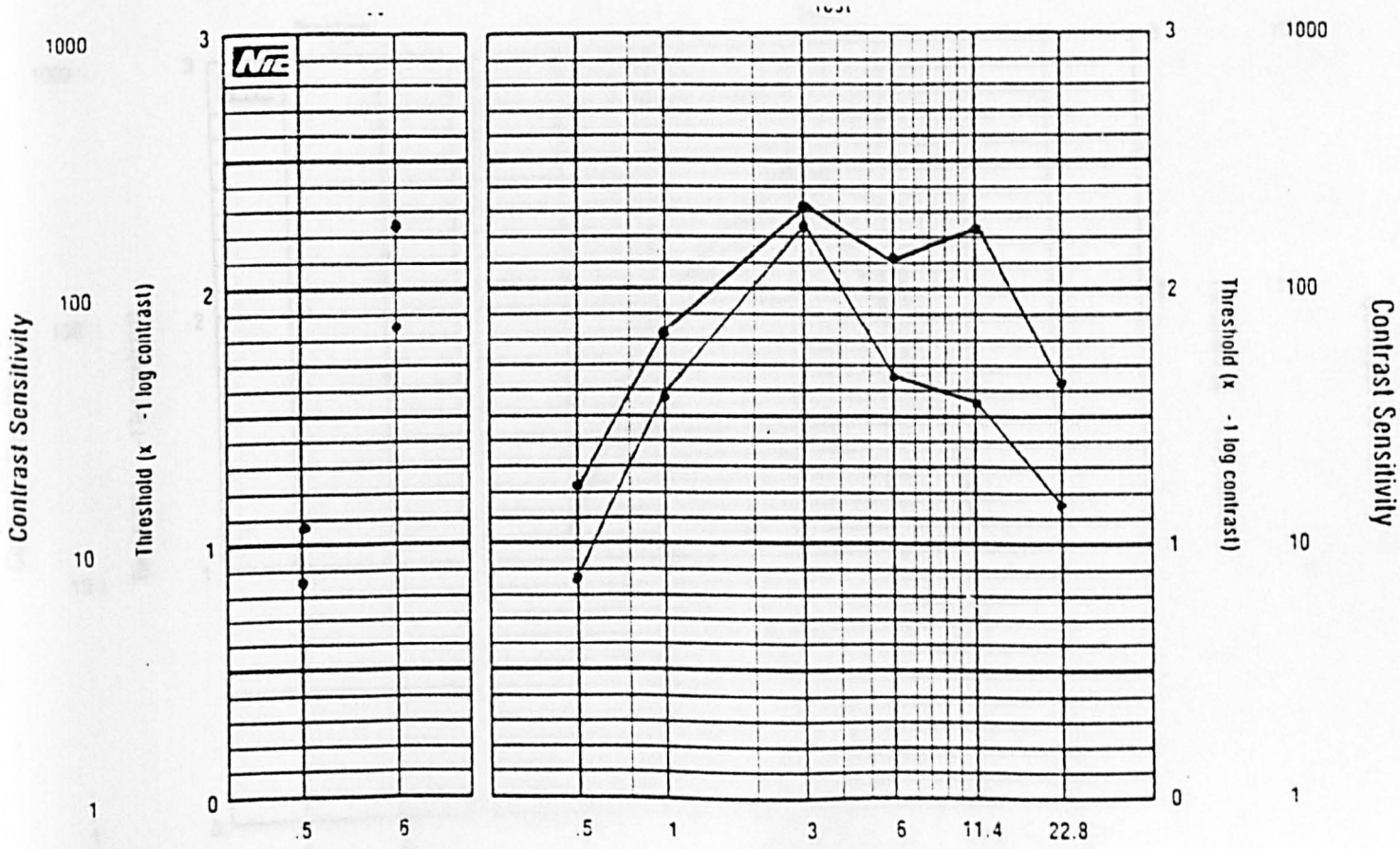
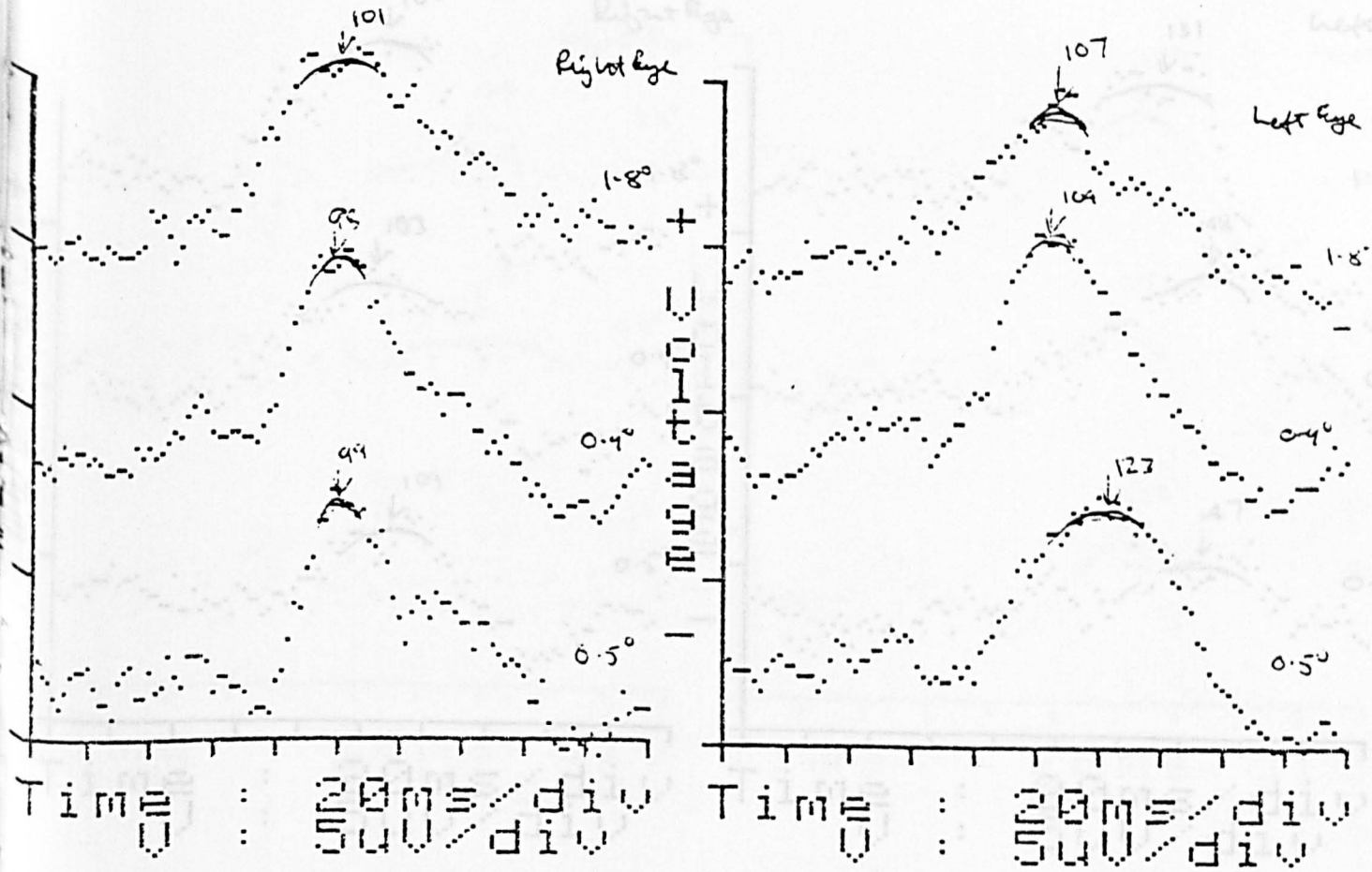


Figure 4.4. Visual Evoked Potentials and Contrast Sensitivity Assessments for Patient 3.



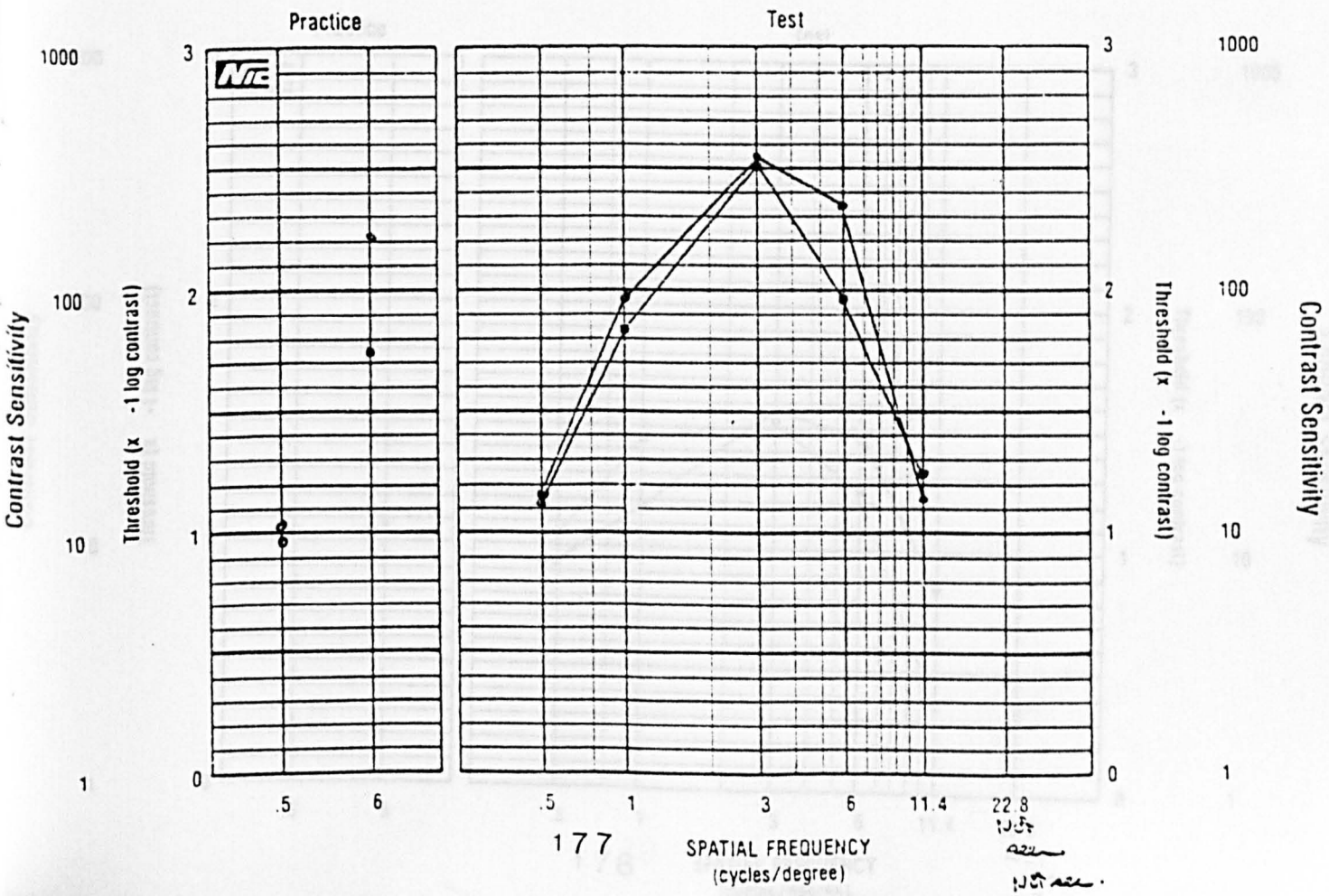
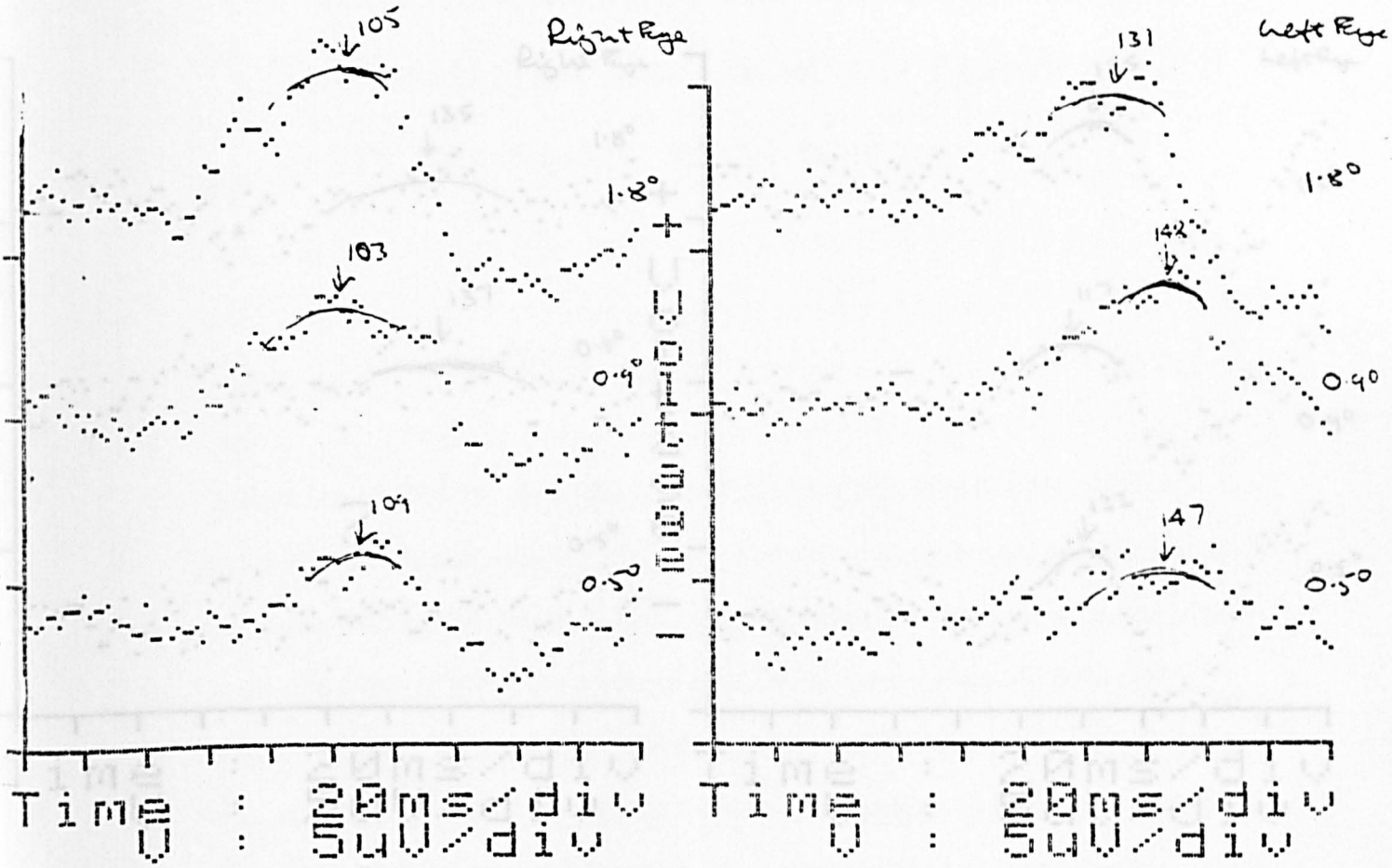


Figure 4.5. Visual Evoked Potentials and Contrast Sensitivity Assessments for Patient 4.



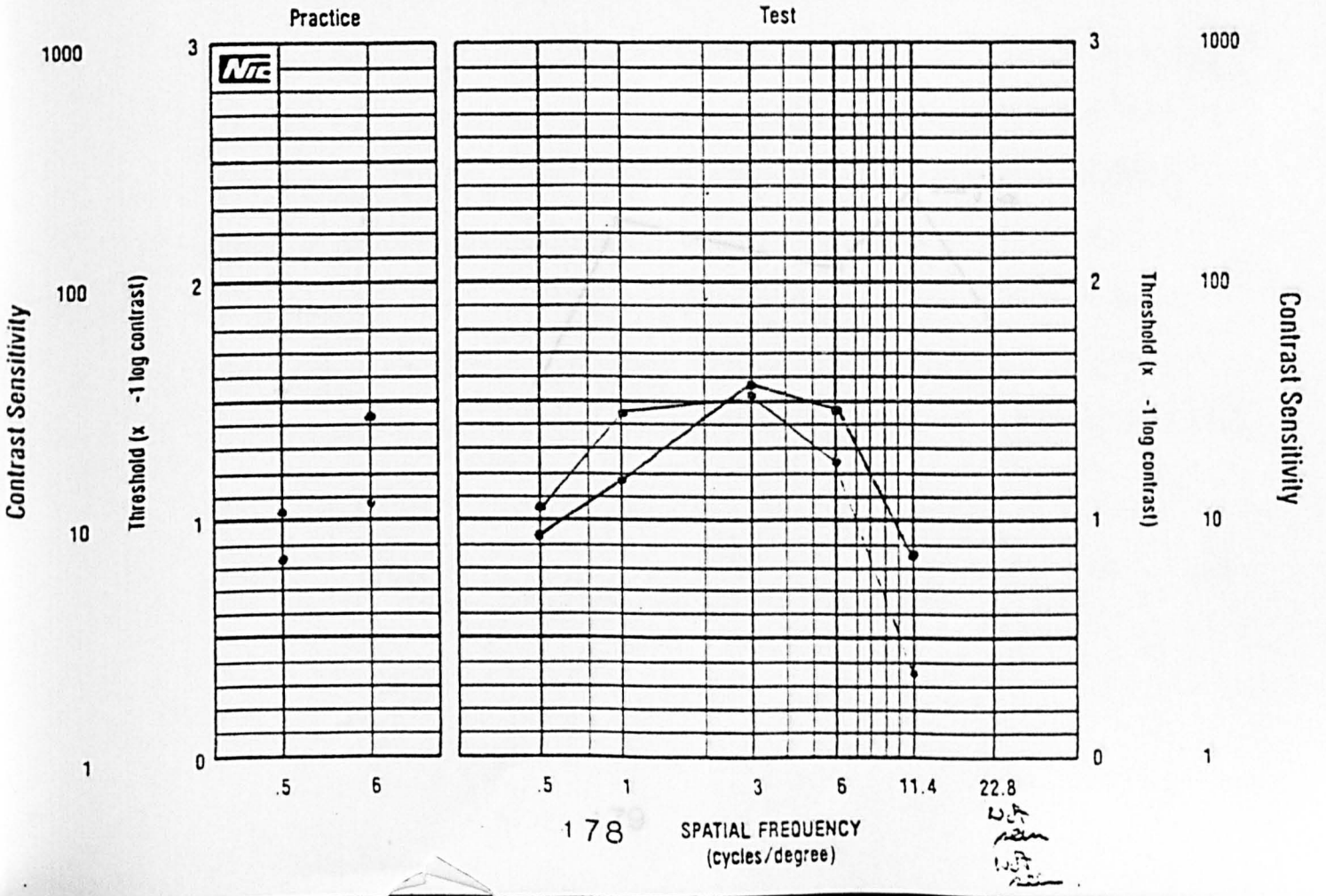
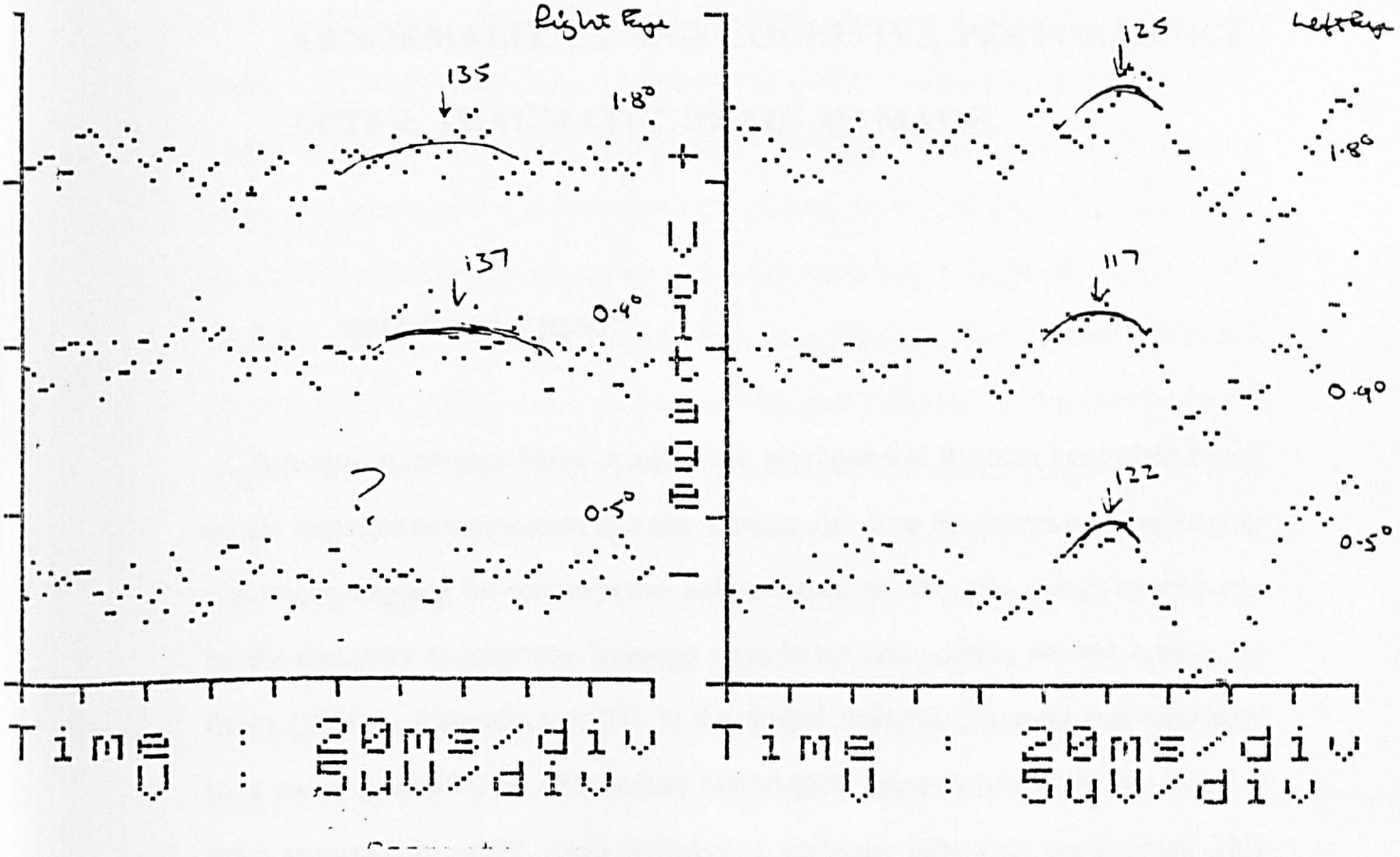
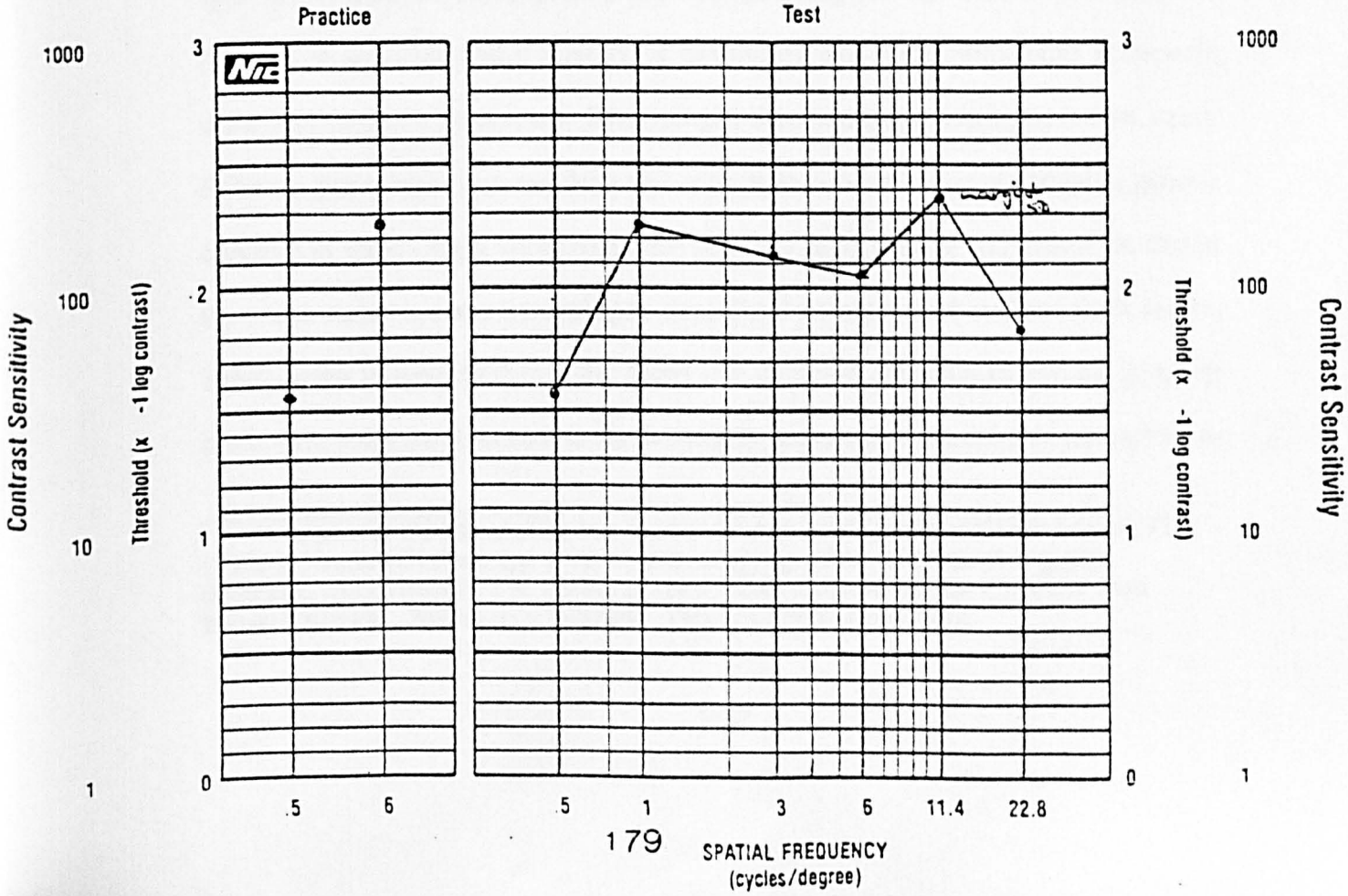


Figure 4.6. Visual Evoked Potentials and Contrast Sensitivity Assessments for Patient 5.





5.0 RELATIONSHIPS BETWEEN STRUCTURAL ABNORMALITIES AND COGNITIVE PERFORMANCE AFTER TRAUMATIC BRAIN DAMAGE.

5.1 INTRODUCTION.[1]

Attempts to correlate brain structure and psychological function have often rested on the implausible assumption that the ultimate aim is to demonstrate an underlying one-to-one mapping between structure and performance. This idea was given credence by the discovery of particular language areas in the brain during the last century by Broca (1861) and Wernicke (1874). In the clinical field this discovery was reinforced by a growing tradition of 19th century neurological research to specifically look for brain abnormalities which could be linked to particular behavioral peculiarities. This approach reached an initial peak in the so-called diagram makers who promoted the fashion of superimposing models of psychological functioning onto schematic drawings of brain structures. Surprisingly this paradigm has survived in many different guises right into our days and appears to continue to haunt people's general concepts of mind - brain interactions. Experiments using cortical stimulation, at first in the motor cortex but later extending to areas like the temporal lobes (Penfield & Jasper, 1954), seem to have furthered the belief that complete mapping of cortical function could eventually be achieved. In the laboratory experiments on animals attempting to

[1] A version of the introduction has been published in: Wiedmann KD & Wilson JTL. (1989). **Neuropsychology and neuroimaging after traumatic brain damage.** In: Crawford J & Parker D (eds.). **Developments in Clinical and Experimental Neuropsychology.** Plenum Press: New York.

map motor functions to particular cortical areas seemed to provide further evidence that the brain is highly modular and each structure appeared to subserve a unique and highly specific function. The paradigm was generalised to attempt mapping of higher cognitive functions such as memory and problem solving and more complex behaviour such as social interaction. However, as far back as 1917 Leyton & Sherrington introduced a note of caution by expressing their skepticism towards this particular method of topological exploration and noted that repeated stimulation of a particular area did not invariably produce the same response. Although it might be argued that their techniques were lacking methodological sophistication, the application of advanced neuroimaging techniques appears to confirm their claim to some extent. Ojeman (1990) using cerebral blood flow technology has shown that brain centres associated with cognitive activity may be highly variable in location between subjects. Earlier, Lashley's statement of the law of mass action although now largely discredited introduced a considerable level of doubt about early attempts at brain mapping (Lashley, 1950). There are two fundamental questions which should be distinguished when attempts are made to establish structure-function relationships:

1) What is the functional significance of particular structural changes?
2) What types of brain abnormalities are associated with particular functional deficits?

These two questions will serve as a guide in this chapter and will be examined for the main part on research in head injury. Answers to these questions provide a particular challenge because of the often diffuse or multifocal nature of brain damage and the complexity of its functional consequences.

5.1.1 Pathology of head injury.

The effects of traumatic brain injury are highly variable but are increasingly well characterised. A variety of different kinds of damage may be sustained, and because of this variability they give rise to a number of areas in which the relationship between structural brain damage and functional deficits can be investigated. Much of our knowledge of the processes involved in severe traumatic brain damage has been derived from neuropathological studies. However, there has been considerable doubt as to whether these findings are generalisable to survivors of head injury; furthermore pathological studies - by the nature of the subject - reveal little about the processes involved during the recovery period.

Blunt head injury results primarily in contusions through contact of the brain with the skull and diffuse axonal injury through shearing forces (Adams, Mitchell, Graham & Doyle, 1977; Adams, Scott, Parker, Graham & Doyle, 1980; Adams, Graham, Murray & Scott, 1982), and secondarily in hypoxic - ischaemic damage (Graham, Adams & Doyle, 1978). With conventional neuropathological methods only larger contusions are detected, and the clinical importance of minor contusions is often played down, despite the fact that they may relate quite closely to psychological deficits. The most common sites of direct impact damage have been found to be the temporal lobes, particularly the lateral and inferior surface, and the orbito-frontal cortex (Adams et al. 1980). Diffuse axonal injury is well recognised at post mortem, and is considered to be the most significant type of primary damage (Adams et al. 1977).

5.1.2 Neuropsychology of head injury.

Studies attempting to relate neuropsychological function to neuroimaging findings have often used measures of psychological outcome. In some studies assessment of outcome after head injury is restricted to physical or neurological indices and the most frequently used categorisation, the Glasgow Outcome Scale, is based on criteria put forward by Jennett and Bond (1975). The scale is limited to four outcome categories: Dead or permanently vegetative, severe disability, moderate disability and good recovery, and therefore provides, even in its extended format (Jennet, Snoek, Bond & Brooks, 1981), insufficient information about the quality of life after head injury and residual cognitive and behavioural deficits. Neuropsychological research has mainly concentrated on patients in the categories moderate disability and good recovery in whom neuropsychological assessment and rehabilitation may be possible. Nevertheless, many patients categorised as 'good recovery' are frequently found to suffer from substantial cognitive, behavioural and social sequelae (Brooks 1984).

In some studies localisation of function appears to be the primary aim. One of the underlying problems, however, when this is attempted, is that there are few if any neuropsychological test procedures which allow for precise inferences about the localisation of specific functions. Traditionally, theories of neuropsychological function have been based on assumptions which in the light of more recent neuroimaging techniques have become largely untenable: One particular source were patients with gunshot wounds (Newcombe, 1969) or other penetrating head injuries (Teuber, Battersby & Bender, 1960) but it was rarely known how deep into the brain an object had actually penetrated. Thus precise knowledge about the actual brain

structures destroyed was rather limited. Another even less accurate attempt was to use site of impact as a means of localisation. Although it was soon discovered by the means of neuropathological investigation that this approach was unsatisfactory its popularity continued into the mid seventies when neuroimaging became more widely available. The dangers and pitfalls of this particular approach will be discussed in more detail later.

McFie (1975) suggested that performance on individual subtests of the Wechsler Adult Intelligence Scales (WAIS) may depend upon the functional integrity and specific involvement of individual cerebral lobes. He proposed a scheme to aid localisation of brain damage by linking impaired performance on specific subtests to particular brain areas which were assumed responsible for that function. However, many studies concentrating on the cognitive effects of head injury have reported generalised overall impairment in performance and slowing of information processing (Mandleberg & Brooks 1975; Brooks & Aughton 1979; Brooks, Aughton, Bond, Jones & Rizvi, 1980). In many reports head injury patients were found to perform worse on timed tasks whereas performance on untimed and verbal tasks were more frequently preserved. Van Zomeren & Deelman (1978) reported a study of 57 young male head injury patients who were followed up over a period of two years. They found that choice reaction times discriminated better than simple reaction times between subgroups and revealed a highly significant improvement during follow-up. This was shown to be independent of a mere training effect. Levin, Grossman, Rose & Teasdale (1979) assessed 27 long-term survivors of head injury neuropsychologically and found that all severely and some moderately disabled patients exhibited unequivocal cognitive and emotional sequelae even three years after

injury. McKinlay, Brooks, Bond, Martinage & Marsall (1981) interviewed a close relative of 55 head injury patients at 3, 6 and 12 months post injury and found that the most frequently reported residual disorders were emotional disturbances, poor memory and subjective symptoms. Dikmen, Reitan & Temkin (1983) studied 27 patients over a 18 months period during which patients were assessed three times. They found that higher level cognitive functions like reasoning, concept attainment and flexibility of thought processes were more vulnerable than lower level functions like finger tapping and grip strength, and that higher level functions proved more resistent to recovery. Encouraging findings were that improvement appeared to continue for complex as well as simple tasks over a much longer period than previously accepted. In a similar study Tabaddor, Mattis & Zazula (1984) examined the course of recovery in 68 patients with severe or moderate head injury and observed improvement for all cognitive functions assessed over a one year period. The authors showed that all patients had sustained significant mental impairment after severe to moderate injury but found that in spite of significant improvement patients continued to show marked impairment in cognitive functions. Williams, Gomes, Drudge & Kessler (1984) used multiple regression statistics to identify the most powerful predictors of outcome in their sample of 96 patients. Best predictors for post-injury IQ were coma grade and premorbid IQ, and coma grade, mass lesion, and skull fracture for the Halstead Impairment Index.

Summarising, it appears that deficits traditionally associated with focal or unilateral brain damage resulting from head injury are by far less common than generalised cognitive and emotional problems. Attempts to localise neuropsychological function may therefore be misguided and methods used to study focal brain lesions may prove

inappropriate for the study of traumatic brain injury. Newcombe (1982) advocated "a different approach and new techniques" (p.112) for the study of traumatic brain damage. A more differentiated approach to categorisation and intervention remains to be achieved.

5.1.3 Neuroimaging in head injury.

The term neuroimaging refers to a number of radiological investigation techniques concerned with the pathology of the nervous system, predominantly the brain and the spinal chord. Early attempts at neuroimaging including arteriography and pneumoencephalography are now largely discredited for their unreliability and potential (and proven) health risks. Angiograms have also become less common in the diagnosis of head injury and are mostly restricted to investigations of vascular abnormalities and to serve as a map in guiding surgery.

Computed (Axial) Tomography (CT) is the prevailing investigation technique in head injury but also for many other neurological conditions. The technique has undergone dramatic improvements since its introduction for clinical use in the early 1970's (cf. Ambrose 1973; New, Scott & Schnur, 1974), including an impressive enhancement in spatial resolution and a significant reduction in the amount of radiation exposure thus reducing the health risk involved. However, limitations remain with respect to resolution and the choice of angles for sectioning. These factors as well as problems with bone artifacts restrict its usefulness to both clinical diagnosis and to research, and there is a residual health risk arising from ionising radiation which sets limits to repeatability.

Problems with angle sectioning, ionising radiation and to some extent with resolution have been overcome with the introduction of Magnetic Resonance Imaging (MRI). Although nuclear magnetic resonance technology has been used in physics for decades its clinical application only started in the early seventies. In its medical application it is based predominantly on the magnetic properties of hydrogen atoms which are found in abundance in the human body. In simplistic terms MRI measures the distribution of water in the body. There are almost no restrictions to slice positioning, thus allowing for transverse, saggital and coronal sectioning at any desired angle, and slice thickness in high-field imagers can be less than 1mm with the additional advantage of real-time imaging. This has resulted in an enormous increase in information available to both the clinician and the research worker. Further advantages are a high level of gray-white matter contrast, lack of bone artifact, an abundance of imaging sequences, increased sensitivity to pathological change, and the absence of known health risks. More recent applications have progressed from mere structural imaging to employing the technology to functional aspects such as blood flow and energy consumption by focusing on phosphor rather than hydrogen molecules. Major drawbacks of MRI are seen in the relatively high purchasing costs and the potential hazards associated with working in a strong magnetic field, particularly with respect to imaging acutely ill patients.

The progress in neuroimaging over the last two decades with Computed Tomography and Magnetic Resonance Imaging providing dramatically enhanced resolution, has revolutionised our ability to study the brain in vivo. In addition to accurately locating abnormalities in the brain, neuroimaging can supply us with information about the nature of the damage (haematoma, contusion, oedema, brain

swelling), about the extent or size of lesions and the number of abnormalities. These categories can be divided further for example into extracerebral and intracerebral haematoma, haemorrhagic vs non-haemorrhagic contusions etc. Furthermore, CT and MRI can provide more accurate information about ventricular enlargement and cortical atrophy which are common late complications after head injury than previous techniques (cf. Meyers, Levin, Eisenberg & Guinto, 1983). However, studies of ventricular enlargement based on CT have been criticised for suffering from a considerable error rate, even when ventricular- brain ratios (VBRs) are determined by digitized computer aided analysis. Wyper, Pickard & Matheson (1979) have estimated that assessing ventricular enlargement with conventional methods gives an error rate as high as 20% to 30%. More recently Condon, Patterson, Wyper, Hadley, Grant Teasdale & Rowan (1986) have devised a technique employing specific MR sequences to determine cerebrospinal fluid (CSF) volume which allows assessment of ventricular size to a much higher degree of accuracy. This technique has been successfully employed in a study by Grant, Condon, Lawrence, Hadley, Patterson, Bone & Teasdale (1988) in determining fluctuations in CSF during the menstrual cycle in females. The potential importance to head injury research is obvious since interactions between CSF and intracranial pressure (ICP) play an important role in the management of acute head injuries and are often responsible for secondary lesions. Precise assessment of ventricular enlargement as a late sequel is of particular interest as a measure of diffuse brain damage and has been found to correlate with impaired psychological performance (cf. Levin, Meyers, Grossman & Sarwar, 1981).

5.1.3.1 Studies based on Computed Tomography.

This section contains a review of the literature of attempts to combine neuroimaging information with physiological, neurological and neuropsychological findings.

Within a few years of its introduction Computed Tomography had become the standard method of investigation in head injury. In a famous and now considered classic account by French and Dublin (1977) 316 out of 1000 consecutive admissions for head injury had undergone CT investigations. Fifty-one percent of the 316 patients showed brain abnormalities and some relationship with neurological findings was demonstrated. 103 patients had further CT investigations and in 52 of those patients new lesions or deterioration in known lesions were observed. Zimmerman, Bilaniuk, Gennarelli, Bruce, Dolinskas & Uzzell (1978) examined 286 head injury patients on CT and found abnormalities in 58%. The authors concluded that CT could lead to prompt and more efficient treatment and that its use resulted in a significant improvement in mortality rate and in a decrease in the use of arteriography, skull radiography and surgical intervention. Sweet, Miller, Lipper, Kishore & Becker (1978) studied 140 severe head injury cases of whom only 26 had normal scans. The aim of their study was to investigate whether CT information concerning the presence of lesions in the entire brain rather than only the most affected part could be correlated with neurological status and whether this would be of value in predicting outcome. The authors observed that patients with bilateral lesions had increased ICP and poorer outcome than those who only showed slight, homogeneous decrease in density of the brain. Cooper, Maravilla, Moody & Clark (1979) reported findings from serial CT

scans in 58 patients with severe head injury. Over half of their patients developed new lesions within seven days of the initial scan. There was a high correlation between absence of new lesions and good outcome and vice versa. The authors stressed the value of serial CT scans in increasing the confidence and accuracy of prognosis in severely head injured patients. Roberson, Kishore, Miller, Lipper & Becker (1979) presented a more moderate view stating that they found serial scanning only to be necessary under complicating circumstances. However, they suggested an obligatory follow up scan at three months and acknowledged the value of serial scans for research purposes in post traumatic hydrocephalus, delayed intracerebral haematomas, and intraventricular haemhorrage.Van Dongen and Braakman (1980) reported CT results for 97 survivors in a sample of 225 cases with severe head injury. Findings which included infratentorial and focal and diffuse supratentorial atrophy were correlated with overall social outcome, persistent neurological deficit, operations and prognostic features. The authors suggested a comprehensive model for the classification of cortical atrophy/ventricular enlargement following head injury. Holliday, Kelly and Ball (1982) reviewed the effects of increased ICP in relation to CT scans in 160 patients. They concluded that normal CT in patients with closed head injury and pulmonary injury does not preclude the occurrence of increased ICP and that patients with a normal initial CT in the absence of associated extracranial injuries should make a good recovery. In a multicentre study based on a large number of patients with severe head injuries (N=1107), Gennarelli et al. (1982) argued that to predict outcome reliably, information about type of lesion would be necessary in addition to GCS scores indicating depth of coma. They devised a system of seven lesion categories and demonstrated that mere severity of coma was not sufficient to make sound predictions about mortality and overall outcome. The authors stated that

this improvement in predicting outcome would have been impossible without the aid of CT scanning but they acknowledged contributory factors such as age, pre-injury medical status and other neurological variables for a valid prognosis. They concluded that their system allowed the ranking of head injury lesions according to their importance and that it might help improve individual management.

The studies discussed so far have demonstrated that CT findings can be correlated with functional measures such as coma score, neurological status or outcome defined in broad terms. In contrast, the following studies are examples where more specific correlations between CT information and neuropsychological functioning have been attempted.

Bigler (1981) gives an account of five patients who were psychologically evaluated together with CT scans for the purpose of assessing their rehabilitation potential. CT and psychological investigations demonstrated concomitant abnormalities in three cases but disagreed in two. Dolinskas, Zimmerman, Bilaniuk & Uzzell (1978) followed up 153 patients with CT and neurological examinations. Twenty-seven of these patients underwent psychological evaluation. Cerebral parenchymal disruption was the abnormality most likely to result in a fixed neurological or psychological deficit. The site of residual parenchymal damage was associated more frequently with deficits found on psychological testing than with neurologically detected deficits. An approach to localisation/lateralisation was taken by Uzzell, Zimmerman, Dolinskas & Obrist (1979) who examined 26 patients on CT and the WAIS. Only five of their subjects presented with diffuse bilateral damage whereas the rest were diagnosed as suffering from either left or right hemisphere damage.

Using McFie's (1975) scoring method the authors found a significant overall difference between left and right sided lesions and WAIS performance. However, lateralised lesions yielded significant differences for only three individual subtests. The authors concluded that the traditional distinction between Verbal and Performance subtests on the WAIS was valid for CT documented lesions. Tsushima and Wedding (1979) compared the diagnostic conclusions of the Halstead-Reitan battery with a diagnosis based on CT in 45 patients. They claimed that their results indicated no false positive errors with CT and with a clinical interpretation of the Halstead-Reitan tests as compared to a statistical approach. However, only 24 of their patients had a diagnosis of head injury, and CT findings agreed with clinical neuropsychological conclusions in only 56%. Since patients of different etiology had been pooled it is not clear to what extent their findings actually apply to head injury. Timming, Orrison and Mikula (1982) studied 30 patients with severe head trauma after they had undergone an extensive in-hospital multidisciplinary rehabilitation programme. Patients were assigned to one of four categories based on their CT results. Psychological assessment was carried out if the patient's condition permitted but no correlations were attempted between psychometric and neuroimaging findings due to the small numbers in each category. However, they claimed that CT findings were related to outcome and achievement of independence. The study also demonstrated that patients with normal CT's - although achieving greater independence - can show clear psychological impairment. Rao, Jellinek, Harvey & Flynn (1984) studied 30 patients who had undergone CT investigations and found a significant relationship with rehabilitation - functional outcome, demographic characteristics, and predicted goal achievement. Levin, Meyers, Grossman & Sarwar (1981) studied 32 young adults with traumatic brain injury and a control group of similar age. Enlargement of the lateral ventricles

was present in 72% of the head injured subjects which was related to duration of coma, and to psychological performance on psychometric assessment. Significant correlations were found for both verbal and performance measures of the WAIS and right ventricular brain ratios (VBR) but none for left VBRs. Meyers, Levin, Eisenberg & Guinto (1983) studied 39 closed head injury patients and a control group of 51 subjects to assess possible differences in cognitive outcome for early compared to late ventricular enlargement. They found a significant relationship only for the group with late ventricular enlargement on the verbal and performance subtests on the WAIS. Cullum and Bigler (1985) investigated the effects of haematoma on ventricular size, cortical atrophy and memory in 16 patients and compared them with a group without haematoma matched for age, sex, and education but not on measures indicating severity of injury. The haematoma group showed significantly greater cortical atrophy than controls and was inferior in their performance on memory tests. Results reached significance when considering the entire battery (WMS) but only one subtests (Associate Learning) was significant on its own. Finally Cullum and Bigler (1986) assessed ventricular size, cortical atrophy and the relationship to neuropsychological status after closed head injury in 48 patients. They found highly significant correlations between psychological performance and ventricular enlargement. Performance measures showed stronger relationships with ventricular size than verbal measures and a certain degree of lateralisation was observed: performance measures rendered higher correlations for right ventricular enlargement and verbal measures for left ventricular enlargement. However, these relationships were non-linear and more significant correlations were found for the group not falling into the abnormal range. Correlations for cortical atrophy were generally lower and less robust. Unlike Levin et al. (1981) and others (Baron, Jacobs & Kinkel, 1976; Gyldensted 1977; Synek &

Reuben 1976), Cullum and Bigler failed to find a relationship between age and ventricular size.

5.1.3.2 Studies based on Magnetic Resonance Imaging.

Although Magnetic Resonance Imaging (MRI) had been in use in physics research for some decades, trials for clinical applications only started in the early seventies. However, even by 1981 less than 40 cases had been published on cerebral MR imaging. This changed dramatically with the publication of an account by Bydder et al. (1982) reporting brain imaging results for 140 patients of various etiology. The advantages of MRI over CT in imaging of the central nervous system have already been described and the following section will provide an overview of work published using MRI in the diagnosis of head injury.

One of the earliest accounts of the use of MRI in head injury was published by Gandy, Snow, Zimmerman & Deck (1984) who described three single cases in whom standard skull radiography had been unremarkable whereas MRI clearly helped identifying some focal intracranial lesions. Sipponen, Sepponen & Sivula (1984) studied five patients with chronic subdural haematoma and found MRI particularly useful in the detection of isodense collections and of collections in locations where access is difficult for CT because of bone artifact such as the lower aspects of the temporal lobes. The first report with a considerable sample (N = 25) was published by Han et al. (1984). They gave a detailed description of various abnormalities visualized on MRI in their head injured patients and stressed the advantages of multiplanar imaging and increased sensitivity compared to CT but they were unable to determine

the age of blood collections. Jenkins, Hadley, Teasdale, McPherson & Rowan (1986) studied 50 patients who had MRI investigations within one week of injury. They were able to identify abnormalities in 46 patients which was almost twice as many as found with CT. Furthermore there was a relationship between both depth and duration of coma as measured by the Glasgow Coma Scale and depth of MRI abnormality. Snow, Zimmerman, Gandy & Deck (1986) compared the results of MRI and CT from 35 patients after mild to severe head trauma. MRI was reported to be superior in some aspects but the authors were unable to diagnose subarachnoid or acute parenchymal haemorrhage within the first three days after injury. The group advocated continued use of CT as the procedure of choice in diagnosing head injury which is less than 72 hours old. Subsequently it has been shown that acute haemorrhage can easly be visualised on high field (1.5 Tesla; Gomari, Grossman, Goldberg, Zimmerman & Bilaniuk, 1985), and medium field (0.5 Tesla) MR systems (Edelman, Johnson, Buxton, Shoukimas, Rosen, Davis & Brady, 1986) but more recently also on low field (0.15 Tesla) systems (Hadley, Teasdale, Jenkins, Condon, McPherson, Patterson & Rowan, 1988). A further limitation was described by Barnes, McDonald, Johnson, Tofts & Landon (1987) who reported difficulties in discriminating between two types of experimentally induced oedema. However, their findings were applied by Ormerod et al. (1986) to the problem of distinguishing acute from chronic brainstem lesions. Hadley et al. (1988) in a sample of 50 head injury patients found that MRI was more sensitive to cerebral abnormalities associated with traumatic unconsciousness and detected parenchymal lesions both in patients in coma and in those who had lost consciousness for only a few minutes. They found MRI to be an effective alternative to CT and felt that the additional information obtained from MRI should be valuable in increasing the understanding of the early effects and late consequences of head injury.

A study by Groswasser, Reider-Groswasser, Soroker & Machtey (1987) underlined the problems of classifying patients with multiple lesions. CT performed during the rehabilitation period was normal for all of their 11 patients but MRI detected abnormalities in all patients. The temporal lobe was invariably involved and in seven patients, in addition, the frontal lobe. However, in this study no attempts were made to relate findings to outcome or cognitive performance.

All studies discussed so far have been confined to descriptions of neuroradiological aspects sometimes combined with general neurological observations. Neuropsychological outcome or follow-up studies on head injury and MRI are still few to date.

Levin, Kalinski, Handel, Goldman, Eisenberg, Morrison & Von Laufen (1985) gave a detailed description of a patient who had undergone serial neurobehavioural assessment for clinical correlation with abnormalities detected by MRI. The authors attempted to assign deficient psychological performance to structural abnormalities identified by MRI. However, it could be that their interpretation of the results might be confounded with overall generalized impairment since their patient showed abnormalities in almost every hemispheric lobe. Later, Levin, Handel, Goldman, Eisenberg & Guinto (1985) described four patients who had MRI and CT investigations and neuropsychological assessment with a wide spread of post injury intervals (3 months to 5 years). All four patients showed more abnormalities on MRI than on CT and were impaired on most neuropsychological tests but none of them dispalyed signs of hemispheric disconnection. No explicit conclusions concerning localisation of function or generalisations about the usefulness of this technique to aid

neuropsychological investigation were suggested in this study. However, most importantly the authors inferred from their findings that MRI data supported the hypothesis that diffuse, non-missile head injury is in many cases a multifocal insult. Evaluation of this increased sensitivity and its application to neuropsychological outcome formed the basis for a study by Wilson, Wiedmann, Hadley, Condon, Teasdale & Brooks (1988a). In this study the authors attemptedto establish whether the increase in sensitivity would have any clinical relevance or whether it merely served to achieve a better description of the brain damage sustained. Wilson et al. (1988) compared the use of CT and MRI to predict psychological outcome in 25 patients. The number of abnormalities detected by MRI outnumbered those detected by CT by a ratio of two to one indicating increased sensitivity of MRI over CT. The majority of patients showed multiple abnormalities precluding analysis of data on the basis of traditional models of lateralisation or localisation. Alternatively patients were categorised according to depth of abnormality following the centripetal model proposed by Ommaya and Gennarelli (1974). There were no significant correlations between CT findings and neuropsychological outcome neither for investigations during the acute phase nor at follow-up. A weak relationship was established between acute MRI findings and late neuropsychological outcome but for MRI performed at the time of assessment relationships were highly significant (pooled results from cognitive tests: $r=0.75$ $p<0.001$). The usefulness of applying the centripetal model to neuroradiological data was further confirmed in a study by Levin et al. (1988) who found a strong relationship between MRI findings, duration of coma and post traumatic amnesia.

MRI technology has opened a new dimension to head injury research and could potentially lead to a far better understanding of the underlying mechanisms and dynamic processes involved in recovery from traumatic brain damage. The increase of sensitivity and therefore the detection of underlying brain damage is impressive but to some extent the value of this abundance of new information has initially been found difficult to assess. The fact that this wealth of information can cause some problems of selection will be described in a further study of 56 patients which will form the centre of the next section.

5.2 A STUDY OF VISUAL EVENT PERCEPTION FOLLOWING TRAUMATIC BRAIN DAMAGE.

The study reported in the following section formed part of a larger investigation inquiring into the cognitive sequelae of traumatic brain damage and their structural correlates. Although the main interest was in patients' performance on event perception task and the possibilty of establishing relationships between performance and structural abnormalities, patients' performance on other tasks was included where appropriate. The purpose of the present investigation was to find out whether

1. patients could be differentiated on the basis of their performance on visual event perception tasks;
2. the two event perception tasks employed were equally sensitive to traumatic brain damage;
3. there were specific patterns of brain damage which lead to impairment on the event perception tasks?

5.2.1 Methods.

Subjects. Subjects were 47 patients (37 male) with a mean age of 31.4 years and an age range of 16 - 65 years who had been admitted to the Institute of Neurological Sciences in Glasgow following head trauma severe enough to warrant admission to this specialised unit. Twenty -five patients or 53% had been involved in road traffic accidents and 22 or 47% had sustained a fall or assault. Glasgow Coma Score (GCS) (Teasdale, Murray, Parker & Jennett, 1979) on admission ranged from 3 to 14 (mean

= 10.0) (Table 5.1). The range of Post Traumatic Amnesia (PTA) which was determined by interview was 0 to over 3 months (mean = 21.9 days). Follow-up took place five to twelve months (median=184 days) after injury. A group of 14 control subjects with a mean age of 28.4 years (range 15 - 49 years) was recruited from an orthopaedic outpatient clinic at the same hospital. None of the controls had suffered head injury or fractures of the dominant hand nor had they ever suffered from psychiatric illness (see table 5.1)

Assessment procedures. All but the visual memory tests outlined in chapter 2 were administered in the same way as described except for Event Perception Movement which was identical with the version used in chapter 4.

Neuropsychological assessment was carried out within 48 hours of follow-up neuroimaging. The neuropsychological test battery consisted of 20 measures. General intellectual ability was assessed employing six subtests from the Wechsler Adult Intelligence Scales (Wechsler, 1955): Similarities, Digit Span and Vocabulary from the Verbal Scale, and Digit Symbol, Block Design and Object Assembly from the Performance Scale. The National Adult Reading Test (NART) (Nelson, 1981) was used as an estimate of premorbid IQ. For assessment of verbal memory and learning the Logical Memory and Associate Learning subtests from the Wechsler Memory Scales (WMS; Wechsler, 1945) were used. Verbal processing and proficiency were assessed on a Word Fluency Test (Borokowski, Benton & Spreen, 1967), the Graded Naming Task (McKenna & Warrington, 1983), and a computerised Word Recognition task (Wilson, Wiedmann, Phillips & Brooks, 1988b). In addition patients were assessed on Simple and Choice Reaction Times which were divided into decision and

movement times (Van Zomeren, 1981), and for visual processing on a computerised Visual Search task and two computerised visual Event Perception tasks, Event Perception Threshold and Event Perception Movement with the modifications mentioned above. Visual memory and learning was assessed by the Rey Complex Figure Task (Rey, 1941).

Magnetic resonance imaging was carried out on a Picker Vista 1100 0.15 Tesla resistive MR system operating at 6.38 MHz. An initial 2 cm thick spin echo (SE 200/40) pilot image in the sagittal or coronal plane was used to determine the position of 16 slices each 8 mm thick for a T2 weighted spin echo sequence (SE 2000/80), and an 8 slice T1 weighted inversion recovery sequence (IR 1660/400/40) in the axial plane. Total acquisition time was 45 min.

Images were analysed by an experienced neuroradiologist who had no access to neuropsychological test information. Twelve mutually exclusive regions of interest (ROIs) in the cerebral hemispheres, and in addition the basal ganglia, the brainstem, the cerebellum and the corpus callosum were categorized according to whether an abnormality was present or not, and secondly, according to depth of abnormality using the following categories: (1) No parenchymal abnormalities, (2) cortical abnormalities, (3) white matter, and (4) deep white matter and deep structure abnormalities and late ventricular enlargement.

5.2.2 RESULTS.

No significant differences were found for age and premorbid IQ as assessed by the NART between patients and controls and it was therefore felt justified to compare groups without corrections. Table 5.2 shows the results of a comparison of the neuropsychological test performance between all patients and the control group. Since only 3 controls were tested on reaction time tasks these measures were not included in the comparison. Patients performed significantly worse on 10 of the remaining 16 tasks with significantly inferior performance on all computerised tests.

Since one of the aims of this study was to assess the sensitivity of Event Perception tasks to the effects of traumatic brain damage, patients were split into two groups: Those whose score on Event Perception Movement was 1 SD below the control mean (m=29.1 SD=3.6) or any score equal to or lower than 25, and those patients whose score was above 25. With this division 20 patients fell into a low score group and 27 into a high score group. Fifty per cent of the controls achieved the maximum score of 32 indicating that performance on this task was relatively easy for non-brain damaged subjects. Event Perception Movement rather than Event Perception Threshold was chosen because differences between patients and controls were more reliable for Event Perception Movement.

Table 5.3 shows that there were no statistically significant differences between the low and high score groups for age, NART or GCS but patients in the low score group had a significantly longer posttraumatic amnesia (PTA) with a mean of 34.7 days compared to the high score group with 12.5 days ($p<0.01$). This might suggest higher

injury severity for the low score group which may be reflected in worse performance. Comparing test results for the two groups confirmed this suspicion: Low scorers performed significantly worse on 14 of the 20 measures.

Patients' performance on Event Perception Movement and Event Perception Threshold was compared with performance on all other tasks using Pearson correlations. Table 5.4 shows that 17 out of the 19 measures were significantly related with performance on Event Perception Movement and 16 with Event Perception Threshold. The strongest relationships for Event Perception Movement were found to be with Event Perception Threshold ($r= -0.67$ $p<0.001$), Visual Search ($r= -0.63$ $p<0.001$), and Rey Figure Copy ($r= 0.61$ $p<0.001$). For Event Perception Threshold (apart from showing the same relationship with Event Perception Movement, of course), the same tests showed the strongest relationships but with Rey Figure Copy being slightly stronger ($r= -0.67$ $p<0.001$) than Visual Search ($r= 0.66$ $p<0.001$). All four RT measures were significantly related to Event Perception Movement but only the two RT movement measures were related to Event Perception Threshold. There was a significant relationship between Event Perception Movement at $r= -0.44$ $p<0.001$ and PTA but not with Event Perception Threshold.

However, it was found that Event Perception Movement showed a slight but statistically significant relationship with age ($r= -0.39$ $p<0.01$), indicating better performance for younger patients, and Event Perception Threshold with both age and NART ($r= 0.30$ $p<0.05$; $r= -0.28$ $p<0.05$), indicating better performance for younger patients with higher premorbid IQ estimates. A partial correlation procedure was therefore employed controlling for age in the Event Perception Movement condition,

and for age and NART in the Event Perception Threshold condition. This procedure resulted in a slight decrease in many correlation coefficient values but the number of significant relationships remained the same at 17 measures for Event Perception Movement. For Event Perception Threshold the effects of the partial correlation procedure were more drastic since two covariates had to be considered. The number of statistically significant relationships after correction fell to half the number found without correction leaving 8 measures with reduced values for correlation coefficients in all cases but one. The effects of correction worked the opposite way for PTA: The value of the correlation coefficient with Event Perception Movement rose to r= -.058 $p<0.001$ and Event Perception Threshold now showed a significant relationship at r= 0.27 $p<0.05$.

Table 5.5 shows the relationship of PTA to performance on all neuropsychological tasks. Fourteen measures were significantly related with PTA with the strongest relationships found for RT tasks and Event Perception Movement (r= -0.58 $p<0.001$).

Table 5.6 shows the distribution of patients according to the deepest abnormality found in any one patient which was coded as (1) no parenchymal abnormality, (2) cortical abnormality, (3) white matter and (4) deep white matter, or basal ganglia and/or late ventricular enlargement. For comparison the distribution from the study by Wilson et al. (1988a) is also shown.

A comparison between the two studies shows that distributions for early MRI were slightly different insofar as there were more patients in the deepest abnormality category in the current study. However, whereas almost 50% of patients in the Wilson

et al. study fell into category four for late MRI, the distribution in the current study is somewhat more evenly distributed.

Table 5.7 gives an idea of the implications that this difference in distribution had on a comparison between indices of brain damage and performance on neuropsychological tasks. Spearman correlation coefficients were obtained for test performance and the deepest abnormality found in any patient. Only Vocabulary showed a significant relationship with the deepest abnormality for early MRI in the Wilson et al. study but relationships with late MRI were highly significant and very consistent with rather high correlation coefficients on 10 out of 11 measures. In the current study early MRI showed slightly more relationships with neuropsychological test performance with 10 out of 20 measures being statistically significant including Event Perception Movement and Event Perception Threshold. For late MRI 17 out of 20 measures showed a statistically significant relationship with depth of abnormality but the strength of the relationships was weaker than in the Wilson et al. study as expressed by lower correlation coefficients. The strongest relationship was found for Visual Search ($r= 0.46$ $p<0.001$), and an equally strong one for Event Perception Movement and Word Recognition ($r= -/+0.44$ $p<0.001$). Event Perception Threshold was not significantly related to depth of abnormality.

In the next section abnormalities were analysed according to presence and/or depth of abnormalities in 16 regions of interest (ROIs). Table 5.8 gives the meaning of the abbreviations used in the following tables and figures. Figure 5.1 shows a schematic drawing indicating the regions of interest used in the current study. Figure 5.2 shows the distribution of patients with abnormalities for each ROI for early and

late MRI. For early MRI the highest frequencies were found for patients with abnormalities in the left and right frontal areas. The figures for brainstem and corpus callosum abnormalities were unexpectedly high with 41% and 28% respectively. For late MRI there were fewer patients with abnormalities in each ROI but relative percentages were very similar.

Figure 5.3 shows the distribution of patients with abnormalities for each ROI for early MRI with groups split into high and low scorers on Event Perception Movement. For most ROIs there were higher percentages of patients with abnormalities in the low score group. This pattern was almost reversed for late MRI where there was in general a higher percentage of high scorers for the hemispheric ROIs. For deep or midline structures (basal ganglia, brainstem and corpus callosum and cerebellum) proportions of patients with abnormalities were higher for the low score group. It is of importance to note that only 3 of the 11 high scorers with abnormalities in the brainstem continued to show brainstem abnormalities at follow-up whereas 50% of the low scorers continued to show such abnormalities. Likewise only 1 of 6 patients in the high score group continued to show an abnormality in the corpus callosum whereas only 1 of the 7 patients in the low score group recovered from such an abnormality. When all patients with deep or midline structure abnormalities on late MRI were lumped together only 19% of the high score group were found to show such abnormalities whereas evidence of such abnormalities was found in 58% of patients in the low score group (table 5.9). This difference was statistically significant at $p<0.006$ on a chi ^{2} test ($chi^2= 7.62$). On the other hand differences in the number of patients with abnormalities in hemispheric sites were not statistically significant ($chi^2= 1.79$ ns) (table 5.10).

At this point it was felt to be of interest to see whether a similar pattern would emerge when patients are split according to performance on Event Perception Threshold. The same criteria were used as for splitting patients into low and high movement groups: there were 24 patients whose score on Event Perception Threshold was within 1 SD of the control mean, or 49 ms, and 22 patients whose score was higher than 49 ms indicating impaired performance. Table 5.11 and 5.12 show that distributions for patients with abnormalities in both deep structures and hemispheric sites were very similar for both groups and there were no statistically significant differences.

Figure 5.5 shows the distribution for all patients with the total numbers of ROIs rated abnormal for early and late MRI expressed in percentages. From these figures it is clear that many patients had suffered multiple abnormalities although there was a considerable reduction in the number of patients suffering from multiple abnormalities at follow-up.

Figures 5.6 and 5.7 show distributions for the low and high score groups analysed separately for early and late MRI respectively. Distributions were largely similar except for early MRI where the low score group had slightly more patients with a larger number of abnormalities.

There was a significant but rather weak relationship between the number of abnormal ROIs and performance on Event Perception Movement and Event Perception Threshold (table 5.13). Relationships were somewhat stronger for Event Perception Movement and for the high score group.

The frequency with which multiple abnormalities are found in head injury patients comprises a problem when attempting to relate impaired performance to abnormalities in particular areas. An analysis of intercorrelations of ROIs with abnormalities for early and late MRI for all patients was conducted to establish whether any specific patterns of abnormalities would emerge in the present group of patients. Table 5.14 shows the results of this analysis; since this table consisted of 238 correlations (16x16 minus auto-correlations) the level of acceptable statistical significance was raised to $p<0.01$ leaving approximately 2 correlations which could be chance results. Frontal and anterior temporal areas showed the strongest relationships indicating that these two areas are commonly injured together. There were some isolated significant relationships with hemispheric ROIs and deep structures but only one significant relationship amongst the deep structures themselves (see table 5.14: Corpus callosum with cerebellum $r= 0.38$ $p<0.01$) despite their relatively high frequency of occurrence (cf. figures 5.2 to 5.4). The strongest relationships were found for orbitofrontal left with orbitofrontal right for early MRI at $r= 0.62$ $p<0.0001$, and late MRI at $r= 0.64$ $p<0.0001$.

Tables 5.15 to 5.16 show both Spearman and Partial correlations between individual ROIs and performance on Event Perception Movement and Event Perception Threshold. Partial correlations were computed because Event Perception Movement was significantly related with age, and Event Perception Threshold was significantly related with age and NART error score. On the whole these correlations showed few consistent relationships between abnormalities in individual ROIs and the Event Perception tasks. One of the more consistent relationships was between the posterior temporal right area and both Event Perception tasks before and after

correction for age and NART on both early and late MRI with values ranging from r= +/- 0.27 to r= +/- 0.35 (all $p<0.05$). An important result was the significant relationship between abnormalities in the corpus callosum for early MRI after correction for age with Event Perception Movement at r= -0.40 $p<0.01$ (table 5.15). This relationship was also found at follow-up MRI but only before correction at r= -0.34 $p<0.05$ (table 5.16). A sporadic relationship with Event Perception Movement and the cerebellum was also noted (tables 5.15 & 5.16).

5.2.3 DISCUSSION.

A group of 47 head trauma patients and 14 controls were assessed on a battery of 20 neuropsychological measures including two computerised visual event perception tasks, Event Perception Movement and Event Perception Threshold. Insufficient numbers of controls were tested on RT tasks which were therefore not included in a comparison between patients and controls. Patients were significantly impaired on 10 of the remaining 16 measures. The finding of significant impairment on neuropsychological test procedures following head trauma merely confirmed findings from previous studies discussed in the introduction to this chapter and is as such only of relevance in confirming successful selection of a patient group with sufficient cognitive impairment to warrant further investigation.

The different approaches taken in analysing the data from this study correspond to the questions raised initially in the introduction to the current chapter. The approach used to select patients on psychological grounds ie. by performance on Event

Perception Movement corresponds to the second question: trying to find structural abnormalities which might explain impaired performance. The approach by which patients were selected on the basis of their neuroradiological abnormality corresponds to the first question ie. trying to find psychological correlates to identified structural abnormalities.

When patients were divided into a low score and a high score group according to their performance on Event Perception Movement it emerged that groups differed significantly in duration of PTA and hence presumably in injury severity. PTA has traditionally been considered as reflecting injury severity or the degree of brain damage sustained and was initially proposed by Russell (1932) and Symonds and Russell (1943). In the current study depth of coma on admission measured by the GCS was only weakly related to PTA ($r= -0.32$ $p<0.05$). Despite a relatively long delay between the time of the accident and the follow-up interview PTA showed a fairly consistent relationship with a number of measures. PTA was related to performance on Event Perception Movement to a relatively high degree after correction for age ($r= -0.58$ $p<0.001$) but the relationship with performance on Event Perception Threshold was rather weak ($r=0.27$ $p<0.05$). This suggests that duration of PTA or its assumed underlying cause ie. the amount of (diffuse) brain damage, is also to a considerable extent dependent on the sensitivity of the task to which PTA is related. This was demonstrated by the results in table 5.6 were measures traditionally found to be more sensitive to the effects of diffuse brain damage, the performance measures on the WAIS, were significantly related with PTA. RT tasks appeared to be the most sensitive measures and showed the highest correlations with PTA.

There is no a priori reason why patients should be differentially impaired on the Event Perception tasks except if we agree with the assumption that Event Perception Threshold is measuring a different perceptual process as outlined in chapter 1. The correlation between the two Event Perception tasks for this group was r= -0.66 $p<0.001$ which for an $r^2 = 0.396$ explains only about 40% of the variance of patients' performance on these tasks. A number of individual patients were found who were impaired on the one task but showed preserved performance on the other. Using the same criteria as in chapter 3 a double dissociation between Event Perception Threshold and Event Perception Movement could be established. According to these criteria the unimpaired test score had to be within 1 SD of the normal range and the impaired score must be 3 SDs beyond the control mean. If the latter criterion were to be relaxed to 2 SDs a further 5 (2 an 3) individuals would show dissociations between these tasks (see table 5.17).

At this point the question arises whether patterns of brain damage in the low score group were different from the high score group leading to relatively greater impairment on Event Perception Movement, or whether the two tests were simply differentially sensitive to the effects of diffuse brain damage?

Evidence for the latter argument can be found in comparing the strength of the relationship of the two tasks with indices of depth of brain damage found on early and late MRI. For the whole group of patients Event Perception Movement correlated with depth indices on early MRI at r= -0.37 $p<0.01$ and on late MRI at r= -0.44 $p<0.001$. In contrast Event Perception Threshold correlated at r= 0.32 $p<0.05$ for early and at r= 0.16 ns for late MRI. Thus depth of abnormality was related to performance on Event

Perception Movement to an acceptable degree but less so to Event Perception Threshold. This finding strengthens rather than weakens the argument that depth of abnormality or, if the proposition by Ommaya and Gennarelli (1974) is accepted, the degree of diffuse brain damage may be considered a decisive factor in explaining performance on Event Perception Movement. Deep white matter or deep structure abnormalities have been considered as representing more global and more widespread brain damage rather than simply representing damage to the areas in which they are detected (Ommaya & Gennarelli, 1974; Wilson et al., 1988a). Ventricular enlargement following head trauma which also causes patients to be classified in this category is a widely accepted indicator of diffuse brain damage (Levin et al., 1981; Cullum & Bigler, 1986; Meyers et al., 1983). Thus it appears from this analysis that indicators of diffuse brain damage were more strongly correlated with Event Perception Movement than with Event Perception Threshold, or, in other words, that Event Perception Movement may be more sensitive to diffuse brain damage.

For comparison performance on three other tasks will be discussed: Block Design because it showed the highest relationship with depth of abnormality in the Wilson et al. (1988a) study ($r= -0.86$; $r^2 = 0.74$); Rey Figure Copy because it showed the strongest relationship with both Event Perception Movement and Event Perception Threshold in the current study ($r= 0.61$; $r= -0.67$), and Digit Span which was the only task not showing a significant relationship with depth of brain abnormality in the Wilson et al. (1988a) study. Digit Span is generally taken as a measure of short-term memory or attention span and since attention at least contributes to performance on the Event Perception tasks as discussed in chapter 1 it seemed appropriate to investigate the relationship between these tasks.

In the current study Digit Span was significantly lower for the whole patient group as well as for both subgroups independently. It was also significantly related to depth for late MRI for the whole group ($r= -0.43$ $p<0.001$). However, its relationship with performance on the two Event Perception tasks was low and not statistically significant for any of the conditions. Despite a highly significant difference between patients and controls, and being significantly related to depth of abnormality Digit Span and the Event Perception tasks do not appear to have much in common. Digit Span seems to measure different aspects of attention from the type of attention required by the Event Perception tasks.

Over 50% of the patients in the current sample obtained maximum scores on the Rey Figure Copy task and a significant relationship with PTA ($r= 0.47$ $p<001$) suggests that it is mainly patients with more severe brain damage who lose points on this task. Since PTA was also significantly related with the Event Perception tasks it can be assumed that both the Event Perception tasks and Rey Figure Copy are sensitive measures of diffuse brain damage. The tasks appear to be highly unrelated from a theoretical and procedural point of view and yet they showed a fairly strong relationship (table 5.5). The most likely common feature might be impaired performance on both types of task rather than any other intrinsic connection.

Patients as a whole performed only marginally worse from controls on Block Design but the low score group's performance was significantly impaired. Scores on Block Design were significantly related to performance on both Event Perception tasks before and for Event Perception Movement after correction for age (and NART) for the whole group. When the low score and high score groups were evaluated

independently performance on Block Design remained significantly but marginally related to performance on Event Perception tasks. Block Design was significantly related to depth indices for both early and late MRI but for the latter correlation coefficients only reached little more than half the value compared to the Wilson et al. study. Given the relatively low correlations between the Event Perception tasks and Block Design but fairly robust correlations with depth indices it appears that the common feature shared by these measures is their sensitivity to diffuse brain damage rather than any intrinsic relatedness in task performance.

The question whether there were any specific patterns of brain abnormalities for patients leading to differential impairment on the two Event Perception tasks was investigated by analysing 16 ROIs with respect to presence and absence of brain abnormalities. Figure 5.2 showed that the number of patients with abnormalities in any ROI was invariably higher for early than for late MRI. Highest frequencies were found for both left and right frontal areas closely followed by orbitofrontal and anterior temporal areas. This finding confirmed the results in a report by Wilson, Hadley, Wiedmann & Teasdale (1990b) that patterns of lesions found in fatal accidents (Adams et al., 1977; Graham et al. 1989) resemble closely those in survivors of head trauma. The number of abnormalities found in the brainstem and corpus callosum was unexpectedly high especially on early MRI. These latter indices form part of the 'classic triad' for diffuse brain damage identified by Adams, Doyle, Ford, Gennarelli, Graham & McLellan (1989) involving the brainstem, the corpus callosum and, at the microscopic level, diffuse axonal damage. Confirmation that these abnormalities were by no means artifacts was found in a study by Wiedmann, Grant, Hadley & Wilson (1989) who investigated a similar sample of head trauma patients and found that

brainstem abnormalities seen on early MRI were significantly related to persistent neurological deficits such as anosmia and ageusia.

When comparing the low score and high score group the distribution of patients with abnormalities over different ROIs was very similar for early MRI and larger differences were only found for frontal left (low= 65%; high= 51%), and the posterior temporal right area (low= 45%; high= 26%). Brainstem abnormalities were equally common in both groups but the percentage of corpus callosum abnormalities was higher for the low score group (35% and 22%). As for the whole group a general reduction in the number of abnormalities was found on late MRI when examining the two groups independently. For hemispheric ROIs the two groups had roughly identical distributions but the low score group showed more patients with persistent deep structure abnormalities. The largest difference was found for the corpus callosum (low= 30%; high= 4%). These differences support findings by Wilson, Hadley, Wiedmann & Teasdale (1990a) who proposed a division of patients into subgroups according to different patterns of lesions with the aim of obtaining subsamples which are clinically meaningful. When this was attempted in the current study, 8 patients emerged as having both brainstem and corpus callosum abnormalities simultaneously on early MRI, but only 4 of them were members of the low score group. However, as the analysis in figures 5.2 to 5.4 suggested differences in these areas seemed to be more prominent at follow-up MRI. The same analysis was therefore conducted with indices from late MRI. Result proved to be similar: only 3 patients had both brainstem and callosum abnormalities on late MRI and all 3 patients were members of the low score group.

Because there was a majority of patients with multiple brain damage intercorrelations of abnormalities were investigated to see whether distinct patterns of brain damage would emerge (cf. Wilson et al., 1990b). The results of this analysis were given in table 5.15. Neuropathological studies have shown that abnormalities in traumatic brain damage rarely occur in isolation but tend to form particular patterns (eg. Adams et al. 1980; Graham et al. 1989). The functional and theoretical implications if such patterns were also found in survivors of severe head injury are of considerable importance. Such findings would require a shift in the way people approach the question of localisation of function in these conditions and require a new approach in the way such questions are raised. It emerged that not only was the majority of patients with abnormalities found in the frontal and anterior temporal areas but these areas also tended to show the strongest relationships. This means that frontal damage was most frequently paired with damage to the anterior temporal lobes both ipsilaterally and bilaterally.

Finally it was considered whether disruption of particular pathways responsible in information processing of event perception stimuli could be identified, given the improved resolution of MRI over CT. By analysing abnormalities in individual ROIs it was thought possible to identify damage to specific areas which might explain why patients' performance on the Event Perception tasks differed, perhaps as a result of an abnormality in one or more particular brain region. For early MRI the posterior temporal area on the right side was shown to give fairly consistent relationships with both Event Perception tasks. For late MRI both Event Perception tasks were significantly related with both anterior and posterior temporal areas on the right side.

The strongest evidence for a different pattern of brain damage in the low and high score group was found in a statistically significant difference in the number of patients with residual deep structure abnormalities on late MRI. In the low score group more than half of the patients were found to continue to show deep structure abnormalities whereas less than 20% of the high score patients showed evidence of such abnormalities on late MRI. In addition, splitting patients according to performance on Event Perception Threshold showed no such differences. These findings are taken as clear evidence that patterns of brain damage are different for the low and high score group. Conversely, if deep structure damage is accepted as representing more widespread brain damage, Event Perception Movement was more sensitive to the effects of diffuse brain damage than Event Perception Threshold as reflected in the scores of patients with more widespread brain damage.

Two important points must be stressed at this stage: (1) the size of brain abnormality was never taken into account in any of the neuroradiological analyses and hence an abnormality only measuring some cubic millimetres was given the same weight as one of several cubic centimetres. Little definite information is as yet available on the size of abnormalities and its neuropsychological correlates. An analysis of this kind will remain problematic since the importance of lesion size must vary considerably with respect to location, eg. a large intracerebral haematoma in the frontal lobes may be more easily compensated for than a much smaller haemorrhagic contusion in the brainstem. Another variable not taken into consideration was type of abnormality ie. whether the abnormality found was a haemorrhagic contusion, a haematoma, an oedema or any other type of lesion. Both aspects neglected in this study may nevertheless be of importance in capturing the full picture of the intracranial

processes following traumatic brain damage. On the other hand with such relatively few patients statistical management would become even more difficult than it may already have appeared in the present study. (2) It is clear that despite largely improved resolution, MRI is by no means capable of identifying all abnormalities present in the brain of trauma patients. The third hallmark of diffuse axonal damage, for instance, retraction balls and microglial scarring, can only be seen under the microscope and escapes MRI evaluation. Furthermore, MRI can only show structural abnormalities but as the next chapter will demonstrate metabolic abnormalities not demonstrated or even suspected on the basis of MRI investigation may be of importance in explaining the behavioural and cognitive correlates following brain damage. With the possibility of information being patchy at its best assumptions concerning the basis of impairment on the Event Perception tasks can only be tentative.

5.3 CONCLUSIONS.

Two visual event perception tasks have been evaluated in a study of patients with traumatic brain damage. Differences between patients and controls were found to be more reliable on Event Perception Movement than on Event Perception Threshold, and Event Perception Movement was taken to be more sensitive to diffuse brain damage. This assumption was strengthened by the finding of significantly longer PTA in patients with poorer performance on Event Perception Movement. However, a number of individual patients could be identified in whom performance on Event Perception tasks was doubly dissociated.

Indices from both early and late MRI were used to investigate the nature of brain damage in heads injury patients and an attempt was made to relate these indices to performance on the Event Perception tasks. Reliable relationships with depth indices for both early and late MRI could only be established for Event Perception Movement. Identification of any one region of the brain as being particularly responsible for impaired performance on the Event Perception tasks was equivocal due to multiple brain damage sustained by a majority of patients and a resultant high interrelation of brain regions with abnormalities. However, if such an attempt at localisation should be excused, the more consistent relationships between performance on the Event Perception tasks were found with abnormalities in both left and right temporal areas. To carry this idea slightly further it might be argued that these findings are in congruence with the cortical model proposed by Van Essen & Maunsell (1983) who found that movement analysis went as far as the middle temporal area at least in the monkey's visual system (cf. chapter 1). On the other hand much of the evidence

found in the study on solvent abuse described in chapter 2 would support a more subcortically based model for the Event Perception tasks involved in this study. In fact the other areas showing more consistent relationships were the deep structures which were also found to be abnormal in a significant majority of patients with low scores on Event Perception Movement compared to patients with high scores. Unlike experimental lesion studies abnormalities in a sample of head injury patients do not occur in isolation and indices of deeper damage were taken to be representative of more widespread brain damage. When examining a number of possible patterns of brain damage which might discriminate patients with low scores on Event Perception Movement from patients with high scores on this task, the clearest differences in patterns of brain abnormalities were in the number of patients showing persistent deep structure damage. High score patients showed significantly less involvement of deep structure abnormalities on late MRI; the converse was true for patients in the low score group. It can be concluded that Event Perception Movement was sensitive in discriminating patients with differential degrees of brain damage but the nature of the material studied did not allow any firm conclusions about the precise localisation of the perceptual processes involved in this task.

One of the implications of the differential impairment found for the Event Perception tasks might be a confirmation of the assumption that Event Perception Threshold measures aspects of perception which are less susceptible to disruption by traumatic brain damage than the processes involved in Event Perception Movement. In fact, it appears plausible to apply one of the arguments raised to explain impaired performance on Event Perception Movement in optic neuritis patients in chapter 4: if signals arising in response to movement are mediated by smaller nerve fibres than

those arising in response to appearances, it could be assumed that smaller fibres are also more vulnerable to the effects of diffuse brain damage than larger fibres. Although differences in performance on the two tasks were not as pronounced as in the optic neuritis patients, the significant relationship with deep structures and the significant proportion of patients with low scores on Event Perception Movement and deep structure abnormalities strengthens this possibility.

Studying structural correlates of traumatic brain damage is only one route in the attempt to capture the processes following head trauma. A more dynamic picture is provided by techniques allowing the study of indices of metabolic changes following trauma. The next chapter will report a study of head trauma patients in whom cerebral bloodflow was measured by Single Photon Emission Computed Tomography (SPECT).

TABLES AND FIGURES

Table 5.1: Demographic background of head injury patients and controls.

	Patients N=47			Controls N=14		
	m	SD	range	m	SD	range
AGE (years)	33.8	15.4	16-65	28.4	8.4	15-49
NART (max.50)	21.2	10.2	3-46	25.4	7.8	11-39
GCS (3-15)	10.0	3.5	3-14			
PTA (days)	21.9	26.8	0-99			

NART = National Adult Reading Test; GCS = Glasgow Coma Scale;
PTA = Posttraumatic Amnesia

TABLE 5.2: T-tests comparing all patients with the control group.

TEST	All Patients N=47 Score/SD	Controls N=14 Score/SD	t-value	p
Age (years)	31.4 / 15.5	28.4 / 8.4	-1.3	ns
NART (max=50)	21.2 / 10.2	25.4 / 7.8	1.4	ns
Similarities+	13.7 / 4.7	16.4 / 4.4	1.6	ns
Digit Span+	11.6 / 2.4	14.6 / 1.6	4.6	0.001
Vocabulary+	41.3 / 15.7	45.2 / 14.2	0.7	ns
Digit Symbol+	40.7 / 15.6	62.7 / 6.2	7.1	0.001
Block Design+	30.1 / 9.5	34.7 /7.0	1.4	ns
Object Assembly+	25.5 / 8.4	29.8 / 6.4	1.5	ns
Rey Copy (max=36)	33.1 / 4.6	34.9 / 1.9	2.0	0.05
Rey Recall (max=36)	18.6 / 6.9	22.1 / 5.8	1.6	ns
Logical Memory (max=23)	11.1 / 4.1	13.1 / 2.8	1.8	ns
Assoc. Learning (max=21)	14.0 / 3.6	16.2 / 2.5	2.2	0.05
Word Fluency	34.1 / 10.2	51.9 / 8.7	5.5	0.001
Graded Naming (max=30)	17.9 / 5.7	21.2 / 3.9	2.1	0.05
EP Threshold (ms)	68 / 78	39 / 10	-2.5	0.01
EP Movement (max=32)	24.3 / 6.8	29.1 / 3.6	3.4	0.001
Visual Search (ms)	4625 / 1468	3211 / 597	-5.3	0.001
Word Recognition (ms)	82 / 54	50 / 24	-3.2	0.001

Level of significance: * = $p < 0.05$ ** = $p < 0.01$ *** = $p < 0.001$ denotes significantly different from controls

+ = Raw Scores EP = Event Perception GCS = Glasgow Coma Scale PTA = Post-traumatic Amnesia RT = Reaction Times Assoc. Learning = Associate Learning

TABLE 5.3: T-tests comparing patients with low and high scores on EP movement.

TEST	Low Move N=20	High Move N=27	t-value	p
Age (years)	37.0	31.4	- 1.2	ns
Nart (max=50)	18.8	22.8	1.3	ns
GCS	9.6	10.3	0.7	ns
PTA (days)	34.7	12.5	-3.1	0.01
Similarities+	12.9	14.3	1.0	ns
Digit Span+	11.3	11.9	0.9	ns
Vocabulary+	38.7	43.2	0.9	ns
Digit Symbol+	31.0	47.8	4.3	0.001
Block Design+	24.6	34.2	3.9	0.001
Object Assembly+	22.3	27.9	2.3	0.05
Rey Copy (max=36)	31.5	34.3	2.1	0.05
Rey Recall (max=36)	15.1	21.2	3.4	0.001
Logical Memory (max=23)	9.4	12.3	2.6	0.01
Assoc. Learning (max=21)	13.1	14.6	1.4	ns
Word Fluency	33.9	34.2	0.1	ns
Graded Naming (max=30)	17.0	18.6	0.9	ns
EP Threshold (ms)	102	42	- 2.8	0.01
EP Movement (max=32)	18.3	28.8	7.3	0.001
Visual Search (ms)	5404	4047	- 3.5	0.001
Word Recognition (ms)	98	68	- 1.9	0.05
Simple RT Decision (ms)	396	300	- 3.4	0.001
Simple RT Movement (ms)	312	244	- 2.8	0.01
Choice RT Decision (ms)	464	328	- 3.8	0.001
Choice RT Movement (ms)	308	248	- 2.3	0.05

+ = Raw Scores EP = Event Perception GCS = Glasgow Coma Scale PTA = Post-traumatic Amnesia RT = Reaction Times Assoc. Learning = Associate Learning

TABLE 5.4 Pearson and Partial Correlations between performance on EP tasks and performance on other tasks for all patients (N=47).

	Pearson Corrs		Partial Corrs	
TEST	EP Move	EP Treshold	EP Move	EP Treshold
Age (years)	-0.39**	0.30*	- - -	- - -
Nart (max=50)	0.18	-0.28*	- - -	- - -
GCS	-0.07	0.14	0.15	0.03
PTA (days)	-0.44***	0.21	-0.58***	0.27*
Similarities+	0.45***	-0.42***	0.31*	-0.06
Digit Span+	0.23	-0.28*	0.24	-0.20
Vocabulary+	0.25*	-0.37**	0.29*	-0.14
Digit Symbol+	0.56***	-0.45***	0.48***	-0.20
Block Design+	0.60***	-0.42***	0.50***	-0.16
Object Assembly+	0.45***	-0.37**	0.43***	-0.27*
Rey Copy (max=36)	0.61***	-0.67***	0.45***	-0.40**
Rey Recall (max=36)	0.53***	-0.42***	0.45***	-0.24
Logical Memory (max=23)	0.52***	-0.35**	0.48***	-0.06
Assoc. Learning (max=21)	0.33**	-0.20	0.29*	0.15
Word Fluency	0.16	-0.34**	0.21	-0.21
Graded Naming (max=30)	0.37**	-0.42***	0.40**	-0.29*
EP Threshold (ms)	-0.67***	- - -	-0.55***	- - -
EP Movement (max=32)	- - -	-0.67***	- - -	-0.52***
Visual Search (ms)	-0.63***	0.66***	-0.57***	0.58***
Word Recognition (ms)	-0.42***	0.57***	-0.48***	0.59***
Simple RT Decision$	-0.42***	0.20	-0.50***	0.15
Simple RT Movement$	-0.56***	0.51***	-0.44**	0.31*
Choice RT Decision$	-0.45***	0.22	-0.54***	0.20
Choice RT Movement$	-0.45***	0.40**	-0.37**	0.24

+ = Raw Scores $ = scores are in ms EP = Event Perception GCS = Glasgow Coma Scale PTA = Post-traumatic Amnesia RT = Reaction Times Assoc. Learning = Associate Learning

TABLE 5.5 Partial correlations controlling for age between PTA and test performance for all patients.

TEST	All Patients N=47
NART	-0.07
GCS	-0.32*
Similarities	-0.20
Digit Span	-0.16
Vocabulary	-0.18
Digit Symbol	-0.45***
Block Design	-0.39*
Object Assembly	-0.39**
Rey Copy	-0.47***
Rey Recall	-0.38**
Logical Memory	-0.50***
Assoc. Learning	-0.12
Word Fluency	-0.16
Graded Naming	-0.10
EP Threshold	0.27*
EP Movement	-0.58***
Visual Search	0.40**
Word Recognition	0.45***
Simple RT Decision	0.58***
Simple RT Movement	0.53***
Choice RT Decision	0.61***
Choice RT Movement	0.54***

Level of significance: * = $p < 0.05$ ** = $p < 0.01$ *** = $p < 0.001$

EP = Event Perception GCS = Glasgow Coma Scale PTA = Post-traumatic Amnesia RT = Reaction Times Assoc. Learning = Associate Learning

TABLE 5.7 Spearman correlation coefficients between the deepest abnormality detected on late MRI for an earlier study[1], early and late MRI for the current study and neuropsychological test performance.

TEST	EARLY MRI N=25	LATE MRI N=25	EARLY MRI N=46	LATE MRI N=47
Similarities	-0.24	-0.58***	-0.26*	-0.35*
Digit Span	-0.21	-0.24	-0.22	-0.43***
Vocabulary	-0.43*	-0.48**	-0.19	-0.25*
Digit Symbol	-0.14	-0.73***	-0.28*	-0.37**
Block Design	-0.21	-0.86***	-0.42***	-0.47***
Object Assembly	-0.21	-0.73***	-0.22	-0.36**
Rey Copy	-0.10	-0.50**	-0.31*	-0.35**
Rey Recall	0.04	-0.58***	-0.22	-0.42***
Logical Memory	-0.09	-0.51**	-0.17	-0.14
Assoc. Learning	-0.02	-0.53**	-0.20	-0.14
Word Fluency	-0.26	-0.56**	-0.24*	-0.26*
Graded Naming	- - -	- - -	-0.33**	-0.37**
EP Threshold	- - -	- - -	0.32*	0.16
EP Movement	- - -	- - -	-0.37**	-0.44***
Visual Search	- - -	- - -	0.30*	0.46***
Word Recognition	- - -	- - -	0.39**	0.44***
Simple RT Decision	- - -	- - -	0.17	0.26*
Simple RT Movement	- - -	- - -	0.20	0.31*
Choice RT Decision	- - -	- - -	0.22	0.28*
Choice RT Movement	- - -	- - -	0.17	0.27*

Level of significance: * = p< 0.05 ** = p< 0.01 *** = p< 0.001
EP = Event Perception Assoc. Learning = Associate Learning

[1] Wilson JTL, Wiedmann KD, Hadley DM, Condon B, Teasdale GM & Brooks DN. (1988). Early and late magnetic resonance imaging and neuropsychological outcome after head injury. J. Neurology, Neurosurgery & Psychiatry, 51, 391-396.

Table 5.6 Distribution of patients according to deepest abnormality found for early and late MRI.

Distribution in the study by Wilson et al. (1988a):

Lesion Category	I	II	III	IV
Early MRI N = 25	2 = 8%	6 = 24%	10 = 40%	7 = 28%
Late MRI N = 25	5 = 20%	3 = 12%	5 = 20%	12 = 48%

Distribution in the current study:

Lesion Category	I	II	III	IV
Early MRI N = 46	4 = 9%	5 = 11%	17 = 37%	20 = 43%
Late MRI N = 47	9 = 19%	13 = 28%	8 = 17%	17 = 36%

Table 5.8 Abbreviations used for Regions of Interest (ROIs)

OFL	orbitofrontal left	OFR	orbitofrontal right
FRL	frontal left	FRR	frontal right
ATL	anterior temporal left	ATR	anterior temporal right
PTL	posterior temporal left	PTR	posterior temporal right
PAL	parietal left	PAR	parietal right
OCL	occipital left	OCR	occipital right

GANG	basal ganglia
STEM	brainstem
CC	corpus callosum
CB	cerebellum

Table 5.9 LATE MRI: Distribution of patients with low scores and high scores on Event Perception Movement with deep structure abnormalities.

	Deep structure abnormalities	
	YES	NO
HIGH	19%	81%
EP Movement score		
LOW	58%	42%

Chi^2= 7.62 p<0.006; Pearson's/Spearman's r= 0.41 p<0.0025

Table 5.10 LATE MRI: Distribution of patients with low scores and high scores on Event Perception Movement with hemispheric abnormalities.

		Hemispheric abnormalities	
		YES	NO
EP Movement score	HIGH	89%	11%
	LOW	74%	26%

Chi^2= 1.79 ns; Pearson's/Spearman's r= -0.20 ns

Table 5.11 LATE MRI: Distribution of patients with low scores and high scores on Event Perception Threshold with deep structure abnormalities.

	Deep structure abnormalities	
	YES	NO
EP Threshold score HIGH	36%	64%
LOW	33%	67%

Chi^2= 0.05 ns; Pearson's/Spearman's r= 0.03 ns

Table 5.12 LATE MRI: Distribution of patients with low scores and high scores on Event Perception Threshold with hemispheric abnormalities.

		Hemispheric abnormalities	
		YES	NO
EP Threshold score	HIGH	86%	14%
	LOW	79%	21%

Chi^2= 0.41 ns; Pearson's/Spearman's r= 0.09 ns

Table 5.13: Pearson correlations between number of abnormal ROIs and performance on Event Perception Movement and Event Perception Threshold.

	EP Move		EP Threshold	
	Early	Late	Early	Late
All Patients	-0.30*	-0.32*	0.22	0.26*
Low Move	-0.29	-0.40*	0.24	0.28
High Move	-0.47**	-0.43*	0.24	0.36*

TABLE 5.14: Spearman correlations showing interrelation of ROIs for all patients - early and late MRI.

ROI	OFL	OFR	FRL	FRR	ATL	ATR	PTL	PTR	PAL	PAR	OCL	OCR	GANG	STEM	CC	CB
OFL	-	.62***	.37*		.59***	.42**	.39**									
OFR	.64***	-				.46**										
FRL	.45**	.48***	-	.54***												
FRR		.55***	.52***	-												
ATL	.41**				-		.44**				.35*			.37*		
ATR	.44**	.60***				-		.45**				.33*				
PTL	.34*				.50***		-									
PTR						.45**		-				.45**				
PAL									-	.46**						
PAR						.35*				-						
OCL											-					
OCR												-				
GANG													-			
STEM				.43**										-		
CC															-	.38**
CB		.35*														-

Level of significance: * = p<0.01 ** = p<0.001 *** = p<0.0001 Upper diagonal: Early MRI Lower diagonal: Late MRI

TABLE 5.15 EARLY MRI: Spearman and Partial correlations between abnormalities found in any one ROI and performance on EP Movement and Threshold for all patients (N=47)

	Spearman Corrs		Partial Corrs	
ROI	EP Move	EP Threshold	EP Move	EP Threshold
OFL	-0.22	0.26*	-0.13	0.19
OFR	-0.12	0.08	-0.14	-0.7
FRL	-0.14	0.08	-0.10	0.11
FRR	-0.07	-0.06	-0.03	0.21
ATL	-0.16	0.36**	0.08	-0.01
ATR	-0.23	0.28*	-0.32*	0.21
PTL	0.01	0.15	0.29!	-0.15
PTR	-0.31*	0.32*	-0.30*	0.27*
PAL	-0.18	0.11	-0.06	0.10
PAR	-0.09	0.05	-0.20	0.12
OCL	-0.03	0.14	0.05	-0.08
OCR	-0.16	0.13	-0.03	-0.10
GANGLIA	0.07	0.04	-0.15	-0.02
BRAINSTEM	-0.07	0.20	0.07	0.26
CORPUS CALL.	-0.13	-0.13	-0.40**	0.08
CEREBELLUM	-0.24*	0.12	-0.13	0.20

Level of significance: * = $p < 0.05$ ** = $p < 0.01$ *** = $p < 0.001$! = $p < 0.05$ counter to predicted direction

EP = Event Perception Corpus Call. = Corpus Callosum
Covariates were age for EP Movement and age and NART for EP Threshold

TABLE 5.16 LATE MRI: Spearman and Partial correlations between abnormalities found in any one ROI and performance on EP Movement and Threshold for all patients (N=47)

	Spearman Corrs		Partial Corrs	
ROI	EP Move	EP Treshold	EP Move	EP Threshold
OFL	-0.23	0.24*	-0.08	-0.03
OFR	-0.20	0.16	-0.08	0.01
FRL	-0.09	0.08	-0.14	0.17
FRR	-0.02	-0.09	-0.16	0.07
ATL	-0.09	0.25	-0.06	-0.09
ATR	-0.29*	0.38**	-0.27*	0.30*
PTL	0.18	0.12	0.04	-0.11
PTR	-0.28*	0.30*	-0.35*	0.26
PAL	-0.01	-0.20	-0.29*	-0.11
PAR	-0.10	0.15	-0.26*	0.12
OCL	0.11	-0.12	-0.05	-0.01
OCR	-0.17	0.15	-0.10	-0.06
GANGLIA	-0.20	0.10	-0.08	0.02
BRAINSTEM	-0.14	0.01	-0.15	-0.10
CORPUS CALL.	-0.34*	-0.02	-0.25	0.25
CEREBELLUM	-0.18	0.19	-0.26*	0.15

Level of significance: * = $p < 0.05$ ** = $p < 0.01$ *** = $p < 0.001$
EP = Event Perception Corpus Call. = Corpus Callosum

Covariates were age for EP Movement and age and NART for EP Threshold

Table 5.17 Individual head injury patients showing double dissociations on Event Perception Movement and Event Perception Threshold.

	UNIMPAIRED		
	EP Movement	EP Threshold	
EP Movement	12	30 ms	Patient 1*
	17	50 ms	Patient 2
IMPAIRED			
EP Threshold	68 ms	26	Patient 3

	CONTROL VALUES		
	MEAN	SD	NORMAL RANGE
EP Move (max=25)	29.1	3.6	25.5 - 32.0
EP Thresh (ms)	39	10	29 - 49

* Difference = 4 SDs.

Table 5.1 Schematic drawing of the brain to indicate regions of interest used for neuroradiological analysis.

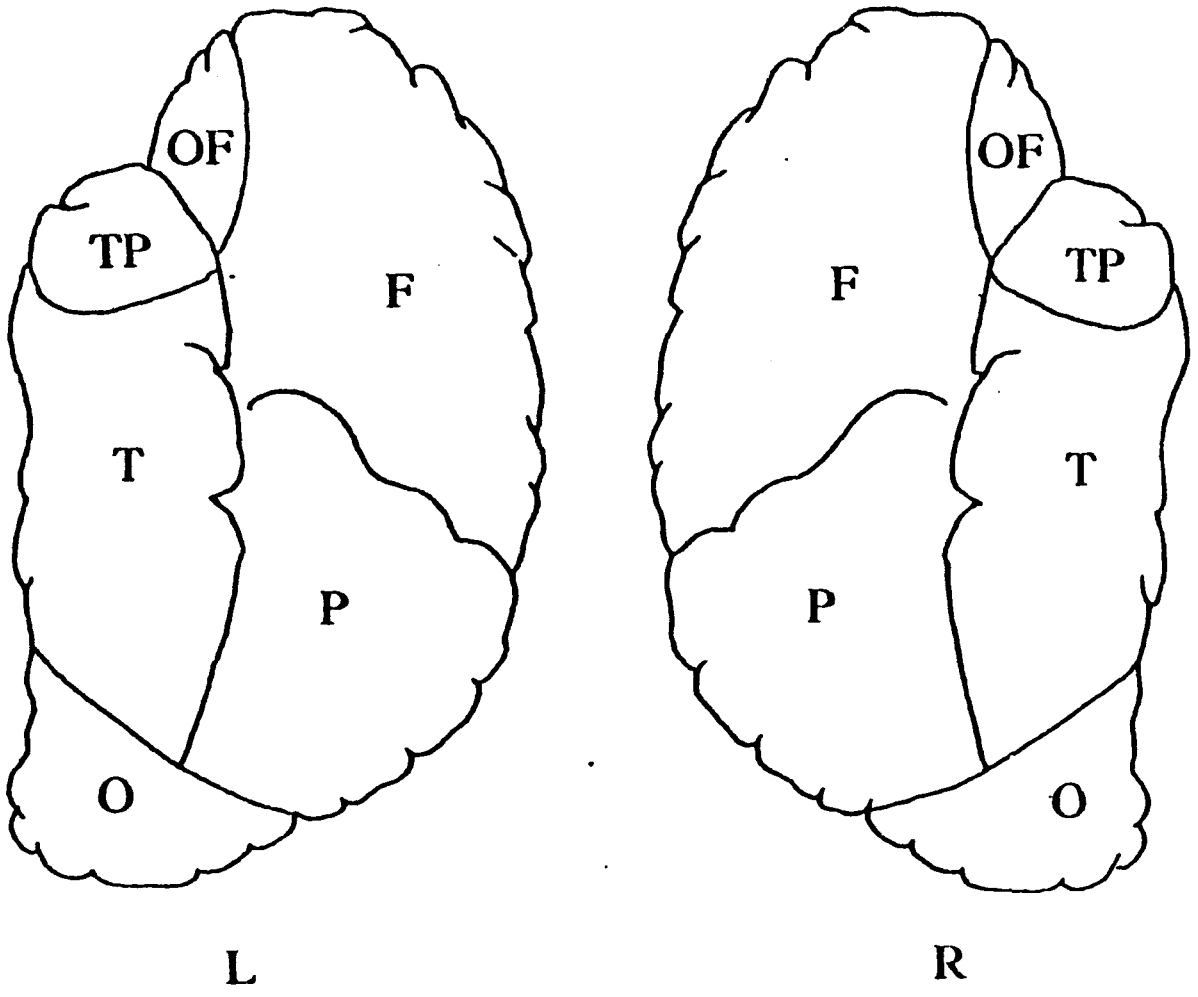


Figure 5.2 Early and late MRI: Distribution of patients with abnormalities for each ROI.

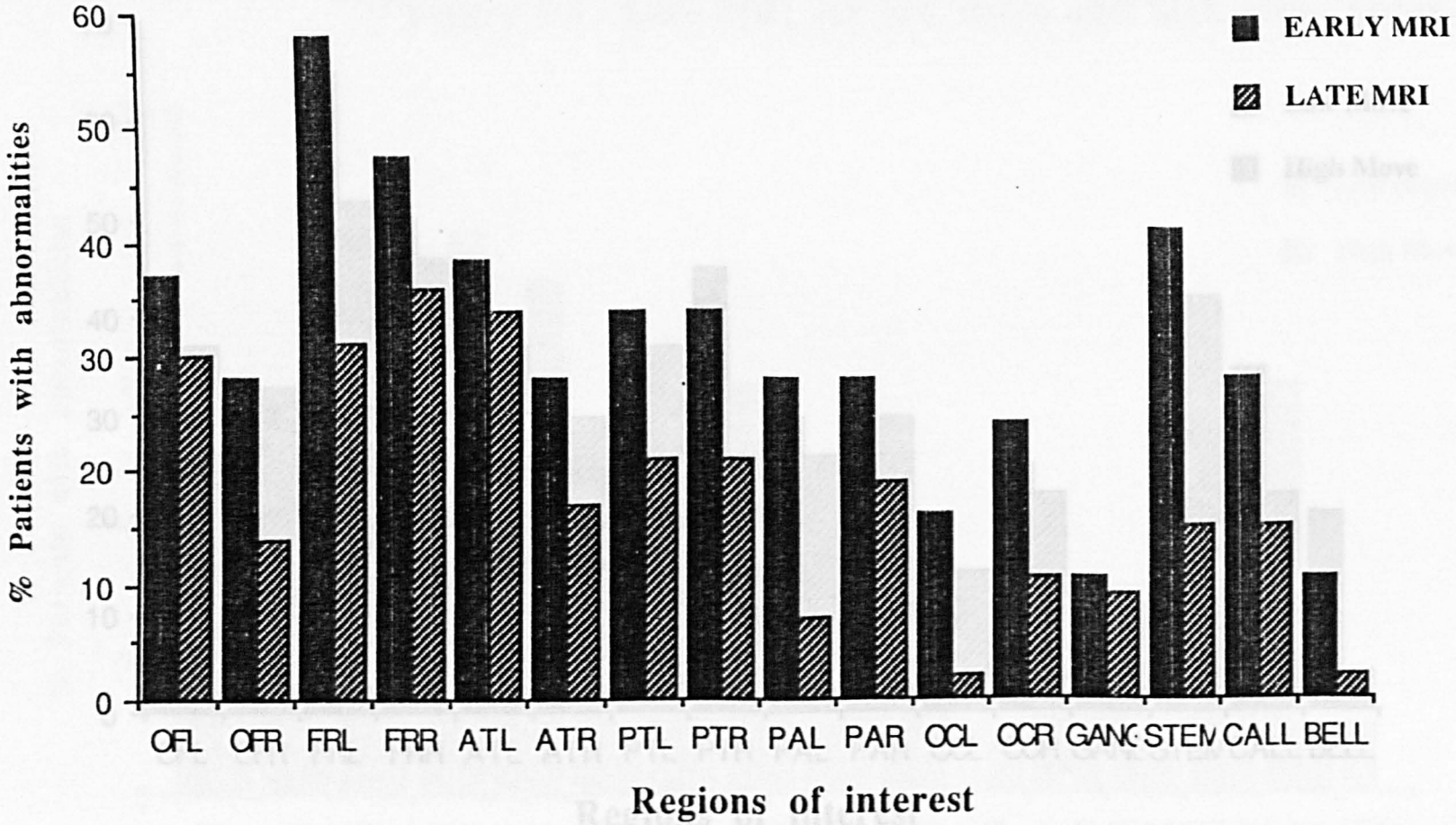


Figure 5.3 Early MRI for low move and high move group

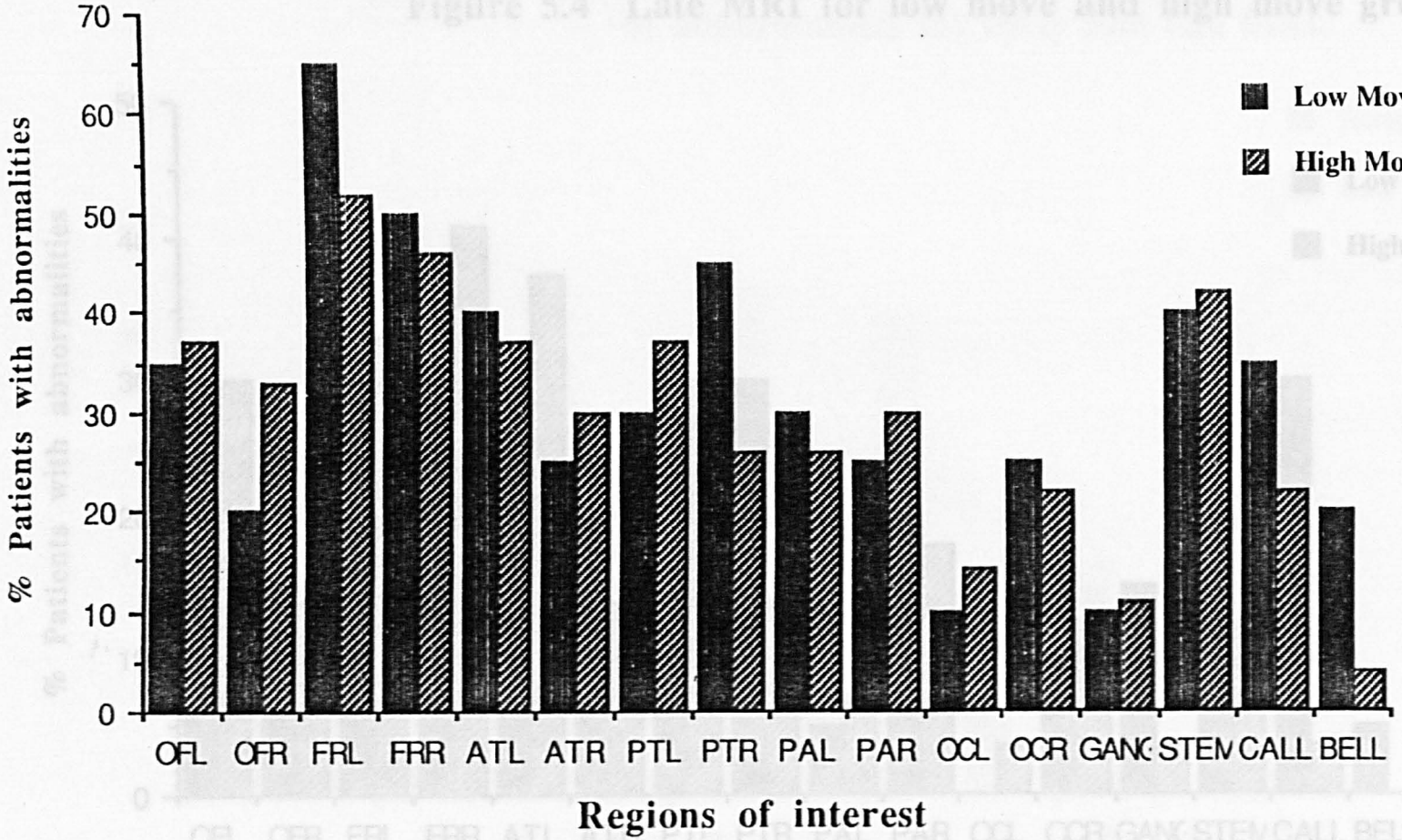


Figure 5.4 Late MRI for low move and high move group

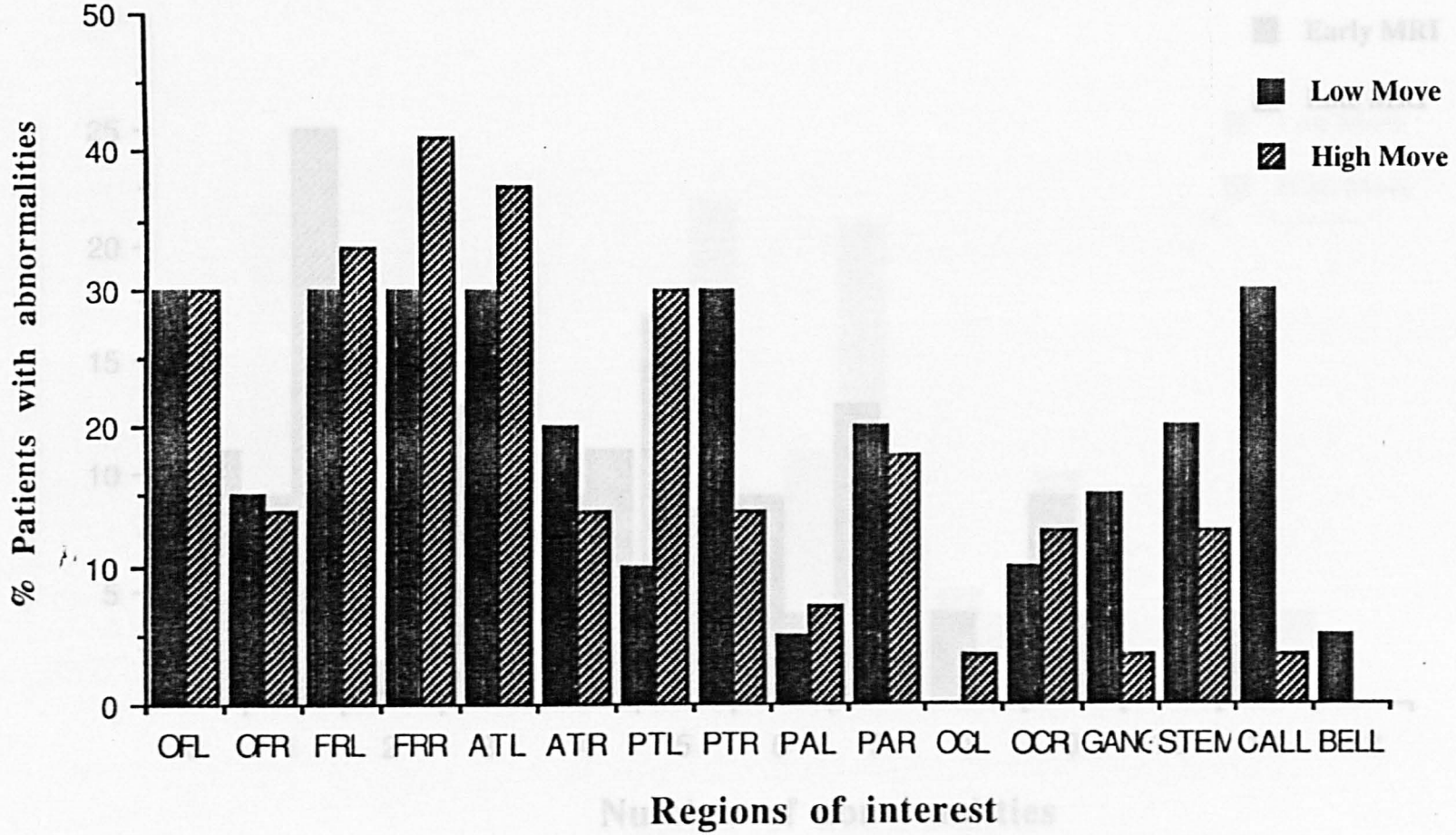


Figure 5.5 Distribution of patients with total number of abnormalities for early and late MRI.

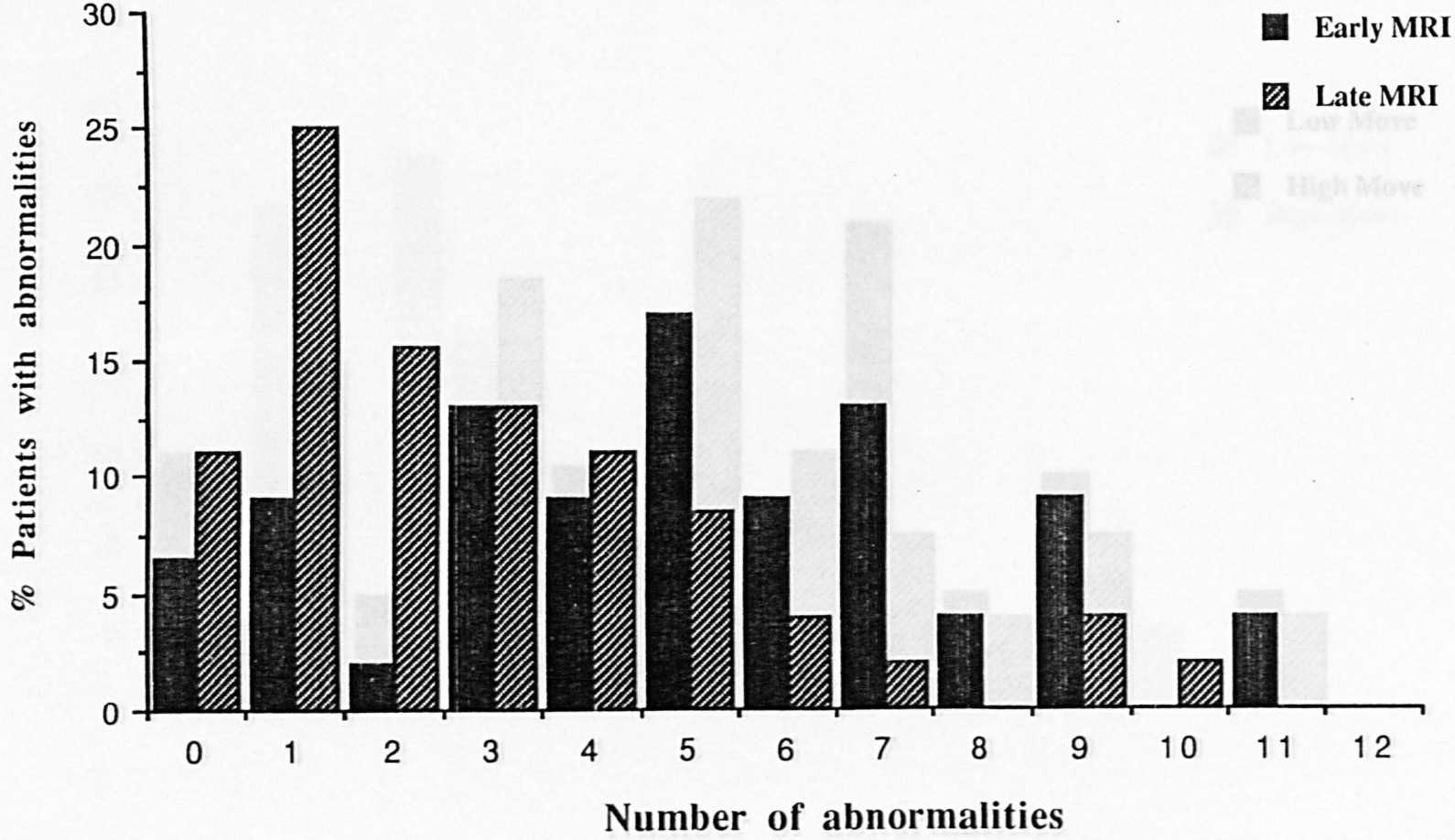


Figure 5.6 Distribution of patients with total number of abnormalities for EARLY MRI for low and high move group

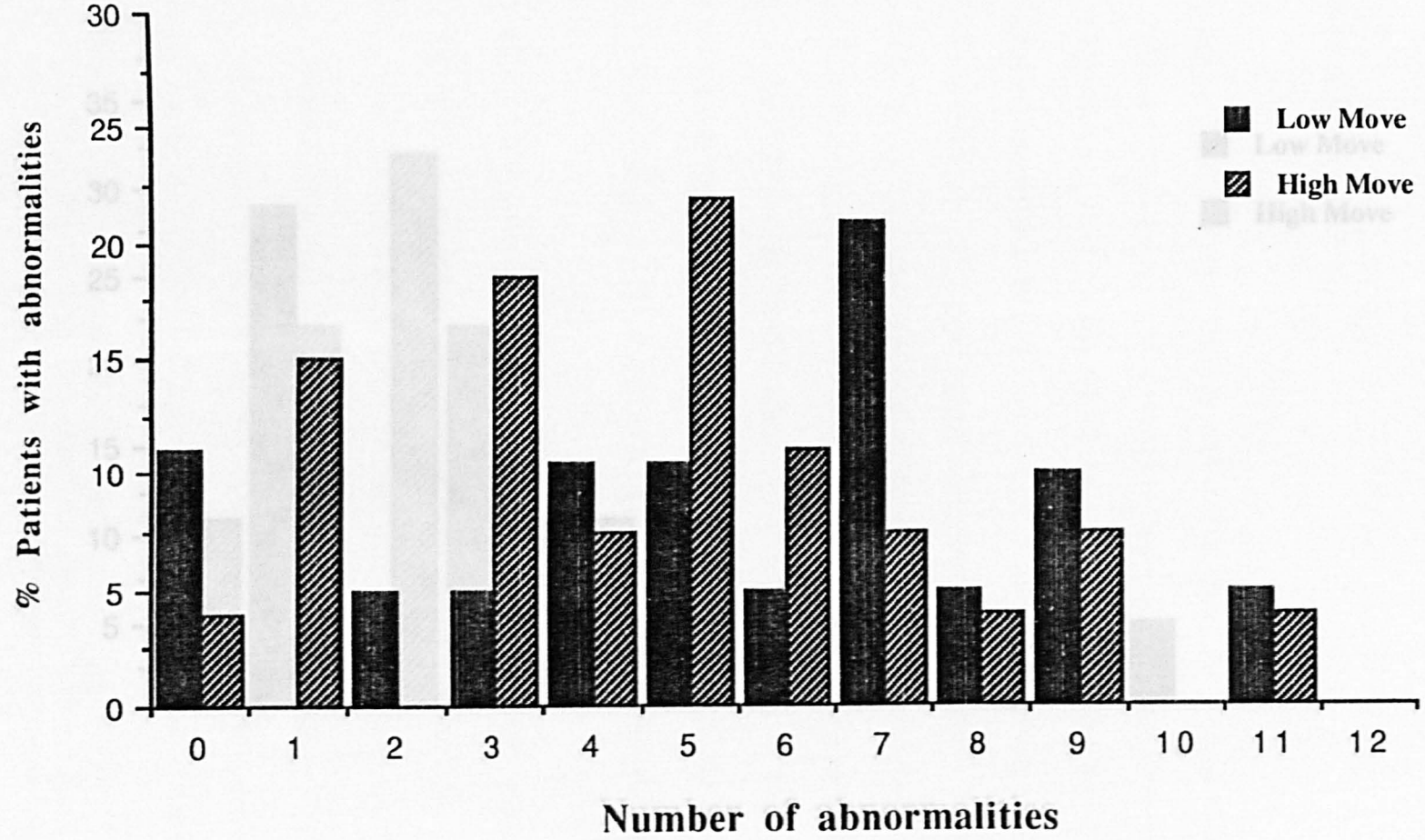
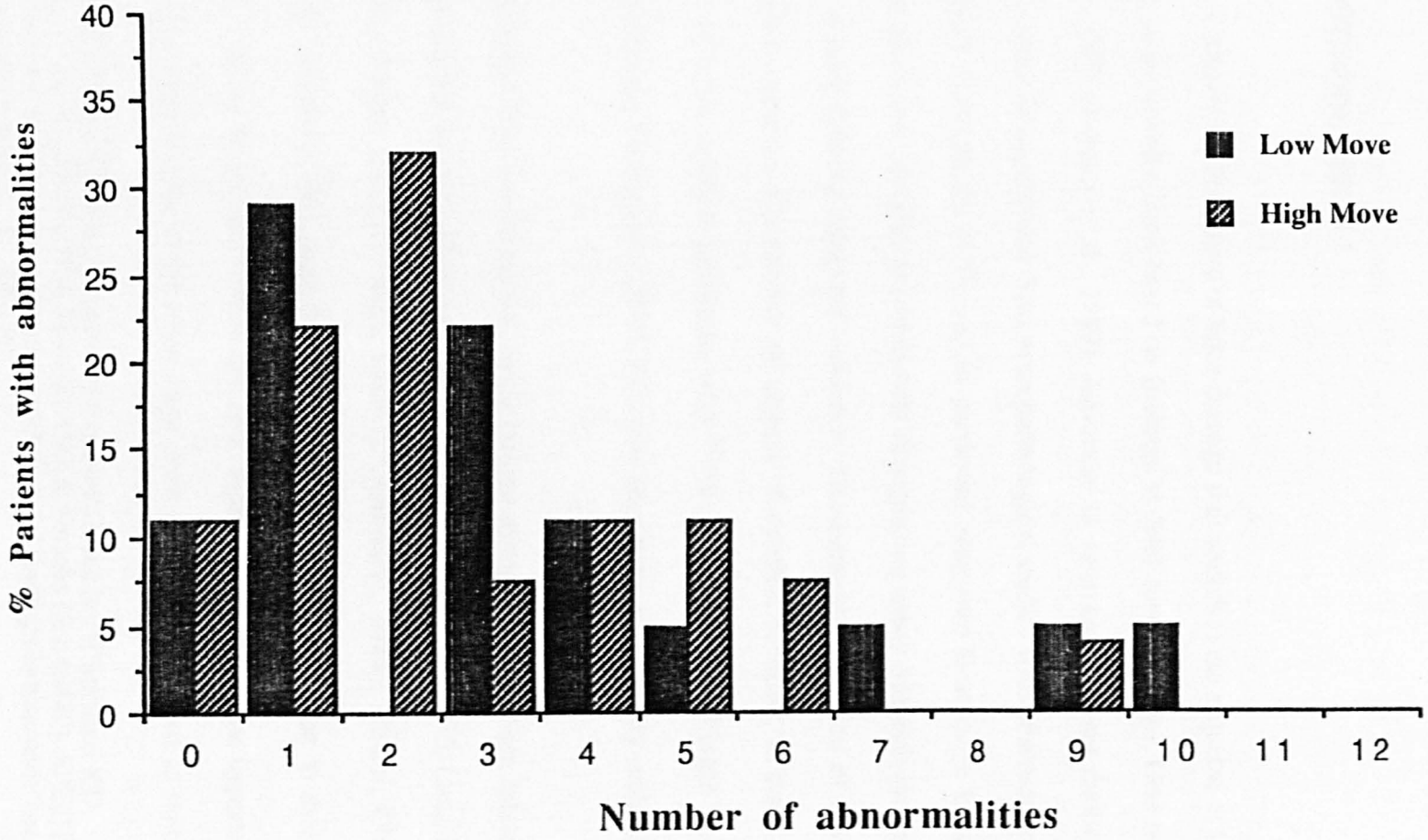


Figure 5.7 Distribution of patients with total number of abnormalities for LATE MRI for low and high move group.



6.0 Cerebral bloodflow and visual event perception after traumatic brain damage.

6.1 INTRODUCTION.[1]

Concepts concerning the nature of brain damage that underlies the sequelae of head injury have, until recently, been based on findings in fatal cases (Adams, Graham & Gennarelli, 1985; Graham et al., 1989). Advances in neuroimaging are making it possible to replace extrapolations from neuropathological studies with observations in life. Computed Tomography (CT), and in particular Magnetic Resonance Imaging (MRI), have given new insights into structural changes, but many dynamic processes can occur without leaving structural evidence. Tomographic detection of isotope tracers enables mapping of a number of aspects of cerebral function; in particular assessment of local cerebral perfusion with ^{99m}Tc HM-PAO and Single Photon Emission Computed Tomography (SPECT) is now becoming more widely available.

Cerebral blood flow measurements, using isotope techniques have been related to the sequelae of head injury in several studies (Gobiet, Grote & Bock, 1975; Langfitt & Obrist, 1981; Obrist, Langfitt, Jaggi, Cruz & Gennarelli, 1984). Uzzell, Obrist, Dolinskas & Langfitt (1986) used the ^{133}Xenon intravenous technique to measure hemispheric CBF in 42 patients with severe head injury. They found that hyperaemia and intracranial hypertension in the acute stage were significantly related to outcome

[1] A version of this chapter has previously been published in: Wiedmann KD, Wilson JTL, Wyper D, Hadley DM, Teasdale GM & Brooks DN. (1989). SPECT cerebral bloodflow, MR imaging and neuropsychological findings in traumatic head injury. **Neuropsychology, 3,** 267-281.

and neuropsychological performance at follow-up. All patients suffered from neuropsychological dysfunction but patients with hyperaemia in the acute stage showed greater impairment of overall intellectual and memory functions than those without intracranial pressure elevations.

SPECT in conjunction with a rotating gamma camera has become available in recent years along with the development of photon emitting radiopharmaceuticals. Initial drawbacks were the lack of reliable radioligands and insufficient spatial resolution - that is regions of interest (ROIs) were often restricted to entire cerebral hemispheres. For single photon imaging, ^{99m}Technetium labelled substances have been shown to offer significant advantages (Ell et al., 1985). The tracer ^{99m}Tc-hexamethyl propyleneamine oxime (HM-PAO) in combination with a good tomographic imaging device can be used to produce images of cerebral blood flow distribution with transverse resolution of less than 10mm and a slice thickness of 13mm. Medial structures such as the caudate nucleus can be identified on the imager. Uptake of HM-PAO is very rapid and it stays trapped for many hours, allowing injection at a critical moment, for example, during an operation. Imaging may be postponed for several hours. The fraction of the administered dose which is retained by the brain reaches a peak after 40 to 50 seconds, then decreases by 10 per cent within the first ten minutes and subsequently by only 0.4 per cent per hour (Andersen, Friberg, Schmidt & Hasselbach, 1988). Bullock, Park, McCulloch, Patterson & Wyper (1989) used a double label autoradiographic technique to compare the spatial distribution of ^{99m}Tc HM-PAO with rCBF determined by ^{14}C iodoantipyrine autoradiography in the rat's brain and have shown that the distribution of HM-PAO

was in good agreement with regional cerebral perfusion.

Abdel-Dayem et al. (1987) studied thirteen head injury patients using HM-PAO SPECT and CT and found SPECT to be superior at detecting lesions. SPECT detected more lesions than CT, and made it possible to identify some lesions earlier. A pilot study conducted in our laboratory suggested that CBF abnormalities might follow structural lesions more closely in focal brain damage, whereas abnormalities detected on SPECT and MRI seemed to vary considerably more in their location in a group of patients with diffuse brain damage (Wiedmann, Patterson, Hadley, Teasdale, Wilson & Brooks, 1989).

The current study aimed to examine the value of SPECT in detecting abnormalities in head injury and to explore whether these related to impaired neuropsychological test performance particularly on visual event perception tasks. The purposes of the current study were to find out if SPECT with HM-PAO would detect patterns of cerebral blood flow characteristic of focal and diffuse traumatic brain damage; provide relevant information not demonstrated by structural imaging, establish relationships between CBF-SPECT abnormalities and neuropsychological impairment, and show specific patterns of CBF abnormalities related to impairment on the visual event perception tasks.

6.2 PATIENTS AND METHODS.

6.2.1 Subjects.

Two groups of patients were studied: a group of sixteen patients for whom the primary clinical diagnosis was diffuse or contusional brain damage and a group of eight patients who had space occupying lesions. Patients were classified employing a rating scale which weighted the contribution of three intracranial lesion categories to a patient's condition. These categories were: (1) diffuse shearing lesion, (2) contusional lesion, and (3) space occupying mass lesion. All patients had been referred from a primary surgical unit. Patients had MRI and CBF-SPECT investigations and neuropsychological assessment at follow-up 5-12 months after injury (median 6 months). Patients were compared for neuropsychological test performance with a control group of 16 orthopaedic outpatients who had sustained bone fractures but without involvement of the head and who had not sustained a head injury at any time before (see Table 6.1). Apart from an additional 2 subjects employed in the comparison between focal and diffuse patients the control group was identical to that in the previous chapter.

Diffuse group. In this group of 16 patients (12 male) 9 patients had been involved in road traffic accidents and the remaining 7 had sustained falls, three from a considerable height. The age range was 17 to 64 years with a mean of 38.6 years. Glasgow Coma Score (GCS) (Teasdale, Murray, Parker & Jennett, 1979) on admission ranged from 3 to 14 (mean = 10.0) (Table 6.1). The range of Post Traumatic Amnesia (PTA) determined by interview was 0 to 3 months (median = 23.5

days) (tables 6.1 and 6.2). Table 6.2 shows that the distribution of patients with diffuse brain damage differed considerably with respect to GCS and PTA from the focal group. There were more patients in the diffuse group who had a lower GCS on admission indicating deeper coma than in the focal group. Almost two thirds of the patients in the diffuse group had a PTA of more than 15 days. Ten patients sustained a skull fracture; three patients had undergone an operation and 13 had been treated conservatively. Follow-up took place five to twelve months (median=190 days) after injury. All patients were right handed both before and after the accident. Only two patients were working at the time of the follow-up assessment.

Focal group. In this group of eight patients (one female) seven had sustained falls (six of them under the influence of alcohol) and one was the victim of an assault. The age range was 24 to 62 years with a mean of 53.1 years. GCS on admission ranged from 10 to 15 (mean=12.1) (tables 6.1 and 6.2). PTA ranged from 4 to 35 days (median=8 days) (tables 6.1 and 6.2). Four patients sustained a skull fracture and two had undergone surgery. Follow-up took place 3 to 11 months (median=207 days) after injury. Six patients were right handed, one left handed and one ambidextrous. Three patients were working at the time of the follow-up assessment.

6.2.2 Neuroimaging.

Magnetic resonance imaging was carried out on a Picker Vista 1100 0.15 Tesla resistive MR system operating at 6.38 MHz. An initial 2 cm thick spin echo (SE 200/40) pilot image in the sagittal or coronal plane was used to determine the position

of 16 slices each 8 mm thick for a T2 weighted spin echo sequence (SE 2000/80), and an 8 slice T1 weighted inversion recovery sequence (IR 1660/400/ 40) in the axial plane. Total acquisition time was 45 min. Cerebral blood flow investigations were carried out on a Novo 810 Tomograph following intravenous injection of 600 mBq of HM-PAO (Ceretec, Amersham Int.). Patients were instructed to keep their eyes closed both during the injection and for the following 20 s to minimize variations in visual stimulation. SPECT images were acquired in the orbito-meatal plane with 10mm spacing starting just above the base of the skull. Imaging time required for each slice was 3 min totalling to 24 min for 8 slices.

Images from both investigation modalities were analysed by an experienced neuroradiologist and a clinical physicist who had no access to neuropsychological test information. For MRI 12 mutually exclusive regions of interest in the cerebral hemispheres were categorized according to whether an abnormality was present or not. For the analysis of SPECT abnormalities 12 regions of interest were employed which corresponded as closely as technically possible to those for MRI. SPECT ROIs were rated as indicating (1) normal flow (2) decreased flow (3) zero or near to zero flow, and (4) increased flow (cf. figure 5.1).

6.2.3 Neuropsychological assessment.

Neuropsychological assessment was carried out within 48 hours of follow-up neuroimaging. The neuropsychological test battery consisted of 24 measures. General intellectual ability was assessed employing six subtests from the Wechsler Adult

Intelligence Scales (Wechsler, 1955): Similarities, Digit Span and Vocabulary from the Verbal Scale, and Digit Symbol, Block Design and Object Assembly from the Performance Scale. The National Adult Reading Test (NART) (Nelson, 1981) was used as an estimate of premorbid IQ. For assessment of verbal memory and learning the Logical Memory and Associate Learning subtests from the Wechsler Memory Scales (WMS; Wechsler, 1945) were used. Verbal processing and proficiency were assessed on a Word Fluency Test (Borokowski, Benton & Spreen, 1967), the Graded Naming Task (McKenna & Warrington, 1983), and a computerised Word Recognition task (Wilson, Wiedmann, Phillips & Brooks, 1988b). In addition patients were assessed on Simple and Choice Reaction Times which were divided into decision and movement times (Van Zomeren, 1981), and for visual processing on a computerised visual search task and two computerised visual event perception tasks (Wilson et al., 1988b). Visual memory and learning was assessed by the Rey Complex Figure Task (Rey, 1941) and computerised visual span and learning tasks (Wilson, Wiedmann, Hadley & Brooks, 1989).

6.3 RESULTS.

6.3.1 Neuroimaging.

Diffuse group. Twelve (75%) patients had abnormalities on MRI and 14 (87.5%) on SPECT. Only one patient had no abnormalities on either MRI or SPECT. Over 70% of all patients with bloodflow abnormalities had abnormalities in more than one area on SPECT. Four patients had areas of increased flow but the most frequent abnormality visualized was slightly decreased flow (18 regions). Table 6.3 shows the areas in which abnormalities were found on MRI and SPECT in individual patients. Although the total number of abnormalities detected in the 12 hemispheric areas did not differ greatly on either imaging modality (MRI=44; SPECT=36) there was considerable variation in the actual location of abnormalities. SPECT and MRI abnormalities coincided in 18 locations but differed in another 18 ROIs for SPECT and in 26 ROIs for MRI. Figure 6.1 allows comparison between MRI and SPECT for different regions of interest; left and right ROIs are collapsed in this figure. SPECT identified abnormalities in the parietal lobes in more patients whereas MRI detected abnormalities in more patients in the orbito-frontal and anterior temporal regions.

Focal group. All eight patients showed abnormalities on both SPECT and MRI. However, there were again differences in the location of abnormalities. Twenty-four abnormalities were detected on SPECT and 29 on MRI. SPECT and MRI abnormalities coincided in 13 locations but differed in 11 for SPECT and 16 for MRI (see Table 6.3). Figure 6.2 gives a comparison of SPECT and MRI for the focal group. For the focal group there were more patients showing abnormalities on SPECT

in the orbito-frontal and frontal areas while MRI detected abnormalities in more patients in anterior temporal and parietal areas.

6.3.2 Neuropsychology.

Tables 6.4 an 6.5 give the mean scores and t-test differences on neuropsychological performance for the diffuse, the focal and the control group. The diffuse group showed statistically significant differences on all but two tasks (Associate Memory and Path Span) compared to the control group. The focal group showed significant differences on 18 of the 24 measures. However, when comparing the head injury patients and orthopaedic controls, the NART yielded a statistically significant difference at the $p< 0.01$ level suggesting differences in premorbid IQ for both groups.

Diffuse group. Since patients in this group differed significantly from controls on NART errors an ANCOVA was therefore conducted controlling for NART differences. With correction, 13 out of the 24 measures remained statistically significant. Impaired performance was mainly found for tests requiring speed and rapid information processing. The diffuse group was significantly impaired on all Reaction Time measures and particularly on decision time, the cognitive component, in the four choice condition. Decision time in this condition showed an increase of 70 msecs when compared to decision time for the simple condition; although some rise in reaction time is expected reflecting the increase in complexity, this was more than twice the time observed in the controls (patients: 70 msecs, controls: 32 msecs; difference patients/controls: $t=-2.7$ $p<0.01$). Information processing speed was also

significantly impaired on the Visual Search task and the Digit Symbol task. Patients were impaired on short-term memory span procedures: Digit Span and its visual analogues Pattern and Path Span, suggesting a deficit in attention. On pattern span patients recalled only 7.6 blocks on average compared to 9.4 for controls. On Path Span, although relatively small in absolute terms, scores were consistently lower for the patients (patients: 4.9; controls: 5.3). Furthermore patients were impaired on a measure of visual learning, Pattern Learning Items, which is the visual long-term memory analogue of Pattern Span (see Wilson et al., 1989). Differences on measures of verbal memory and learning disappeared when controlling for NART differences but there were highly significant differences on Word Fluency.

Focal group. In addition to NART differences age was also significantly higher when comparing the focal group with orthopaedic controls. When controlling for age and NART differences the focal group showed impaired performance on three out of the twenty-four measures. Significant impairment was found on Digit Span, Word Recognition which requires rapid processing of visually presented verbal information and Visual Search. All three tests required rapid processing of information and/or sustained concentration.

When comparing the focal and the diffuse group there was no significant difference on the NART but the age difference (see Table 6.1) reached statistical significance at the $p < 0.01$ level. Differences in test performance between the two head injured groups were only found for Digit Span (Focal=9.4; Diffuse=11.2; $p < 0.05$; WAIS age corrected scores).

6.3.2.1 Performance on Event Perception tasks.

All 16 patients in the diffuse group had been evaluated on Event Perception tasks but only one patient in the focal group. The following analysis was therefore based entirely on findings from the diffuse group who formed a subsample of the patients studied in the previous chapter. Since only 14 controls had been assessed on Event Perception tasks t-tests were repeated and the revised values are shown in table 6.6. Patients now performed significantly worse on 12 of the remaining 16 tasks. Groups also differed significantly on age and premorbid IQ estimates with patients being older and scoring lower on the NART. Scores on all assessment procedures were lower than in the previous study suggesting greater impairment in this group which was probably a result of selecting patients with respect to diffuse damage.

Table 6.7 shows Pearson correlations between the two Event Perception tasks and all other measures for the whole group. No significant relationships were found for Event Perception Movement with age, NART or GCS but PTA was significantly related at $r= -0.45$ $p<0.05$. Event Perception Threshold was significantly related to age at $r= 0.44$ $p<0.05$ but to none of the other demographic variables. Significant relationships were found with Event Perception Movement and 14 of the 20 measures and the strongest relationships were with RT measures. Nine measures were significantly related with Event Perception Threshold, the strongest being Visual Search and Word Recognition at $r=0.81$ $p<0.001$ and $r=0.76$ $p<0.001$. Since Event Perception Threshold was significantly related with age and closely but not significantly with NART a partial correlation procedure was used to control for these variables. After correction 11 measures were significantly related with Event

Perception Movement and 5 with Event Perception Threshold. The relationship between PTA and Event Perception Movement was now highly significant at $r=0.78$ $p<0.001$.

6.3.3 Neuropsychology and Cerebral Blood Flow.

Diffuse group. For a regional analysis of SPECT findings areas were coded as having normal or abnormal flow and patients with CBF abnormalities in specific ROIs were compared with patients not showing an abnormality. For this analysis only those tests were used which showed reliable differences from the control group after correction for NART and age differences. To illustrate relationships with traditional memory tests findings for Logical Memory and Rey Figure copy and recall were also included. The Mann-Whitney U statistic was computed for tests and ROIs comparing the mean rank of patients with and without an abnormality in a specific region (table 6.8). Differences in rank order were statistically significant in 11 cases. Two tests, Word Fluency and Event Perception Threshold, indicated better performance for patients with abnormalities. Performance on Digit Span, Path Span and on Reaction Time measures did not seem to be related to CBF defects in any particular ROI. Digit Symbol, Rey Figure copy and recall, and Visual Search were related to CBF abnormalities in the right anterior temporal area. In addition Rey Figure recall was related to abnormalities in the left orbito-frontal and right posterior temporal areas. Pattern Span and Pattern Learning Items were related to CBF defects in the left and right orbito-frontal area; Pattern Learning also showed a relationship with abnormalities in the right posterior temporal and parietal areas. Nonverbal tests showed a consistent relationship with the right anterior temporal regions whereas

performance on the Logical Memory test was related to left anterior temporal functioning. Pattern Span and Pattern Learning Items showed in addition a relationship with both left and right orbito-frontal regions and with right posterior temporal and parietal areas.

An analysis collapsing results into a left-right dichotomy to look at lateralisation of function or dividing patients into anterior versus posterior groups rendered inconsistent results. Only Rey Figure recall and Pattern Learning Items showed significant relationship but they were almost equally strongly correlated for left versus right as for anterior versus posterior regions.

Focal group: For the focal group only one of the three measures which continued to show statistically significant impairment after correction for age and NART differences was systematically related to CBF defects: Word Recognition showed a relationship with CBF defects in the right frontal area. A relationship between Pattern Span and the right posterior temporal region could also be demonstrated: performance on Pattern Span was actually poorer than for the diffuse group (Focal=7.3, Diffuse=7.6; Control=9.4).

Event Perception groups. Only two ROIs showed statistically significant relationships with performance on the Event Perception tasks. For the whole group of 16 patients there was a relationship between Event Perception Threshold and the anterior temporal area left but this was found to be counter to the predicted direction.

6.4 DISCUSSION.

Previous studies have demonstrated that it is possible to establish meaningful relationships between structural indices of brain damage following head injury and neuropsychological outcome measures. Investigation of such relationships was undertaken in the present study for functional measures of CBF employing SPECT with ^{99m}Tc HM-PAO. Two groups of head injury patients were investigated. The groups differed in diagnosis: a group with diffuse or contusional brain damage and a group with space occupying lesions. Groups differed significantly on GCS admission score and on PTA, indicating greater injury severity for the diffuse group. They also differed in neuropsychological test performance. The diffuse group showed statistically significant differences on 13 out of 24 measures compared with a control group after correction for premorbid differences whereas the focal group was significantly impaired on only three tests after correction for age and NART differences.

Differences in diagnosis and type of brain damage must be taken into account in relating neuroradiological data in a meaningful and systematic manner to neuropsychological outcome measures. Mass lesions often extend over several ROIs and yet appear to be less disruptive of function than several isolated lesions; the focal group had approximately one third more ROIs with abnormalities than the diffuse group. In the focal group abnormalities typically extended over both the anterior and posterior temporal ROIs ipsilaterally, but this pattern was less frequent in the diffuse group. For the diffuse group SPECT seemed to be more sensitive than MRI to abnormalities in the parietal areas but the converse appeared to be true for the focal

group. At this stage it is not clear whether this finding is due to a shift in sensitivity between the two imaging modalities, whether it is due to a rater bias, or a relatively small patient group sample.

Differences in patterns of CBF between diffuse and focal head injury were established. For the focal group SPECT identified more CBF defects in the anterior regions and the orbito-frontal and frontal areas, but more posterior abnormalities were found in the diffuse group. The fact that 50% of all the bloodflow abnormalities identified by SPECT were found to occur independently from sites of structural damage visualized on MRI demonstrates that SPECT can provide additional information not revealed by structural imaging techniques.

For the diffuse group neuropsychological test performance showed consistent relationships with CBF abnormalities in specific regions. The most consistent relationships were found for non-verbal tasks and CBF defects in the right anterior temporal area. Visual memory tasks like Pattern Span and Pattern Learning showed in addition a relationship with CBF abnormalities in both left and right orbito-frontal areas. On the other hand Word Fluency and Event Perception Threshold indicated relationships with CBF abnormalities counter to the predicted direction. It is important to note from these results that task performance was not simply related to ROIs showing the highest frequency of abnormality.

The lack of consistent relationships with bloodflow abnormalities was rather surprising. For the whole group the only relationship found was for Event Perception Threshold with the anterior temporal area left but this was counter to the predicted

direction. The fact that the temporal lobes had been the most likely candidates for some form of localisation for the Event Perception tasks with respect to MRI findings makes it even more surprising that this area should show the opposite for bloodflow measurements.

A weakness in this study was that no bloodflow information had been obtained for deep structures which had shown reliable relationships with MRI, and which may be of particular importance to performance on the Event Perception tasks. The reasons for this omission were both anatomical and practical. The corpus callosum consisting mainly of white matter and with no major blood vessels in its vicinity is not represented on bloodflow images because of its very low perfusion rate. Similar arguments apply for the brainstem but in addition major arteries feeding the entire brain pass close by and make it difficult to evaluate bloodflow in this area. The basal ganglia could be identified but using the method of visual inspection rather than quantitation as a means of analysis it was felt to be too unreliable to make sound judgments about abnormalities in this area. The cerebellum is a structure generally allowing good identification of bloodflow abnormalities but in many patients in this study the tomographic sequences did not include a clear enough image of the cerebellum to allow unequivocal judgments.

6.5 CONCLUSIONS.

Considering the diffuse nature of abnormalities in head injury and the fact that a majority of patients had abnormalities in more than one area, it is important to emphasize the difficulty of showing differential localization for this population. Relationships between bloodflow abnormalities and performance on Event Perception tasks were found to be inconsistent. However, the study did show that SPECT was able to identify abnormalities in areas where no abnormalities had been suspected on the basis of MRI investigations, and that these abnormalities were related to performance on neuropsychological tasks. In addition SPECT suggested different patterns of bloodflow abnormalities depending on the type of brain injury sustained. These patterns could not have been predicted on the basis of structural information.

It remains a plausible aim to construct models which will allow extraction and integration of information from both structural and functional imaging and their relationship to neuropsychological performance.

TABLES AND FIGURES

Table 6.1: Demographic background of head injury patient groups and controls.

	A	B	C
	DIFFUSE GROUP N=16	FOCAL GROUP N=8	CONTROLS N=16
AGE	38.6 (17-64)[B]	53.1 (24-62)[C]	35.7 (16-63)
SEX	12 MALE	7 MALE	13 MALE
GCS	10.0 (3-14)[B]	12.1 (10-15)	--
PTA	23.5 (0-99)[B]	8.0 (4-35)	--
FOLLOW-UP	190 (161-237)	207 (93-405)	--
SKULL FRACT.	10	4	--
SURGERY	3	2	--
BACK AT WORK	2	3	--
PREMORBID IQ	101.7 (92-114)[C]	101.1 (92-110)[C]	108.4 (95-124)

Notes: [B] **denotes significantly different from group B at p<0.01**

[C] **denotes significantly different from group C at p<0.01**

TABLE 6.2: Distribution of Glasgow Coma Score on admission and Post-traumatic Amnesia.

GROUP	GCS	3-8	9-12	13-14	Total
DIFFUSE		6	4	6	-	16
FOCAL		-	4	3	1	8
GROUPS N	PTA (days)	0-1	2-7	8-14	=>15	Total
DIFFUSE		2	2	2	10	16
FOCAL		-	4	3	1	8

Table 6.3 Distribution of abnormalities: SPECT and MRI for diffuse and focal group.

DIFFUSE GROUP:

PATIENT_NO	ROI OFL	OFR	FRL	FRR	ATL	ATR	PTL	PTR	PAL	PAR	OCL	OCR
1	MS	MS	M	M				S				
2	MS		M		MS			MS		S		M
3									S	S		
4												
5				S					S			
6	MS	MS	MS	MS	M	M	S	MS	M	MS		
7				S	M		MS	S				
8	M		MS	M			M	M				
9	M	M	M	MS		M				S		
10								S				
11					M							
12				M	S							
13			S	S	MS	S	M	M				
14	M				M	MS	M	MS		MS		
15		S			M	S						
16			S	M								M

FOCAL GROUP:

PATIENT_NO	ROI OFL	OFR	FRL	FRR	ATL	ATR	PTL	PTR	PAL	PAR	OCL	OCR
1			MS		M		M					
2	M	MS		MS	M	M	MS				MS	M
3			S	S		M		MS		M		
4						M		MS		M		
5	MS		MS		MS		M					
6			S	S	M	MS	M	S	M			
7	S		S	MS	M	MS		S				
8				S	M		S				S	

Notes: S = SPECT abnormality M = MRI abnormality

TABLE 6.4 Means for test results, T-test results, and ANCOVA results on neuropsychological test performance for diffuse, focal and control group.

A: GENERAL INTELLECTUAL ABILITY

TEST	A DIFFUSE (N=16)	B FOCAL (N=8)	C CONTROL (N=16)	ANCOVA (F- values) DIFFUSE	FOCAL
SIMILARITIES	12.9**	11.4**	17.2	1.1	.1
DIGIT SPAN	11.6****	9.6****	14.2	8.8**	26.6****
VOCABULARY	36.8**	40.3	49.8	.1	.5
DIGIT SYMBOL	37.9****	35.4****	60.7	10.9***	3.9
BLOCK DESIGN	28.1*	26.6**	35.8	1.5	0.3
OBJECT ASSEMBLY	23.2*	22.8	29.8	.9	0.9

B: VERBAL MEMORY AND VERBAL PROFICIENCY

LOGICAL MEMORY	9.6**	8.6**	12.9	3.8	0.7
ASSOCIATE MEMORY	13.8	12.0*	16.1	.9	0.1
WORD FLUENCY	32.5****	30.9***	49.3	10.5***	3.4
GRADED NAMING	16.0***	14.5***	22.0	.5	0.2
WORD RECOGNITION@	72****	82	48	2.4	36.0****

NOTES: All measures in this table represent raw scores; @ = scores are in milliseconds: higher values indicate impaired performance; '*' denotes statistically significant from group C: * = $p < 0.05$ ** = $p < 0.01$ *** = $p < 0.001$ **** = $p < 0.0001$. ANCOVA= Analysis of Covariance between diffuse and control, focal and control: Covariates for diffuse group = NART Score; covariates for focal group = NART Score and age.

Table 6.5 Means for test results, T-test results, and ANCOVA results on neuropsychological test performance for diffuse, focal and control group.

C: REACTION TIMES AND VISUAL PROCESSING

TEST	A DIFFUSE (N=16)	B FOCAL (N=8)	C CONTROL (N=16)	ANCOVA (F- values) DIFFUSE	FOCAL
RT SIMPLE DECISION@	353**	341	271	7.4**	0.4
RT SIMPLE MOVEMENT@	301**	298***	215	6.6**	1.7
RT CHOICE DECISION@	423**	391	302	8.9***	0.8
RT CHOICE MOVEMENT@	307**	313*	211	7.9**	2.1
VISUAL SEARCH@	4700****	4900	3300	11.9***	48.5****

D: VISUAL MEMORY AND LEARNING

REY COPY	32.8**	31.8*	35.3	2.2	0.1
REY RECALL	18.5*	14.5***	23.2	.2	0.1
PATTERN SPAN	7.6****	7.3***	9.4	16.6****	.3
PATH SPAN	4.9	4.6*	5.3	5.7*	.2
PATTERN LEARNING ITEMS	145.3*	134.3*	163.1	5.0*	.1
PATH LEARNING ITEMS	80.2*	64.7**	94.1	3.2	.1

NOTES: All measures in this table represent raw scores; @ = scores are in milliseconds: higher values indicate impaired performance; '*' denotes statistically significant from group C: * = $p < 0.05$ ** = $p < 0.01$ *** = $p < 0.001$ **** = $p < 0.0001$. ANCOVA= Analysis of Covariance between diffuse and control, focal and control: Covariates for diffuse group = NART Score; covariates for focal group = NART Score and age.

TABLE 6.6 T-tests comparing patients with the control group.

TEST	All Patients N=16 Score/SD	Controls N=14 Score/SD	t-value	p
Age (years)	38.6 / 17.2	28.4 / 8.4	-2.1	0.05
NART (max=50)	18.8 / 7.5	25.4 / 7.8	2.3	0.05
Similarities+	12.9 / 5.4	16.4 / 4.4	2.3	0.05
Digit Span+	11.6 / 2.0	14.6 / 1.6	4.1	0.001
Vocabulary+	36.8 / 11.7	45.2 / 14.2	1.6	ns
Digit Symbol+	37.9 / 15.5	62.7 / 6.2	5.7	0.001
Block Design+	28.1 / 10.0	34.7 /7.0	2.4	0.05
Object Assembly+	23.2 / 9.0	29.8 / 6.4	2.5	0.05
Rey Copy (max=36)	32.8 / 5.0	34.9 / 1.9	2.3	0.05
Rey Recall (max=36)	18.5 / 7.1	22.1 / 5.8	1.8	ns
Logical Memory (max=23)	9.6 / 3.4	13.1 / 2.8	2.8	0.05
Assoc. Learning (max=21)	13.8 / 3.6	16.2 / 2.5	2.0	ns
Word Fluency	32.5 / 10.3	51.9 / 8.7	5.3	0.001
Graded Naming (max=30)	16.0 / 6.1	21.2 / 3.9	2.9	0.01
EP Threshold (ms)	54 / 66	39 / 10	-1.9	ns
EP Movement (max=32)	23.4 / 7.9	29.1 / 3.6	3.1	0.01
Visual Search (ms)	4700 / 1764	3211 / 597	-3.7	0.001
Word Recognition (ms)	72 / 57	50 / 24	-2.3	0.05

Level of significance: * = p< 0.05 ** = p< 0.01 *** = p< 0.001 denotes significantly different from controls

+ = Raw Scores EP = Event Perception GCS = Glasgow Coma Scale PTA = Post-traumatic Amnesia RT = Reaction Times Assoc. Learning = Associate Learning

TABLE 6.7 Pearson and Partial Correlations controlling for age and NART between performance on EP tasks and performance on other tasks for patients (N=16)

	Pearson Corrs		Partial Corrs	
TEST	EP Move	EP Treshold	EP Move	EP Treshold
Age (years)	-0.26	0.44*	- - -	- - -
Nart (max=50)	0.31	-0.42	- - -	- - -
GCS	-0.07	0.23	-0.12	0.23
PTA (days)	-0.45*	0.03	-0.78***	0.44
Similarities+	0.45*	-0.52*	0.27	-0.21
Digit Span+	0.12	-0.37	0.05	-0.32
Vocabulary+	0.33	-0.35	0.44	-0.33
Digit Symbol+	0.59**	-0.42*	0.49*	-0.12
Block Design+	0.59**	-0.37	0.48*	0.08
Object Assembly+	0.58**	-0.41	0.46	-0.13
Rey Copy (max=36)	0.52*	-0.70***	0.38	-0.52*
Rey Recall (max=36)	0.50*	-0.37	0.42	-0.12
Logical Memory (max=23)	0.58**	-0.31	0.61*	-0.31
Assoc. Learning (max=21)	0.30	-0.05	0.49*	-0.14
Word Fluency	0.22	-0.36	0.20	-0.34
Graded Naming (max=30)	0.40	-0.42*	0.37	-0.24
EP Threshold (ms)	-0.70***	- - -	-0.63*	- - -
EP Movement (max=32)	- - -	-0.70***	- - -	-0.63*
Visual Search (ms)	-0.63**	0.81***	-0.52*	0.72***
Word Recognition (ms)	-0.56**	0.76***	-0.56*	0.83***
Simple RT Decision$	-0.78***	0.26	-0.83***	0.23
Simple RT Movement$	-0.76***	0.54*	-0.88***	0.54*
Choice RT Decision$	-0.71***	0.38	-0.78**	0.39
Choice RT Movement$	-0.65**	0.50*	-0.78**	0.53

+ = Raw Scores $ = scores are in ms EP = Event Perception GCS = Glasgow Coma Scale PTA = Post-traumatic Amnesia RT = Reaction Times Assoc. Learning = Associate Learning

Table 6.8 Psychological test performance and SPECT regional bloodflow abnormalities for diffuse group: Mann-Whitney U-tests.

TEST \ ROI	OFL	OFR	FRL	FRR	ATL	ATR	PTL	PTR	PAL	PAR
DIGIT SPAN										
DIGIT SYMBOL						6.0*				
LOGICAL MEMORY					2.5**					
WORD FLUENCY							2.0!		4.0*	
VISUAL SEARCH						7.0*				
EVENT THRESHOLD					0.0!!					
EVENT MOVEMENT										
REY COPY						5.5*				
REY RECALL	6.0*					4.5*		2.5**		
PATTERN SPAN	5.0*	2.0**								
PATH SPAN										
PATTERN LEARN. ITEMS	0.0**	5.0*						10.0*		13.0*

NOTES: Statistically significant at * = p< 0.05 ** = p< 0.01
! = p< 0.05 !! = p< 0.01 counter to predicted direction

Figure 6.1 Diffuse group: frequency distribution of ROIs showing number of patients with abnormalities.

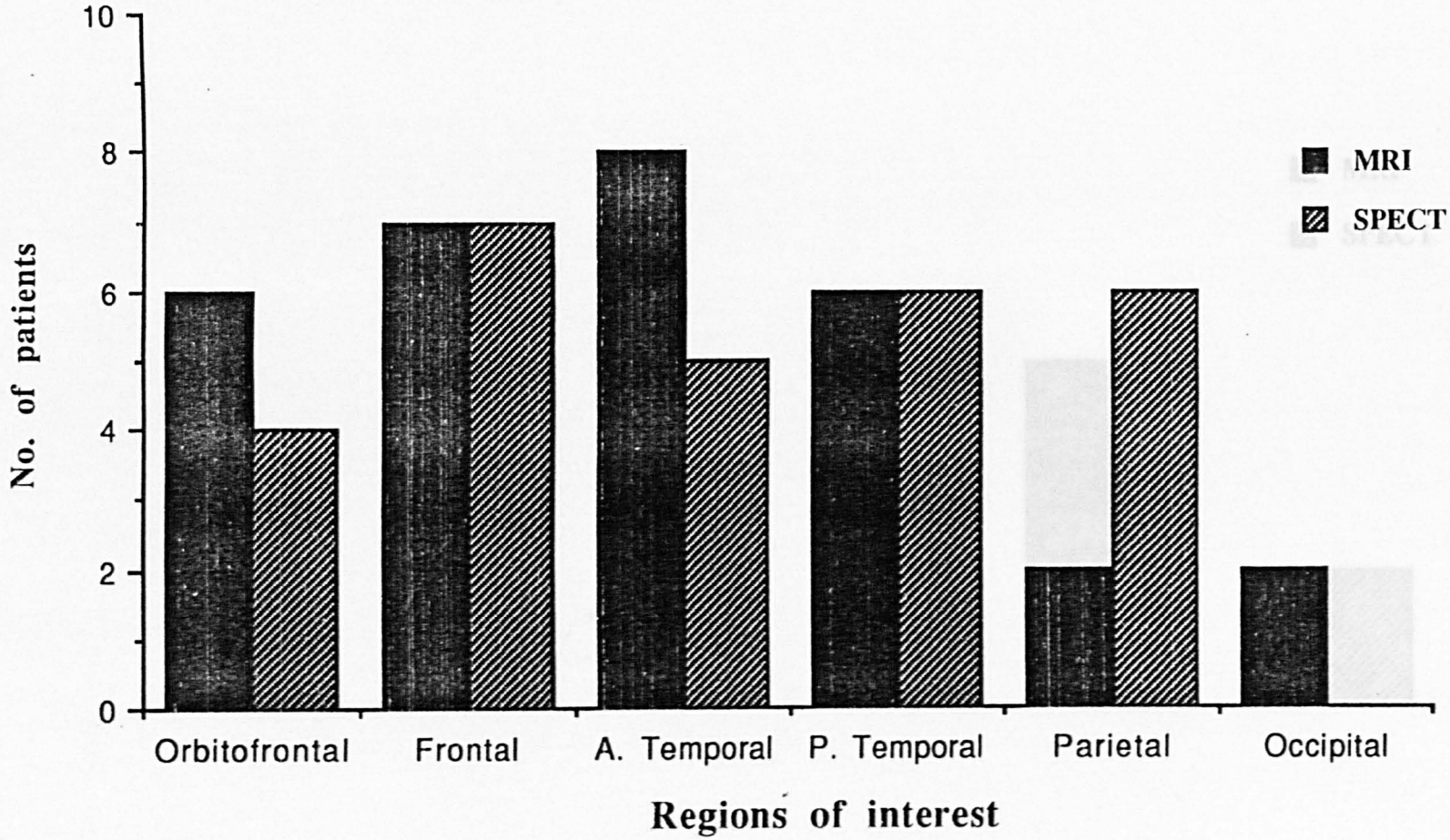
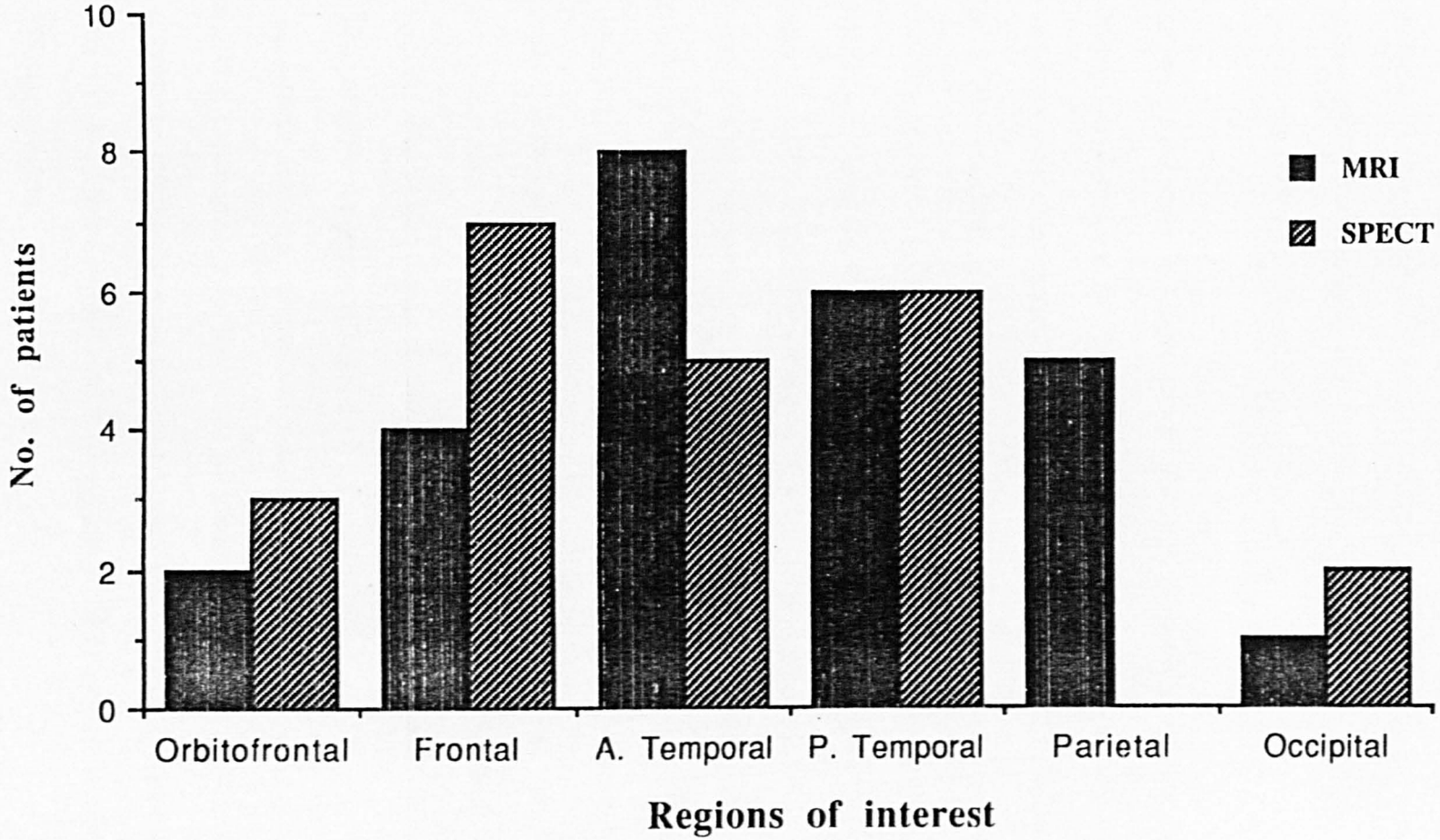


Figure 6.2 Focal group: frequency distribution of ROIs showing number of patients with abnormalities.



7.0 SUMMARY AND GENERAL CONCLUSIONS.

The aims of this project were (1) to investigate two forms of event perception: perception of movement and perception of sudden appearance, (2) to develop event perception procedures which could be applied to testing clinical populations, and (3) to relate event perception to abnormalities shown by neuroimaging.

Computerised procedures were developed which allowed manipulation of relevant parameters affecting the perception of appearing or moving stimuli. A model of neuronal processes involved in the perception of visual events was proposed based on work by Phillips & Singer (1974) and Singer & Phillips (1974). In its essence the model states that perception of appearing stimuli depends on the production of transient neuronal signals triggering the attention system linked to transient processes. On the other hand psychophysical evidence was provided to show that short range movement does not produce transient appearance signals to the background pattern. Yet short range movement was found to be sufficient to attract attention as reflected in high detection rates in a condition where the background was steady and the target only produced a single movement. The means by which transient appearance signals were thought to be suppressed was the mechanism of lateral reciprocal inhibition of ON and OFF neurons. The spatial limits of this lateral inhibition were found to be approximately 30 min/arc for the present conditions.

It was thought that by studying appropriate groups of patients with neurological disorders, a double dissociation in performance on these tasks might be found providing further evidence that the neuronal coding strategies were distinct. In addition some insight into the properties underlying coding might be gained from the pathologies in different groups.

In chapter 2 a single case study was reported, and a study of 12 chronic solvent abusers whose performance was compared to 12 non-solvent abusing matched controls. Four solvent abusers were followed up over a period of 12 months. Previous studies had shown that solvent abuse might lead to differential impairment depending on the substances involved: n-hexane appears to act predominantly on the peripheral nervous system resulting in both sensory and motor polyneuropathies whereas toluene has been found to exert its toxicity and subsequent degenerative effects more exclusively on the central nervous system. This distinction was based on laboratory and industrial studies of exposure to a single toxic agent rather than on studies of solvent abuse since the latter rarely provides a clear picture of the number and amount of substances involved. This was confirmed in the current study where most subjects had used a substance containing a mixture of both toluene and n-hexane. Event Perception tasks were highly sensitive in measuring the effects of solvent abuse on the nervous system. Individuals with prolonged histories of chronic solvent abuse performed significantly worse on Event Perception Threshold and Event Perception Movement than matched non-solvent abusing controls.

The results from this study are consistent with the hypothesis that performance on the Event Perception tasks depends largely on the capacity of both individual and groups of neurons to efficiently separate and process transient signals arising from ON and OFF retinal activity. If this capacity is compromised by - as in this instance - toxic agents, the resulting increased variability in latencies and noise in neuronal channels impairs temporal separation of neuronal signals. Longer temporal separation is therefore required between background and target onset resulting in higher (impaired) scores on the Event Perception Threshold task. However, increased noise and decreased amplitudes may have resulted in significantly lower (impaired) scores in the

Event Perception Movement task which according to one interpretation is assumed not to require transient signals to attract attention. The relatively small increase in sustained firing in response to target movement could be lost in an environment producing abundant spontaneous firing as a result of nerve fibre damage caused by toxins. An already weakened increase in amplitude in response to the moving target may therefore easily go unnoticed. However, an alternative interpretation is based on possible impairment of proper fixation related to cerebellar dysfunction. Subjects had been instructed to maintain fixation throughout the task but no formal assessment of eye movements was attempted. The possibility of cerebellar involvement was also indicated by the relationship of Body Sway with simple and choice RT movement and Visual Search. It was therefore concluded that the results of this study could corroborate the theoretical framework for the Event Perception tasks but other interpretations are possible.

Chapter 3 reported a study of detoxified alcoholics and matched controls. A group of 40 alcoholics was compared with a group of 40 moderately or non-drinking controls on a number of neuropsychological assessment procedures. Alcoholics performed significantly worse than controls on 11 of the 19 procedures during initial assessment. At follow-up alcoholics were significantly impaired on only 2 measures. Performance on all three Event Perception measures was significantly impaired in alcoholics on initial assessment. Alcoholics continued to show significant impairment on Event Perception Threshold at follow-up but were not impaired on Event Perception Movement.

It was concluded that these deficits did not reflect a general deficit of visual attention because of unimpaired performance on other visual processing tasks but that

they represented a rather specific failure of the processes involved in attracting attention in response to rapid change. It was thought that the deficit might occur at levels at which attention is drawn to ON and OFF responses in the visual system. The possible underlying condition was thought to be a subclinical form of alcoholic amblyopia which is caused by pathological changes of nerve fibres in the visual system in response to the toxic effects of alcohol and its metabolites. These nerve fibre changes were related to neurophysiological findings from other studies reporting decreased amplitudes, increased noise and increased latencies in alcoholics in response to visual stimulation. The resultant impairment in performance observed in alcoholics on the visual event perception tasks was in agreement with the rationale proposed in chapter 1 suggesting disruption of stimulus processing if transient signals are degraded. Alcoholics were unique amongst the different patient groups studied in showing a persisting deficit on Event Perception Threshold. As a possible explanation it was thought that channels that are low spatial and high temporal frequency might be involved in relaying appearance signals in this task which took longer to recover than the channels involved in signalling movement.

Chapter 4 reported a study of 5 patients suffering from optic neuritis and compared performance on the Event Perception tasks with patterned visual evoked potentials (VEPs) and contrast sensitivity assessments obtained from the same patients. This study showed that the two Event Perception tasks were differentially sensitive to disruption of nerve conduction. In the case of Event Perception Threshold differences between affected and unaffected eyes were found to be rather small and for all but one testable eyes within the normal range although SOAs were generally higher for the eye showing increased latencies. Event Perception Movement proved to be more easily

disrupted and more sensitive to nerve fibre pathology in the patients studied. Except for one patient binocular detection rate was always at least one SD below the control mean. Performance in the affected eye was considerably worse than in the unaffected eye in all patients. There was a strong relationship between increased latencies and impairment on both Event Perception tasks except for one patient.

Results in this study provided further evidence that the two Event Perception tasks may be mediated by two distinct neural coding processes. Event Perception Threshold, although obviously affected by increased variability in conduction latencies, only showed relatively slight increases in mean SOAs. Although VEP amplitudes were sometimes decreased in the affected eyes, this was far less consistent than the latency changes observed. The trend observed between increased latencies and longer SOAs is consistent with the idea that the important factor for performance on Event Perception Threshold are conduction latencies. This is in agreement with the model proposed in chapter 1. The absence of a clear peak in response to a patterned stimulus from the checkerboard VEPs which - given the angle of displacement - should produce transient signals, suggests that the attention mechanism linked to the transient system may have been disrupted in some patients for selected spatial frequencies. It was also considered possible that signals produced in response to movement are relayed by smaller diameter nerve fibres which in turn might be affected more severely and at an earlier stage by the demyelination process and result in impaired performance on the Event Perception Movement task.

In chapter 5 the results from a study of 47 patients with traumatic brain injury and 16 orthopaedic controls were reported. Impairment was found to be more consistent on Event Perception Movement which was interpreted as being the more sensitive task

to traumatic brain injury. This assumption was strengthened by the finding of significantly longer PTA in patients with poorer performance on Event Perception Movement than with Event Perception Threshold. Event Perception Movement was therefore successful in identifying patients with more severe brain damage. Indices from both early and late MRI were used to investigate the nature of brain damage in these patients and an attempt was made to relate these indices to performance on the Event Perception tasks. Reliable relationships with depth indices could only be established for Event Perception Movement for both early and late MRI. It was difficult to identify any one region of the brain as being particularly related to impaired performance on the Event Perception tasks due to multiple brain damage sustained by a majority of patients and a resultant high interrelation of regions with abnormalities. However, the most consistent relationships between performance on the Event Perception tasks and hemispheric abnormalities were found with both left and right temporal areas. Other areas showing consistent relationships were the deep structures which were found to be abnormal in a significantly larger proportion of patients with low scores on Event Perception Movement compared to patients with high scores. Patterns of brain damage did not differ when patients were split on the basis of their performance on the Event Perception Threshold task. However, these abnormalities did not occur in isolation and indices of deeper damage were taken to represent more widespread brain damage. It was therefore concluded that Event Perception Movement was sensitive in discriminating patients with differential degrees of brain damage but the nature of the material studied did not allow any firm conclusions about the exact localisation of the perceptual processes involved in this task.

In chapter 6 a study of cerebral bloodflow abnormalities in 24 patients with traumatic brain damage was reported using Single Photon Emission Computed Tomography (SPECT) in combination with the tracer ^{99m}Tc-hexamethyl propyleneamine oxime (HM-PAO). Two groups of head injury patients were investigated with a differing diagnosis: a group with diffuse or contusional brain damage and a group with space occupying lesions. Groups differed significantly on GCS admission score and on PTA, indicating greater injury severity for the diffuse group. They also differed in neuropsychological test performance. Differences in patterns of CBF between diffuse and focal head injury were established. For the focal group SPECT identified more CBF defects in the anterior regions and the orbito-frontal and frontal areas, but more posterior abnormalities were found in the diffuse group. The fact that 50% of all the bloodflow abnormalities identified by SPECT were found to occur independently from sites of structural damage visualized on MRI demonstrates that SPECT can provide additional information not revealed by structural imaging techniques. For the diffuse group neuropsychological test performance showed consistent relationships with CBF abnormalities in specific regions. The most consistent relationships were found for non-verbal tasks and CBF defects in the right anterior temporal area. Visual memory tasks like Pattern Span and Pattern Learning showed in addition a relationship with CBF abnormalities in both left and right orbito-frontal areas. On the other hand Word Fluency and Event Perception Threshold indicated relationships with CBF abnormalities counter to the predicted direction. The lack of consistent relationships with bloodflow abnormalities was rather surprising. For the whole group the only relationship found was for Event Perception Threshold with the anterior temporal area left but this was found to be counter to the predicted direction. The fact that the temporal lobes had been the most likely candidates

suggesting some form of localisation for the Event Perception tasks on MRI makes it even more surprising that this area should show up the opposite way for bloodflow measurements.

The fact that in general patients appeared to show greater impairment on Event Perception Movement than on Event Perception Threshold could be taken to mean that Event Perception Threshold is the less sensitive measure. However, it could also mean that this task is measuring a more basic aspect of visual event perception which is less prone to disruption by the effects of neurological disease and probably a more distributed process than the perception of short-range apparent movement. This view may also be acceptable from an intuitive perspective given that detection of appearances and disappearances of visual stimuli are amongst the most basic visual functions imaginable. However, stimuli in the Event Perception Movement paradigm were essentially based on the same principles: the perception of motion was induced by a stimulus disappearing at one location and reappearing at another. The quintessential difference must therefore lie in the neuronal coding processes between the two tasks. It has been argued earlier that the Event Perception Movement task may involve a different attention mechanism not involving transient processes. It is likely that a comparison based on only minor variations in the sustained neuronal signal will be more vulnerable than a mechanism for which the basis of comparison are much larger differences in the neuronal signal. It is therefore assumed that differences in performance on the two tasks are dependent on the vulnerability of comparison processes or the level of degradation in the neuronal signal. The clinical studies in this thesis provide support for this broad interpretation.

One of the ideas expressed in the introduction was that impairment on basic aspects of visual information processing might be reflected in impairment for higher cognitive functions. It is difficult to determine to what extent the hierarchical view of cognitive processing can be applied in interpreting the results from the individual studies in this thesis. The notion that these tasks measure basic processes of visual perception is probably easily acceptable. However, it is a much more contentious issue to argue that performance on other tasks requiring higher levels of processing could be predicted from the performance on the Event Perception tasks. Performance on other tasks was significantly related to performance on the Event Perception tasks especially in the low movement group in the head injury study in chapter 5. It is not immediately clear what aspects each of these tests showing significant correlations might share with the Event Perception tasks. Of course, in none of these cases has there been a perfect relationship, leaving (at times considerable) room for other factors to contribute to performance. This point might enhance the argument that some of the variance is shared with the more basic processes measured in the Event Perception tasks. On the other hand it cannot be ruled out that these relationships merely represent impaired performance on both tasks. The finding in chapter 3 where alcoholics were found not to be impaired on RT decision times which is also a measure of visual attention, or on Word Recognition, a task measuring visual processing with clear involvement of semantic processing, would contradict the view that attention processes involved in Event Perception tasks generalise to higher cognitive functions.

In conclusion both the laboratory studies and the clinical studies have provided evidence to corroborate differential neuronal coding for appearance and movement of visual stimuli within a short range of visual angle. A dissociation between these tasks was established in that performance on Event Perception Movement was found to be more severely impaired than on Event Perception Threshold. Double dissociations in performance on these tasks were found amongst alcoholics and head injury patients. A comparison with neuroimaging has shown that patients with deep structure abnormalities tend to perform worse on Event Perception Movement. Patterns of brain damage were significantly different from patterns in patients with unimpaired performance.

The studies in this project have shown that Event Perception tasks are of value in the assessment of neurological patients: they allow assessment of functions which are not usually evaluated in neuropsychological examinations, and facilitate detection of subtle deficits which may be present at an early stage. The evidence provided has shown that Event Perception tasks are specific in the assessment of particular aspects of neuropsychological functioning and they are more sensitive than many traditional neuropsychological test procedures. Tests with a theoretical basis are better suited to clinical research in neuropsychology than many traditional tasks because they potentially allow more precise assessment and explanation of the abnormal processes under investigation.

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