The Genetics of Affective Cognition:

Electrophysiological Evidence for Individual Differences in Affective Picture Processing, Attention and Memory

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For Esmerelda Weatherwax

- mind how you go.

Declaration

The work presented in this thesis was completed under the supervision of Professor David I. Donaldson, Professor Jeremy Hall and Professor Stephen M. Lawrie and conducted at the University of Stirling, United Kingdom.

I declare that this thesis is a presentation of my original work that has not been submitted for any other degree or award. All additional sources of contribution have been acknowledged accordingly.

Johanna Simpson

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Abstract

Affect and cognition have traditionally been considered mutually exclusive domains and their study has evolved into two separate research fields. In recent years, however, there is increasing evidence of affective modulations of cognitive processes and interest in the study of affective cognition has grown. This thesis presents analyses of data collected in four mixed-design experiments between 2009 and 2011, which were designed to investigate affective memory and its electrophysiological correlates, individual differences in said affective memory and electrophysiological correlates, the time-course of affective memory and attentional disengagement from affective stimuli respectively. The first aim of the research presented here was to further understanding of how affective content influences picture processing and memory. Event-related potentials (ERPs) provide a valuable tool for the investigation of modulations of cognitive processes, as their excellent temporal resolution allows for the dissociation between different processes contributing to behavioural outcomes.

Several important results for the study of affective cognition are reported: The late positive potential (LPP) was shown to be modulated differentially by affective content when compared to a behavioural attentional disengagement task. While the behavioural measure of attention replicated findings from participants' self-report of arousal, LPP enhancement did not. This novel finding demonstrates that the affective modulation of the LPP cannot be used as an electrophysiological marker of slowed attentional disengagement as is common in the literature.

In the domain of recognition memory, affective modulation of performance was shown to be time-sensitive, with effects developing faster for negative than for positive picture content.

Affective pictures were associated with a less conservative response bias than neutral pictures but only negative pictures elicited better discrimination performance, driven by an increased in the rate of "remembered" as compared to merely familiar pictures. This was reflected in an increase of the ERP old/new effect for negative pictures in the 500 to 800ms time window, the purported correlate of recollection. The late right-frontal old/new effect between 800 and 1500 ms post stimulus onset was shown to be attenuated by affective content, supporting the interpretation of the late right-frontal effect as a correlate of relevance detection over a retrieval success interpretation. In combination, the findings add weight to the conclusion that affective content enhances memory through selective memory sparing for affective stimuli.

Novel evidence for gender differences in affective cognition was found. Comparisons between female and male participants revealed that the affective modulation of the late right-frontal effect differs between the genders, underlining the importance of assessing and understanding gender differences as part of the study of affective cognition. Brain-derived neurotrophic factor (BDNF) gene val66met single nucleotide polymorphism (SNP), a small genetic change that affects the functioning of BDNF, a protein that plays an important role in neuron growth, differentiation and survival, is shown here to also affect the interaction of affect and cognition. BDNF val66met genotype modulated the early "familiarity" old/new effect selectively in response to positive pictures. The present study clearly demonstrates the value of the ERP technique in the investigation of individual differences in affective and cognitive processing and the need to take such individual differences into account as part of the endeavour to fully understand the mechanisms of affective processing, cognition and affective cognition. A better understanding of the role of gender and genetic differences in the affective modulation of affective processing and memory will have important practical implications in fields where affect and cognition interact.

Contents

Chapter 1: Memory and Affect

This chapter introduces the separate research fields of affect and cognition, with a specific focus on the cognitive literature on recognition memory. Important findings on both the behavioural level and the structural and functional neural levels are discussed. An overview over the field of affective cognition, investigating the affective modulation of cognitive functions, is also given and relevant research summarised and assessed, culminating in a summary of the main research questions pertaining to the investigation of affective recognition memory in the present thesis.

1.1 Memory

Memory is a fundamental aspect of human cognition. The ability to remember the past allows us to understand the world around us in the context of not just the current situation but the whole spectrum of our previous experiences. While many other species show evidence of memory to some extent, from simple pain avoidance learning in fruit flies (Quinn, Harris, & Benzer, 1974) to gorillas being able to remember what food they received and who provided it 7 minutes and 24 hours after the episode (Schwartz, Hoffman, & Evans, 2005), memory is also a prerequisite to many higher order phenomena that are uniquely human. Our everyday functioning draws on memory in countless

ways, from remembering how to ride a bike to remembering the way to the supermarket and which items to buy when we get there.

1.1.1 Organisation of memory

Although the real picture is almost certainly a lot more complex, for the purpose of studying memory it is helpful to distinguish different sub-types of memory. One often cited memory model is that proposed by Atkinson and Shiffrin (1968). It distinguishes between sensory memory, short-term memory and long-term memory (see Figure 1.1). Although the specifics of the proposed sub-systems have been much discussed and expanded on (see Raaijmakers, 1993), the basic distinction between short-term, or working memory, and long-term memory is still widely used.

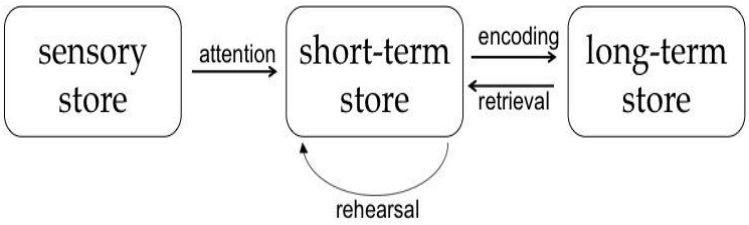


Figure 1.1 *Atkinson and Shiffrin's (1968) multistore model of memory*

Short-term memory is, as the name suggests, characterised by short duration, lasting only as long as information is actively rehearsed, and a limited capacity of around 5 to 9 items (Miller, 1994). Baddeley and Hitch (1974) later proposed their more detailed model of working memory to replace Atkinson and Shiffrin's (1968) sensory and short-term stores.

The work presented in this thesis, however, focuses on long-term memory. The term describes memory that is potentially infinite both in capacity and duration. Tulving (1987) subdivides long-term memory into episodic, semantic and procedural memory. In reviewing other classificatory schemes of the time, he notes that Weiskrantz (1968) broadly shares his classification, referring to event memory, knowledge systems and associative memory/priming respectively. Episodic or event memories and semantic memories or knowledge systems are explicit, that is they are subject to conscious retrieval. Procedural memory on the other hand is implicit, as is the case with Weiskrantz (1968) associative memory/priming.

Cohen and Squire (1980), Kinsbourne (1986) and Schacter (1985) all distinguish between only two long-term memory systems: declarative, episodic or explicit memory in contrast with procedural, semantic or implicit memory. Tulving (1987) describes procedural memory as the learning of connections between stimuli and responses, which can happen slowly. Retrieved procedural memories are expressed through behaviour rather than verbally, a process that can happen without conscious effort or attention. Procedural memory stores information on how to do things.

Semantic memory is memory for knowledge or facts. It can be shared between people and is not connected to the episode during which it was acquired. Episodic memory, finally, is memory for personally experienced episodes that can be mentally relived as the memory is retrieved. Tulving (1987) differentiates between recall and recognition here, recall being the retrieval of memory without any perceptual support and recognition being the identification of a stimulus as previously encountered. Episodic recognition memory and its neural correlates, their modulation by affective content and individual differences in these measures are the focus of the present thesis.

1.1.2 Episodic memory processes: Encoding, consolidation, storage, retrieval

Episodic memory consists of a sequence of processes, all of which can be individually influenced by a range of factors to modulate the overall memory outcome. When a stimulus is first encountered, it must be encoded. During encoding, a mental representation of the stimulus in memory is created. An important factor in the successful encoding of stimuli is attention. When attention is divided, i.e. less attention is paid to the stimulus to be encoded, encoding is impaired (Craik, Govoni, Naveh-Benjamin, & Anderson, 1996). Once encoded, the resultant memory trace is consolidated or stabilised. Consolidation is variably seen as a sub-process of encoding or retention. It is achieved on the neural level by long-term potentiation, a process which strengthens the connections between synchronously firing neurons. After

initial, fast synaptic consolidation which results in a memory representation in the hippocampus, a second slower process called systems consolidation moves the memory to neocortical regions where it is more permanent and independent of the hippocampus (Dudai, 2004). Sleep has been repeatedly shown to be an important factor in memory consolidation, likely by affecting changes in neurotransmitter levels and neurohormones (Payne, 2011). Memory storage refers to the retention of a memory. Finally, the memory can be retrieved when relevant to the situation or task at hand. As mentioned above, retrieval can take the form of recognition, which the process of identifying a given stimulus as previously encountered or new, or recall, i.e. without being confronted with the original stimulus. Recall can be free, i.e. spontaneous, or cued by related information or stimuli.

1.1.3 Theories of recognition memory

Recognition memory, as discussed above, is the ability to identify previously encountered material as old and distinguish it from not previously encountered new material. This recognition can be based on familiarity, a sense of having encountered the stimulus at hand before, or recollection, the retrieval of details of that previous encounter and of the stimulus itself (Yonelinas, 2002). In everyday life, one might see a person in the street and get the feeling of knowing them from somewhere (familiarity) or remember that they are the cashier at the local supermarket (recollection). The relative contribution of

familiarity and recollection to recognition memory is often estimated using the Remember/Know paradigm (Tulving, 1985). If an item is classed as "old" in a recognition memory task, the participant is then asked to indicate whether they remember specific details of their encounter with the item at study or whether they merely feel they know that the item is old because it feels familiar. Theories of recognition memory can be divided into two categories, based on whether they postulate that familiarity and recollection are two distinct processes or two aspects of the same process.

Single process theories see recollection and familiarity as two points on a continuum of memory strength which underlies all recognition memory retrieval. Most prominent among single process theories is the single process signal detection model (see Wixted, 2007). Signal detection theory posits memory strength or "familiarity" to be a single, quantitative, unidimensional variable. At retrieval, familiarity associated with each stimulus is compared to a set response criterion. If familiarity exceeds the response criterion, the stimulus is classed as "old", if familiarity falls short of the response criterion, the stimulus is labelled "new". Importantly, in this model, both old and new items are associated with some level of familiarity and the distributions of familiarity levels for new and old items overlap, meaning that there can never be absolute certainty in a memory decision. Familiarity and recollection are seen in this framework as purely representing weak memories and strong memories respectively (Squire, Wixted, & Clark, 2007).

Dual process theories, in contrast, posit that familiarity and recollection are two separable processes, supported by distinct neural networks, either of which can lead to recognition of an item. Yonelinas (1994) proposes that familiarity is indeed a signal-detection process but that recollection is a separate, thresholded process. Familiarity is continuous and an old decision is made on the basis of familiarity exceeding a certain level. Recollection results in one of two discrete states: either an item is recollected or it is not.

Whether single or dual process theories best describe recognition memory is an ongoing and hotly contested debate in the memory literature (Medina, 2008). The research presented in this thesis, however, was not designed to decide between these theoretical accounts. While a dual process view of recognition memory is adopted throughout, based on a large body of evidence dissociating the two processes (Yonelinas, 2002), the results reported do not test this assumption and could equally be interpreted from a single process point of view.

1.1.4 Neural correlates of recognition memory

The modern study of the brain areas and systems underlying memory was inspired only 60 years ago by what is now the most famous case study in cognitive psychology, the case of patient H.M. (Scoville & Milner, 1957). Before then, memory had been thought to be integrated with other cognitive functions and to be widely distributed across the cortex (Squire, 2009). Patient H.M.

showed extensive memory impairment, including the complete inability to form new episodic memories, as a result of surgical removal of the bilateral hippocampus, amygdala and adjacent parahippocampal areas. H.M.'s intellectual and perceptual faculties were unaffected and he could retain information such as short series of digits as long as his attention was not diverted (Squire, 2009). The focussed memory impairments created by the bilateral Medial Temporal Lobe (MTL) resection in patient H.M. provided initial evidence of the importance of the MTL in episodic memory.

Evidence from animal lesion and neuronal recording studies, human clinical studies and more recently functional brain imaging studies in humans have since confirmed the importance of the hippocampus in memory and identified a second crucial brain area, the perirhinal cortex. Brown and Aggleton (2001), reviewing the literature, proposed that the hippocampus and the perirhinal cortex support two dissociable aspects of memory. They conclude that a perirhinal system underlies familiarity based memory for single objects, while the hippocampal system underlies recollection based memory for more complex associational, spatial or multi-item information.

A number of functional brain imaging studies have confirmed a dissociation in activity associated with familiarity and recollection. Yonelinas et al. (2005), for example, report increased activity associated with recollected words in the hippocampus, the anterior medial prefrontal cortex, the inferior lateral parietal cortex and posterior cingulate. Words that were recognised based on familiarity, in contrast, were associated with increased activation in different

brain regions, including the lateral prefrontal cortex, the superior lateral parietal cortex and the precuneus.

Electrophysiological studies have also provided evidence of a dissociation of neural systems involved in familiarity and recollection by showing that the electrophysiological correlates of familiarity and recollection are distinct in timing and topography. For words, familiarity based recognition is associated with an earlier frontal old/new effect from around 300 milliseconds post-stimulus onset, while recollection is associated with a later left-parietal old/new effect onsetting around 500 milliseconds post stimulus onset (Woodruff, Hayama, & Rugg, 2006). The electrophysiological Event-Related Potentials (ERP) technique employed here, along with the familiarity and recollection ERP effects, will be discussed in detail in Chapter 3.

1.2 Emotion/affect

1.2.1 Defining emotion: Emotion vs affect

"Everyone knows what an emotion is, until asked to give a definition" wrote Fehr and Russell (1984, p. 464), pointing out the difficulty of defining a concept so fundamental to our human experience that it is generally assumed to be understood implicitly. And so, the term emotion is laden with diverse, culturally dependent "folk meaning" but rarely examined more systematically in everyday life. Definitions tend to be circular, relating to the terms "feeling"

and "affect", or rely on examples of either specific emotions or causes or consequences of emotion.

Due to its central role, emotion has been a subject in many disciplines from philosophy and the arts to, more recently, psychology and neuroscience. But despite being studied extensively, very little academic consensus on the definition of emotion has been reached. Kleinginna and Kleinginna (1981) reviewed 101 definitions of emotion from the literature of the time and classified them as belonging to one of ten categories (including for example traditional experimental categories, physical categories, and categories of definitions based on overlapping or distinguishing features compared to other concepts). In an attempt to unify these diverse definitions, they define emotion as "*a complex set of interactions among subjective and objective factors, mediated by neural/hormonal systems, which can (a) give rise to affective experiences such as feelings of arousal, pleasure/displeasure; (b) generate cognitive processes such as emotionally relevant perceptual effect, appraisals, labelling processes; (c) activate widespread physiological adjustments to the arousing conditions; and (d) lead to behaviour that is often, but not always, expressive, goal-directed, and adaptive.*" (Kleinginna & Kleinginna, 1981, p. 355).

Partly, the apparent impossibility of arriving at one universally accepted and applicable definition arises from the fact that the term "emotion", in scientific as in lay language, is used to describe many aspects and different levels of a multi-faceted concept.

The term "emotion", especially in the emotional memory literature, is often used synonymous with "core affect". Core affect theory underlies psychological construction models of emotion, which see emotion experience as a function of previous experience, language, executive functioning and affect. Affect varies on the dimensions of valence, from positive to negative, and arousal, from calm to excited (Russell, 2009; for a recent review of core affect theory in relation to other prevalent models of emotion see Gross, 2011). While specific emotions are transient and directed at something, core affect is an underlying neurophysiological state, which changes over time. An individual is always in a particular state of arousal with a particular valence, even though core affect is not necessarily accessed by consciousness. Core affect is a property of the individual but the dimensions of valence and arousal are also commonly used to describe properties of stimuli, which are assumed to cause an emotional response. However, Russell (2009) notes that such a causal relationship between perceptions of affective quality and core affect, although it is a widely employed premise, is an assumption that needs empirical testing.

1.2.2 Eliciting and measuring affect

To be able to study the interactions between affect and other variables, affect has to be elicited in an empirical setting, often a lab environment. Being ubiquitous in our everyday experience and functioning, affect can be influenced by perceptions of all five senses, by auditory, visual, tactile and even

olfactory and gustatory stimuli. However, owing partly to the fact that they are more easily realised in a lab environment, cognitive research typically uses visual and auditory stimuli to elicit affect. Tactile, olfactory and gustatory stimuli also tend to elicit more diverse individual affective reactions. The taste of caviar for example may produce great pleasure in one person while provoking disgust in another. These types of stimuli are also less accessible to language, which further complicates standardisation. Most people would find it difficult for example to verbalise exactly what is pleasant about a specific scent. Auditory and visual stimuli suffer from these problems to a lesser extend but are still extremely difficult to standardise. A researcher investigating the influence of legibility of a stimulus word on memory can manipulate this variable within clearly defined and objective physical parameters such as luminosity, font size, background colour etc. The affective content of a stimulus on the other hand, that is its potential to elicit affect of a certain valence and arousal value, cannot be defined in objective terms but by definition depends on a perceiver. Two physically very similar stimuli can have completely opposing affective contents. For example, consider the difference in affective impact between a picture of a smiling child holding a water pistol and a picture of the same smiling child holding a real firearm. Therefore the affective content of a stimulus can only ever be determined by people's reported reaction to it. In view of this inherent subjectivity, the best option available to ensure standardisation of stimuli is the use of large samples of ratings of the valence and arousal, or in some cases the specific emotion, associated with stimuli.

There are a number of such standardised affective stimulus sets available to researchers, including collections of affective sounds such as International Affective Digitized Sounds (IADS; Bradley & Lang, 1999b), and words such as Affective Norms for English Words (ANEW; Bradley & Lang, 1999). The most widely used types of stimuli, especially in cognitive research, are pictures in general and pictures of faces more specifically. Face stimuli are typically classified in terms of a small set of basic emotions and include the Pictures of Facial Affect (POFA; Ekman & Friesen, 1979), Karolinska Directed Emotional Faces (KDEF; Lundqvist, Flykt, & Öhman, 1998), the Montreal Set of Facial Displays of Emotion (Beaupré, Cheung, & Hess, 2000) and the NimStim (Tottenham et al., 2009). Affective picture sets are generally classified in terms of the dimensions of core affect, i.e. the arousal and valence associated with stimuli. At the time of data collection for this thesis, the only large standardised set of affective pictures available was the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1999), which is still the most widely used stimulus set of this type. It comprises of 1196 pictures varying in the two primary dimensions of valence and arousal as well as a third dimension of dominance. Ratings for each picture were obtained from approximately 100 participants. The set includes a range of different picture contents, from simple objects to depictions of complex social scenes.

While standardizing affect elicitation in experimental settings is certainly challenging, accurately measuring affect is probably even more complex as it aims to objectively record what are by definition wholly subjective experiences.

Measurements of experienced valence rely on either self-report or observation, for example of facial expression. While self-report can be confounded by aspects such as social desirability or ability to verbalise one's state of affect, observation is further complicated by observer interpretation. Especially cognitive paradigms commonly favour one of the more direct self-report measures. The Semantic Differential Scale (Mehrabian & Russell, 1974), for example, uses ratings on 18 bipolar semantic differentials to arrive at scores for valence, arousal and dominance. The very popular Self Assessment Manikin (SAM; Bradley & Lang, 1994) is a non-verbal, picture-based self-report measure for these three dimensions, avoiding confounds rooted in language. There are a number of physiological methods seeking to avoid the inherent subjectivity of self-report and observation. These include electrodermal methods such as Skin Conductance Level (SCL) or Skin Conductance Response (SCR) and cardiovascular methods such as measures of heart rate or blood pressure. These methods rely on measuring Autonomic Nervous System (ANS) activation and are typically viewed as measures of arousal only.

1.2.3 Valence and arousal – Two independent dimensions?

As noted above, affect and affective stimuli are commonly characterised by variations in two dimensions: valence and arousal. Although additional dimensions have also been proposed, most conceptualisations of affect include valence and arousal (see for example Barrett & Russell, 1999; Fontaine, Scherer,

Roesch & Ellsworth, 2007; Lang, 1995; Reisenzein, 1994; Russell, Weiss, & Mendelsohn, 1989; Watson & Tellegen, 1985). Both of these dimensions are considered continuous and theoretically independent. The valence of a stimulus therefore allows no conclusions about its arousal level and vice versa.

In practice, however, valence and arousal are related in a v-shaped or u-shaped fashion, with extreme negative and positive valences more likely to be associated with high arousal and neutral valence more likely to be associated with low arousal. Warriner, Kuperman and Brysbaert (2013), for example, report such a v-shaped relationship between valence and arousal for a large set of nearly 14000 affective English words. Lang (1995) reports the same relationship for IAPS pictures, calling it a boomerang relationship as he plots arousal along the x-axis. Bernat, Patrick, Benning and Tellegen (2006) also report a v-shaped relationship between IAPS picture valence and arousal, confirming arousal ratings with the physiological measures of startle blink magnitude, skin conductance and corrugator muscle reactions. A similar relationship between valence and arousal is found when mood is induced using Velten statements (Jennings, McGinnis, Lovejoy, & Stirling, 2000), a series of self-referential statements that are read aloud by participants to induce either positive or negative mood. Kuppens, Tuerlinckx, Russell and Barrett (2013) add the finding that there is significant variability between participants in the relationship between valence and arousal.

1.2.3 Neural correlates of affect

Affect is a multi-faceted phenomenon, ranging from simple approach or avoidance reflexes to complex processing of affective meaning. These multiple levels of affective processing are implemented on multiple neural levels. Generally speaking, the complexity of affective processing increases along the neuraxis going from caudal to rostral in the central nervous system (Norris, Gollan, Berntson, & Cacioppo, 2010). Since the present thesis is concerned with affect at the level of processing of the affective content of stimuli under simple viewing conditions, specifically neural correlates indexing affect perception will be discussed here.

The amygdala's association with affective processing has been known for such a long time through findings from animal studies (e.g. Weiskrantz, 1956) that it is now considered common knowledge. Human lesion studies have confirmed impaired identification of facial emotions as a consequence of amygdala damage (Adolphs, Tranel, Damasio, & Damasio, 1994) or amygdalotomy (Young, 1995).

While animal research and human lesion studies have their place in the investigation of the neural basis of behaviour, emotion is both highly subjective, making it difficult to assess the appropriateness of animal models, and likely to be impacted by the experience of trauma, limiting the generalisability of human lesion studies, where damage is seldom restricted to one brain area or system. Knowledge about the neural correlates of affective

perception has therefore been advanced most by functional imaging studies of healthy human participants. Viewing emotional compared to neutral faces has been shown to be associated with increased activity, as measured by blood oxygenation level dependent (BOLD) response, in the amygdala, hippocampus, parahippocampal gyrus and cingulate gyrus (Gur et al., 2002). Although the amygdala has historically been most associated with fear processing, fMRI has also shown it to be reactive to positive facial affect (Pohl, Anders, Schulte-Rüther, Mathiak, & Kircher, 2013), along with the insula.

A number of fMRI studies have sought to dissociate the specific effects of stimulus valence and arousal on brain activation. Although there is some variation in the specific brain regions reported as being neural correlates of changes in valence and arousal respectively, all studies show regions that are sensitive to each of the dimensions but not the other. Studies converge on reporting insula and dorsolateral prefrontal cortex regions as correlates of valence, while the amygdala, parahippocampus and thalamus are reported to index stimulus arousal (Anders, Lotze, Erb, Grodd, & Birbaumer, 2004; Colibazzi et al., 2010; Lewis, Critchley, Rotshtein, & Dolan, 2006; Posner et al., 2009).

Affective stimulus content has also been shown to modulate the electrophysiological correlates of picture processing. Early ERP components between 100 and 200 milliseconds post stimulus onset have been shown to be modulated by affective stimulus content, but reported effects are variable. Arousing stimuli have been shown to elicit an early posterior negativity (EPN)

around 200 to 300 milliseconds post stimulus onset when compared to neutral stimuli (see Olofsson, Nordin, Sequeira, & Polich, 2008 for review). The most extensively reported ERP component that is modulated by affective content is the Late-Positive Potential (LPP), a positive going deflection maximal over central midline electrodes that is increased for affective stimuli. It is discussed in detail in Chapters 3 and 5.

1.3 Affective memory

Although cognition and affect were historically considered fundamentally distinct and their study developed in two independent fields, there has been increasing interest in the interplay of affect and cognition in recent years. Affective stimulus content has repeatedly been shown to have a powerful effect on attentional and perceptual processes. In visual search tasks, for example, participants are faster to detect schematic drawings of faces displaying negative than positive emotions. When faces are inverted, which reduces whole-face processing and therefore affect recognition, the effect disappears (Eastwood, Smilek, & Merikle, 2001). Affective content of spatial cues has also been shown to improve perception. If a stimulus is preceded by an affective spatial cue, then the contrast threshold above which an orientation perception task can be performed successfully on the stimulus is lowered (Phelps, Ling, & Carrasco, 2006). Affective stimulus content also overrides the attentional blink, a temporary attentional blindness to target stimuli presented after preceding

detected targets. Negative words are significantly less likely to be missed when presented in the attentional blink window than neutral words (Anderson, 2005).

Affective stimulus content also modulates memory. Flashbulb memories are an extreme example of vivid and long-lasting memory for an autobiographical event based on its strong affective content (Brown & Kulik, 1977). Flashbulb memories can be created by both negative content, such as hearing news of the terrorist attacks on the World Trade Centre in 2001 (Hirst et al., 2009), and positive content, such as learning of the fall of the Berlin Wall in 1989 (Bohn & Berntsen, 2007). The focussing on affective aspects seen in flashbulb memories can also be demonstrated under conditions of overall much lower affective arousal variation. Affective pictures shown as part of an experiment under controlled conditions in a lab elicit much smaller affective arousal changes than affective life events. Nevertheless, a memory difference can be produced by affective picture content. Under passive viewing conditions, affective components of the foreground of picture stimuli are better remembered than their neutral background (Kensinger, Piguet, Krendl, & Corkin, 2005).

However, affective content does not necessarily interfere with memory for context information. In fact, a number of studies have shown improved source memory for affective over neutral material. Participants were more accurate in remembering the colour of words at study for affective over neutral words (D'Argembeau & Van der Linden, 2004; Doerksen & Shimamura, 2001), as well as in remembering the spatial location in which words had been presented

(D'Argembeau & Van der Linden, 2004). D'Argembeau and Van der Linden (2005) also showed that participants performed significantly better in a temporal information task, where they had to indicate the test list in which each test picture had been presented at study, if the test picture was of negative affective content, compared to neutral and positive pictures. Recognition memory performance was enhanced for both negative and positive relative to neutral pictures.

Affective stimuli are also typically associated with an increased contribution of recollection, relative to familiarity. Participants give a higher proportion of "remember" judgments in response to negative or positive words (Kensinger & Corkin, 2003; Mickley & Kensinger, 2008) and pictures (Mickley & Kensinger, 2008), compared to neutral stimuli.

Functional imaging studies have provided evidence for an interaction between amygdala and hippocampal activation in affective memory (Phelps, 2004). Positron Emission Tomography (PET) first showed that increased amygdala activity during the viewing of affective video clips is associated with later improved recall of the clips (Cahill et al., 1996; 2001). Interestingly, the lateralisation of amygdala activity correlating with improved recall differed between men and women. Chapters 2 and 7 will discuss gender differences in affective memory and its neural correlates in more detail. A review of functional imaging studies of the retrieval in affective memory concluded that affective memory retrieval is implemented in a system consisting of the amygdala, hippocampus and prefrontal cortex (Buchanan, 2007).

1.4 Research questions – affective memory

The central focus of the present thesis is the affective modulation of recognition memory and its electrophysiological correlates. Chapter 6 below discusses relevant electrophysiological research and presents behavioural findings of affective memory and neural correlates of affective memory.

The main research questions addressed in this context are:

- Does processing of, and memory for, affective material differ by stimulus valence or arousal or a combination of both?
- Is the late positive potential an electrophysiological correlate of attention capture by affective stimuli?
- How do the effects of affective content on recognition memory change with increasing retention intervals?
- Is enhanced affective memory associated with increased attention to affective stimuli?

Chapter 2:
Individual Differences in Affect and Cognition

Beyond the tired stereotypical view that "men are from Mars and women are from Venus", research has produced evidence of gender differences in a number of affective and cognitive processes. Additionally, thanks to recent advances in genotyping techniques and growing interest in psychiatric genetics as well as the genetic basis for affect and cognition, small genetic variations with functional outcomes in affective processing or cognition have also been identified. While there is merit in averaging to uncover universal processes and mechanisms of brain function and behaviour, a full understanding of any affective or cognitive domain must also include an understanding of the individual difference factors that modulate it. The present chapter discusses current research on gender and genetic differences in affect and cognition, concentrating on the BDNF val66met polymorphism as a source of variation in behaviour and brain function and ending with a summary of the main research questions addressed by the present thesis.

2.1 Effects of gender

2.1.1 Gender differences in affect

The existence of gender differences is well established in clinical psychology and psychiatry. Men and women differ significantly in prevalence of a wide range of psychiatric disorders. Interestingly, the disorders that are more common in one gender than the other show a high degree of relatedness. While men are more likely to develop dependence issues, such as to drugs or alcohol, and antisocial personality disorders, women consistently show higher rates of depression and dysthymia, as well as anxiety disorders such as generalised anxiety disorder, panic disorder, social phobia and specific phobia (Kessler, 1993b; Kessler & McGonagle, 1994). Attention deficit/hyperactivity disorder is more prevalent in boys than in girls by a factor of between three and 16 (Nøvik et al., 2006). Some studies find prevalence rates of clinical depression in women up to twice as high as those in men (Kessler, 1993a; Weissman, 1977). Maier et al. (1999) showed that the prevalence of depression was consistently higher in women than in men across 14 international samples including participants in Asia, Africa, Europe and America. While personality disorders are more common overall in men, women have higher rates of paranoid, borderline, avoidant, dependent, histrionic and obsessive compulsive personality disorder than men. Additionally to antisocial personality disorder, men are also more likely to exhibit narcissistic personality disorder (Trull, Jahng, Tomko, Wood, & Sher, 2010). The overall pattern that emerges is one of women being more vulnerable than men to mood disorders. Eaton et al. (2012) showed that women

are more vulnerable to disorders characterised by internalising, such as mood and anxiety disorders and men are more vulnerable to disorders characterised by externalising, such as substance abuse disorders and antisocial personality disorder. The authors argue that the observed gender differences in prevalence are due to gender differences in internalising-externalising liability. Using the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) with a sample size of over 43000 participants, they showed that women, independently of mental health status, score higher in internalising liability than men.

The question that arises from these apparently systematic differences in pathology is whether there are underlying gender differences in affective processing in the healthy population, which may increase liability to certain types of disorders over others. Women have been shown to be more emotionally reactive and expressive than men (Balswick & Avertt, 1977; Bradley, Codispoti, Sabatinelli, & Lang, 2001; Kring & Gordon, 1998; Larsen & Diener, 1987) and better at identifying facial emotion (Thayer & Johnsen, 2000). Grossman and Wood (1993) argue that this increased emotional intensity seen in women is driven by gender role rather than biological difference. They asked participants to rate how frequently and how intensely they experienced and expressed a set of five emotions: love, joy, sadness, anger and fear. Participants were also asked to indicate what they felt was a typical man's and a typical woman's intensity of expression of these emotions. They found that women reported more frequent and more intense experience and expression of all

emotions except anger. The same pattern was found in participants' ratings of the typical man and woman. The authors interpreted the finding that ratings of personal emotional experience correlated with the extent to which participants endorsed stereotypical gender roles in their ratings of the typical man and woman as evidence that individual differences in affect are driven by conformity to gender roles. The authors point out that participants' self-reports, rather than the underlying affective experience, may be skewed by views on gender roles. A second explanation for the correlation that is not considered, is that participants likely derive their view of a typical member of their own gender, at least in part, from their own experience. The study therefore cannot conclusively decide whether "stereotypical" emotional experience arises purely on learned social norms or reflects an actual underlying gender difference in neural anatomy or functioning. It does, however, emphasise the need for more objective measures of affective response, especially when considering individual differences.

Although they cannot distinguish between effects of nature and nurture, i.e. differences in underlying physiology and those that arise due to learning and experience, functional imaging techniques do avoid the confounds of social desirability and skewed self-perception that are likely to affect self-report measures. A number of functional Magnetic Resonance Imaging (fMRI) studies have shown gender differences in brain function during affective processing, both in the presence (Hofer et al., 2006; Hu & Xiao, 2009) and in the absence of behavioural gender differences (McClure, 2004; Wrase et al., 2003). When

asking participants to evaluate face stimuli for how threatening they are, (McClure, 2004) found no gender difference in either adolescent or adult participants' threat ratings. Functional MRI, however, showed a gender difference in neural activation in response to affective face stimuli in adults only. Adult women showed activation in the orbitofrontal cortex and amygdala only when presented with angry faces, i.e. stimuli that convey threat. Adult men and adolescents of both genders did not show such clear discrimination of neural activity by affective face expression. Three fMRI studies have also assessed gender differences in brain activity during viewing of affective IAPS pictures. Greater signal change from the blank screen baseline in men than in women was shown in the extrastriate cortex during passive viewing of erotic but not of family IAPS pictures.

Beyond sexual stimuli, Wrase et al. (2003) showed increased activation in response to positive pictures in men compared to women in the amygdala and frontal lobe, while women showed increased activity compared to men in the anterior and medial cingulate gyrus in response to negative pictures. Behavioural valence and arousal ratings did not differ between the genders, nor did skin conductance response or startle modulation. Hofer et al. (2006) did find a gender difference in participants' affective reaction to negative and positive IAPS pictures as measured by the Positive and Negative Affect Schedule (PANAS; Watson & Tellegen, 1985) during a mood induction task. Participants were instructed to attempt feeling happy or sad with the help of the IAPS pictures presented. PANAS negative score was significantly more

increased compared to baseline during negative picture viewing in women than in men. Men showed more positive signal changes for positive pictures in the right posterior cingulate, left putamen and left cerebellum and more positive signal changes for negative pictures in the bilateral superior temporal gyri and cerebellar vermis. The differences found between men and women in fMRI studies using a range of affective tasks point to a difference in implantation of affective processes in the brain. As De Vries (2004) points out, such gender differences in brain function in the absence of behavioural differences are likely to represent compensatory processes in place to bridge underlying sex differences, such as in neural structure or hormone balance.

It is of note that Soleman et al. (2014) provide evidence against the modulation of affective processing by often cited candidate hormones for gender differences: oestrogen, luteinising hormone (LH) and follicle-stimulating hormone (FSH). Based on a difference in brain activation associated with negative compared to neutral stimuli according to female participants' cycle phase (early vs late follicular), oestrogen, which systematically varies over the course of the female menstrual cycle, has been hypothesised to modulate affective arousal and its neural correlates (Goldstein, 2005). However, assessing brain response to IAPS pictures in 21 female-to-male transsexual participants after an eight week course of suppression of gonadal hormone production and 19 female controls, Soleman et al. (2014) found no association between oestrogen, LH or FSH levels and brain activity associated with affective content.

Although fMRI research is useful in uncovering the neural systems likely to mediate gender differences in affective processing, event-related potential studies, given their much better temporal resolution, provide an important tool for dissociating gender effects on different affective processes. At the time of data collection, gender differences in affective processing had not extensively been studied using ERPs. Gasbarri et al. (2007) assessed gender differences in P300 amplitudes between 300 and 500 milliseconds in response to negative, neutral and positive pictures at left and right frontal and parietal sites (electrodes F3, F4, P3, P4). They showed a lateralisation difference between women and men in response to negative pictures, with women showing larger P300 amplitude increases at right hemisphere electrodes and men showing larger P300 amplitude increases at left hemisphere electrodes (for a discussion of the difference in lateralisation of affective brain activity between the genders, see Chapter 7.1).

2.1.2 Gender differences in recognition memory

Gender differences have also been shown in a range of cognitive functions. Generally speaking, women have been found to have an advantage over men on verbal tests, while men outperform women on visuospatial tasks (Collins & Kimura, 1997; Dabbs, Chang, Strong, & Milun, 1998; Weiss, Kemmler, Deisenhammer, Fleischhacker, & Delazer, 2003)). Guerrieri et al. (2016) showed a persisting advantage for men over women on a series of visuo-spatial tasks

under gonadal suppression, concluding that gender differences on these tasks are not dependent on current levels of oestrogen or testosterone. Hausmann, Schoofs, & Jordan (2009) measured performance on a series of visuospatial and verbal tasks under condition of gender stereotype activation and in a control group. They found the expected gender advantages. Male advantage for mental rotation was driven almost entirely by an effect in the stereotype activation group, which also exhibited 60% higher levels of testosterone than the control group. The authors conclude that testosterone mediates effects of stereotypes on gender differences in affective ability. However, given Guerrieri et al.'s (2016) recent findings of gender differences under gonadal suppression, it is likely that both testosterone levels and visuospatial performance are increased by the activation of male stereotypes but are not functionally related. Although women have been found to outperform men on verbal tasks, a recent review of the literature found no general advantage for women in verbal ability and no consistent gender difference in language-related cortical anatomy (Wallentin, 2009).

There is also evidence of gender differences in memory performance. A study of a very large sample of medical school entry tests of 96,968 men and 90,142 women found three main factors in the test batteries used: reasoning, perceptual speed and memory. While men showed an advantage for reasoning, women outperformed men on the memory factor (Stumpf & Jackson, 1994). One problem that is obvious for this particular study should be highlighted for the literature on gender differences in memory and other cognitive abilities at

large: The sample is not representative of the general population but has undergone selection on the very basis of cognitive ability. What is more, applicants for medical study are not only selected for high cognitive ability but male and female applicants are likely differentially affected by gender stereotypes and inequalities. It is conceivable, given the confidence required to pursue such a high status degree and profession and persistent gender biases in the perception of likely academic and professional success, that the female group was subjected to selection bias to a higher degree than the male group, i.e. the threshold for prospective applicants to deem their cognitive abilities sufficient to pursue a medical degree may be higher for women than for men. The fact that over the nine years for which data were analysed the female memory advantage decreased, coupled with the increasing female to male ratio in higher education over time, supports this hypothesis. Since most psychological research uses undergraduate samples, this potential confound of a differential selection bias for men and women should be kept in mind when considering gender effects on cognition.

In studies of autobiographical memory, women have been shown to report more vivid memories with a stronger focus on their emotional and social context than men (Grysman & Hudson, 2013). Consistent with this stronger emphasis on the social significance of a memory, women have also been shown to have better memory for faces than men (Lewin & Herlitz, 2002; Lewin, Wolgers, & Herlitz, 2001; Rehnman & Herlitz, 2007), face memory arguably being an important prerequisite of successful social interaction. Women's

superior face recognition memory is associated with increased scanning of faces at encoding (Heisz, Pottruff, & Shore, 2013). The gender difference diminishes with repeated exposure to the same stimuli, suggesting it is driven by women's more efficient processing of the stimuli at encoding. Face recognition performance has been shown to be correlated with oestrogen levels in women but gender differences remain when oestrogen levels are matched between male and female participants (Yonker, Eriksson, Nilsson, & Herlitz, 2003).

Herlitz, Airaksinen and Nordström (1999) found an overall memory advantage for women on a series of recall and recognition tests that were either verbal (words) or visuospatial (concrete and abstract pictures) in nature. Despite the expected gender differences in other cognitive tasks, with women outperforming men in verbal production and men outperforming women in mental rotation, women not only showed superior free recall of abstract words but also on free recall of concrete pictures, with a marginally significant higher level of performance in concrete picture recognition. Women have also been shown to have better memory for the location of to-be-remembered items within everyday scenes, another memory task with a strong visuospatial component (De Goede & Postma, 2008). However, in tasks that require more complex visuospatial processing at encoding, an advantage for men over women has been demonstrated (Lewin et al., 2001), suggesting a gender influence at the encoding stage of memory. Krueger and Salthouse (2010) assessed the effect of gender on the acquisition and retention of words using a paradigm in which a study-recall block for the same word list was repeated

four times, followed by a study-recall block using a distractor list and a final free recall phase for the original word list. By analysing gains, i.e. newly recalled words, and losses, i.e. previously recalled words that were not recalled, for each block, they showed that men had overall fewer gains than women and women therefore had an advantage in the acquisition, not the retention, of memory for words. As for face recognition, a female advantage in verbal episodic memory has been shown even in the absence of differences in oestrogen between male and female participants, showing that current circulating levels of oestrogen do not drive these gender differences (Yonker et al., 2003).

Although greater hippocampal volumes have been reported for women when corrected for head size (Filipek, Richelme, Kennedy, & Caviness, 1994; Szabó, Lancaster, & Xiong, 2003), no gender difference in hippocampus volume can be demonstrated when head size is matched across genders (Perlaki et al., 2014), leading to the conclusion that effects observed using proportion head-size correction strategies are driven by effects of these correction strategies rather than real gender differences.

Functional imaging has shown gender differences in recognition memory, even in the absence of behavioural differences, suggesting differences in the neural implementation of memory processes. Using fMRI, (Banks, Jones-Gotman, Ladowski, & Sziklas, 2012) showed increased left hippocampal activation during encoding and recognition of verbal information in women compared to men, while an abstract design learning task was associated with increased right

hippocampal activation in men compared to women. Ino, Nakai, Azuma, Kimura, & Fukuyama (2010) showed that in the absence of behavioural gender differences in face recognition, men show increased neural activity during encoding and retrieval in a number of locations including the hippocampus. They interpret the relatively lower activation seen in women as evidence for increased efficiency of the neural systems involved in face recognition.

Taylor, Smith and Iron (1990) also compared word and abstract shape stimuli in a recurring stimulus task while recording EEG. Behaviourally, women and men did not differ significantly in either accuracy or reaction times. However, they showed an earlier onsetting P3 difference between hits and correct rejections in women than in men, as well as an interaction of location and task, with higher peak amplitudes anteriorly for shapes but posteriorly for verbal stimuli, in women but not in men. More recently, Guillem and Mograss (2005) reported gender differences in recognition memory for faces and its electrophysiological correlates. Female subjects had significantly higher hit rates and discrimination indices d' then males. Consistent with Taylor et al.'s (1990) findings using shape stimuli, Guillem and Mograss (2005) also showed more pronounced old/new effects for faces in women than in men in anterior locations, in the 300 to 500 millisecond N400 time-window. The authors attribute this difference in anterior old/new effect sizes to a gender difference in retrieval strategies.

In sum, although the neural basis for gender differences in recognition memory is not yet well understood, there is clear evidence for such a difference both on a behavioural and neurofunctional level.

2.2 Effects of BDNF val66met genotype

2.2.1 Introduction to Single Nucleotide Polymorphisms (SNPs)

Brain anatomy and function, and therefore human behaviour, are influenced to a large extent by our genes, which carry "building instructions" for our bodies. This information is contained in 23 chromosome pairs, one member of each pair being inherited from each parent. Each chromosome is made up of tightly coiled strands of DNA (or deoxyribonucleic acid). Information is encoded in the sequence of the four chemical bases: adenine (A), guanine (G), cytosine (C) and thymine (T). Adenine pairs with thymine and cytosine with guanine to make the base pairs that are responsible for the iconic double helix structure of DNA. Bases are attached to sugars and phosphates to make up so-called nucleotides, three of which make a codon, which is a template for the production of specific amino acid, the building blocks of proteins. A gene is a series of codons that contains information for the production of a protein.

A Single Nucleotide Polymorphism (SNP) is a very small genetic change of just one of the bases within a codon, which can affect the protein being encoded. Some such polymorphisms have been found to have consequences that are measurable at a neuroanatomical, neurofunctional or behavioural level. One of them is the val66met polymorphism of the brain-derived neurotrophic factor (BDNF) gene at codon 66 on chromosome 11. BDNF val66met is a change from the guanine nucleotide to adenine at codon 66, resulting in a change in amino acids from valine to methionine (Sheikh, Hayden, Kryski, Smith, & Singh,

2010). There are two copies of each chromosome. Alternative forms at the same position on a chromosome are referred to as "alleles". A person can therefore either carry two Val-alleles (Val/Val homozygotes), two Met-alleles (Met/Met homozygotes) or one Val-allele and one Met-allele (Val/Met heterozygotes). Studies comparing all three genotypes typically find a dose-response relationship, i.e. stronger effects with increasing Met-allele load (see Mukherjee et al., 2011). Carrying one or two Met-alleles affects the intracellular distribution and packaging of pro-BDNF, a BDNF precursor that in turn affects post-synaptic activity-dependent secretion of mature BDNF (Egan, Kojima, Callicott, Goldberg, Kolachana, Bertolino, Zaitsev, Gold, Goldman, Dean, Lu, & Weinberger, 2003b). BDNF is a growth factor that has been shown to play a role in neuron growth, differentiation and survival (Acheson et al., 1995; Huang & Reichardt, 2001; Teixeira, Barbosa, Diniz, & Kummer, 2010).

2.2.2 Effects of BDNF val66met on affect

The neurotrophic hypothesis of depression implicates BDNF as a central factor in mood disorders (Duman & Li, 2012). Since the val66met SNP indirectly affects the activity-dependent secretion of BDNF (Egan, Kojima, Callicott, Goldberg, Kolachana, Bertolino, Zaitsev, Gold, Goldman, Dean, Lu, & Weinberger, 2003b), the polymorphism has been hypothesised to play a role in vulnerability to depression and other mood disorders. However, findings are inconsistent and two recent meta-analyses have found no association between

BDNF val66met genotype and anxiety or anxiety-related personality traits (Frustaci, Pozzi, Gianfagna, Manzoli, & Boccia, 2008) or between BDNF val66met genotype and bipolar disorder (Wang, Li, Gao, & Fang, 2014) or Major Depressive Disorder (MDD) overall, although the Met/Met genotype was significantly more common among male MDD patients than controls (Verhagen et al., 2008) and has been shown to moderate the relationship between life stress and depression (Hosang, Shiles, Tansey, McGuffin, & Uher, 2014).

Despite inconsistencies in the findings regarding a link between BDNF genotype and affective disorders, effects of the val66met SNP on behaviour and brain function can be demonstrated. Colzato, Van der Does, Kouwenhoven, Elzinga and Hommel (2011) showed that healthy Met-carriers reported significantly higher levels of anxiety during a cold pressure test and had significantly higher anticipatory cortisol responses. Met-carriers also reported higher average alcohol intake, which could indicate differences in response to different levels of everyday stress between val66met genotypes.

There are several reports of a link between val66met genotype and affective processing. Goldman et al. (2010) reported greater amygdala and anterior hippocampus activations during affective face viewing in adolescent Met-carriers than in Val/Val homozygotes. However, the effect was only present in anxious and depressed adolescents and not in their healthy peers. Mukherjee et al. (2011) did show an effect of BDNF val66met genotype on the neural activation during affective face processing, although not in the amygdala.

Participants viewed blocks of fearful or neutral faces and made a gender decision for each stimulus, while fMRI was recorded. After scanning was completed, participants were tested on facial emotion recognition with a task requiring the naming of the emotion displayed by a series of face stimuli (ten faces each with happy, fearful, surprised, sad, disgusted and angry expressions). When age and IQ were taken into account, Met-carriers performed significantly worse in the fear condition of the emotion identification task. Met-carriers also showed more activation in response to fearful relative to neutral faces than Val/Val homozygotes in areas including the anterior cingulate cortex and parts of the prefrontal cortex, parts of the brain stem and cerebellum and the left insula. Mukherjee et al. (2011) also found reduced connectivity from the anterior cingulate cortex to the left hippocampus.

Using positive, negative and neutral IAPS pictures, Montag, Weber, Fliessbach, Elger and Reuter (2009) did show differences in amygdala activation during affective picture viewing between female Met-carriers and Val/Val homozygotes. A region of interest analysis including bilateral amygdala voxels showed stronger increases of activation for positive over neutral pictures for Met-carriers than for Val/Val homozygotes in the right but not the left amygdala. The same effect was significant between BDNF val66met genotypes for negative compared to neutral pictures but was less pronounced. This stronger amygdala reactivity to affective pictures in Met-carriers was replicated, along with stronger right anterior cingulate cortex reactivity to

affective pictures, by Outhred et al. (2012). Assessing a second polymorphism, 5-HTTLPR, an SNP affecting serotonin transporter, which has been previously linked to emotion processing, Outhred et al. (2012) found an interaction between BDNF val66met and 5-HTTLPR such that participants with copies of both the 5-HTTLPR S-allele and the BDNF Met-allele showed the highest reactivity. This points to the importance of understanding the influence of any particular SNP on the brain and behaviour in the context of other, related SNPs. Nevertheless, mapping the functional implications of individual SNPs in isolation is an important first step in the understanding of genetic differences in affective processing and other domains.

2.2.3 Effects of BDNF val66met on recognition memory

The second main area of focus in research on the functional consequences of the BDNF val66met polymorphism is memory, since BDNF is known to affect hippocampal long-term potentiation (Poo, 2001), a synaptic process crucial in memory formation. The Met-allele of the polymorphism has repeatedly been shown to be associated with a reduction in hippocampal size but the evidence is not unequivocal. A meta-analysis of differences in hippocampal volume by BDNF val66met genotype found no significant reduction in volume in Met-carriers, although the effect was close to significance ($p=.058$). Met-carriers did show significantly smaller hippocampal volumes in studies employing manual tracing of the area of interest (Harrisberger et al., 2014). A second meta-analysis

did find a significant reduction for Met-carriers in both hippocampal volume and activation in memory paradigms, as well as behavioural performance (Kambeitz et al., 2012). However, Dodds, Henson, Miller and Nathan (2013) point out that the effects of the BDNF val66met polymorphism on hippocampal activation may have been overestimated by the latter study, due to the method of voxel selection employed for the meta-analysis. Richter-Schmidinger et al. (2010) report no effect of BDNF val66met genotype on hippocampal volume in a relatively large sample of 135 healthy participants.

Karnik, Wang, Barch, Morris and Csernansky (2010) also did not find an association between BDNF val66met genotype and hippocampal volume and no effect on four memory-related behavioural tests: the Category Fluency Task (Goodglass & Kaplan, 1983) and the Wechsler Memory Scale subscales Logical Memory, Digit Span Forwards and Digit Span Backwards (WMS; Wechsler, 1997). Dempster et al. (2005), however, did show a significant reduction in Met-carriers' performance on the WMS delayed measure of logical memory. Lamb, Thompson, McKay, Waldie and Kirk (2015) also showed poorer performance of Met-allele carriers on the Faces subtest of the WMS, a face recognition task, but no effect of val66met genotype on the Family Pictures subtest, a task requiring recall of visual scenes.

Goldberg et al. (2008) assessed differences in the influence of levels of processing and study-test delay by BDNF val66met genotype in a word recognition paradigm. They found that Met-carriers showed consistently lower memory performance than Val-homozygotes independently of encoding task

(shallow vs deep) and test delay (immediate, 30 minutes or 24 hours). Both Hits and Discrimination Index d' were reduced in Met-carriers compared to Val/Val homozygotes, while Correct Rejections were unaffected.

Met-carriers are also impaired relative to Val/Val homozygotes in working memory performance (Richter-Schmidinger et al., 2010) and show a stronger effect of age on the decline of item memory and prospective memory across the lifespan (Kennedy et al., 2015).

As well as impairing memory performance, the Met-allele of the BDNF val66met polymorphism has also been shown to affect memory-related brain activity. Egan, Kojima, Callicott, Goldberg, Kolachana, Bertolino, Zaitsev, Gold, Goldman, Dean, Lu and Weinberger (2003a) reported lower scores in Met/Met than Val/Val homozygotes on a verbal episodic memory measure from the WMS. Normal disengagement of the hippocampus during an n-back working memory task was interrupted in Met-carriers, pointing to differences in hippocampal function by BDNF val66met genotype.

Hariri, Goldberg and Mattay (2003) demonstrated attenuated hippocampal activation during recognition memory directly. Functional MRI was recorded during encoding and retrieval of novel complex scenes. Met-carriers showed significantly reduced recognition memory performance, expressed in higher numbers of both misses and false alarms. Additionally, Met-carriers showed decreased hippocampal activation during the encoding and retrieval of visual scenes.

Kauppi, Nilsson, Adolfsson and Lundquist (2013) also reported decreased MTL-activation in Met-carriers during a face-name associate memory task in a large sample of 194 participants. However, decreased MTL activation in Met-carriers relative to Val/Val homozygotes was only demonstrated during encoding, not retrieval of face-name pairs. Behavioural differences confirmed a trend towards poorer performance in Met-carriers but did not reach significance. Within the sample of healthy older adults between 55 and 75 years, age did not modulate the BDNF val66met effect.

2.3 Research questions – Individual differences in affective cognition

This chapter discussed gender differences in affective processing on one hand and in memory and its neural correlates on the other. Although the neural basis of gender differences in memory is not yet well understood, it is likely to be modulated by gender differences in affective processing. Exploring the nature of this hypothesised modulation as well as its electrophysiological correlates is a vital step in increasing understanding of individual differences in affective memory, which in turn has implications for the theoretical understanding of memory in general and applications in both clinical practice and optimising normal functioning.

The BDNF val66met polymorphism has also been shown to modulate both affective and memory processes. It is therefore hypothesised that Met-carriers will also differ from Val/Val homozygotes in the modulation of memory

processes by affective content. While a difference in the neural correlates of recognition memory between BDNF val66met genotypes has been established, a modulation of its electrophysiological correlates has not been demonstrated to date. Establishing that the influence of the BDNF val66met polymorphism can be shown on an electrophysiological level would pave the way for ERP investigations of the role of BDNF val66met in recognition memory in general and in affective recognition memory in particular. A better understanding of these relationships, in the light of BDNF val66met's involvement in psychiatric pathology, is likely to have consequences for clinical practice as well as contributing to the knowledge base on individual differences in memory.

In sum, the specific research questions arising from this chapter, which will be addressed in Chapters 7 and 8 respectively, are:

- Are there gender differences in affective modulation of cognitive processes and their electrophysiological correlates?
- Is there evidence for a genetic influence on affective cognition and its electrophysiological correlates?

Chapter 3: The Event-Related Potential Technique

3.1 Introduction

Event-Related Potentials (ERPs) are electroencephalogram (EEG) epochs, which are time-locked to particular events and averaged over many trials. EEG is a continuous recording of fluctuations in electrical brain activity measured at the scalp and has been used in research and clinical settings since Hans Berger's pioneering experiments in 1929 (Berger, 1929). In the 1960s, the wider availability of computers allowed for averaging of large numbers of EEG epochs, enabling the emergence of the ERP technique. Modern cognitive ERP research started in 1964, with the description of the first cognitive ERP component (the Contingent Negative Variation or CNV) by Grey Walter and colleagues (Walter, Cooper, Aldridge, McCallum, & Winter, 1964).

As a technique for imaging cognitive brain activity, ERPs are popular for several reasons. One of them is the relative low set-up and running costs of an ERP lab, which are a fraction of those of other imaging techniques such as fMRI or PET. This, together with the non-evasive nature of the ERP technique, makes it an ideal tool for imaging brain activity for cognitive research. Its biggest advantage over other techniques, however, is its excellent temporal resolution, which is matched only by the related Event-Related Magnetic Field (ERMF) technique. With a temporal resolution in the region of 1ms, electromagnetic

measures (ERPs and ERMFs) lend themselves to exploring fast-paced cognitive processes that hemodynamic measures (fMRI and PET) with their temporal resolution in the range of several seconds have very limited access to.

3.2 Neural origins of the EEG signal

EEG records voltage differences across the scalp, over time. These voltage differences are generated by neural activity. Neurons produce voltage changes in two forms: action potentials and postsynaptic potentials. Action potentials are moving voltage spikes that travel from the cell body to the axon terminal, where they trigger the release of neurotransmitters. The neurotransmitters in turn bind to receptors in the postsynaptic membrane, causing a graded change in the postsynaptic potentials across the cell membrane. The arrangement of axons and the rapid firing rate and short-lived nature of action potentials means that action potential signals from adjacent cells almost always cancel each other out so that they cannot be recorded at the scalp (Luck, 2005).

The signals picked up by EEG recorded at the scalp, in the vast majority of cases, originate in postsynaptic potentials only. These are graded potential changes in the postsynaptic membranes, which are much longer lived than action potentials. A postsynaptic potential creates a dipole between the dendrites and the cell body of the neuron and when many such dipoles in adjacent neurons are spatially and temporally aligned, they can summate to create an "equivalent current dipole" which will produce a measurable signal

at the scalp. This means that only signals from neuron populations with broadly parallel orientations can be recorded through EEG. Cortical pyramidal cells typically show this arrangement and are the main source of the EEG signal. But even when neurons are aligned relative to the cortical surface, cortical folding still leads to some regions not contributing to the EEG due to signal cancellation (Luck, 2005).

Where signals can summate into equivalent current dipoles, these dipoles cause current to spread out throughout the conductive medium of the brain leading to measurable signals at the scalp. However, due to the different tissues composing the brain and their different relative conductivities, signals measurable at the scalp are blurred and distorted and do not necessarily reflect activity in cortical areas close to the recording site.

Importantly, while it is possible to mathematically approximate the distribution of scalp voltages that would be produced by the activation of specific neural generators (the "forward problem"), the inverse is not possible. For any given scalp distribution there is an infinite number of possible combinations of neural generators (Helmholtz, 1853), making ERP source localisation difficult and imprecise, even when additional constraints are added into the algorithms used (see Luck, 2005).

3.3 EEG recording

In the Psychological Imaging Laboratory at the University of Stirling, where data presented in this thesis were collected, EEG is recorded from 62 silver/silver chloride electrodes arranged in an extended version of Jasper's (1958) International 10/20 system (FP1, FPZ, FP2, AF3, AF4, F7, F5, F3, F1, FZ, F2, F4, F6, F8, FT7, FC5, FC3, FC1, FCZ, FC2, FC4, FC6, FT8, T7, C5, C3, C1, CZ, C2, C4, C6, T8, TP7, CP5, CP3, CP1, CPZ, CP2, CP4, CP6, TP8, P7, P5, P3, P1, PZ, P2, P4, P6, P8, PO7, PO5, PO3, POZ, PO4, PO6, PO8, CB1, O1, OZ, O2, CB2) using an elastic EEG cap (Quick-Cap, Neuromedical Supplies: www.neuro.com). Figure 3.1 below schematically shows the arrangement of these electrodes across the scalp. The 10/20 system places electrodes on the intersections of a grid created by dividing the distance from the nasion, the scalp depression between the eyes, to the inion, the most prominent point of the occipital bone, and from one preauricular point to the other, into equal percentages. "F" (Frontal) locations are placed at 30% of the distance from the nasion to the inion, "C" (Central) locations at 50% and "P" (Parietal) locations at 70% of the distance. Midline sites lie equidistant from the two preauricular points and are designated "z". Additional electrodes are distributed equally across the distance between the two preauricular points and labelled with increasing odd numbers going left from the midline and increasing even numbers going right. All electrode labels therefore indicate the precise location of the electrode on the scalp.

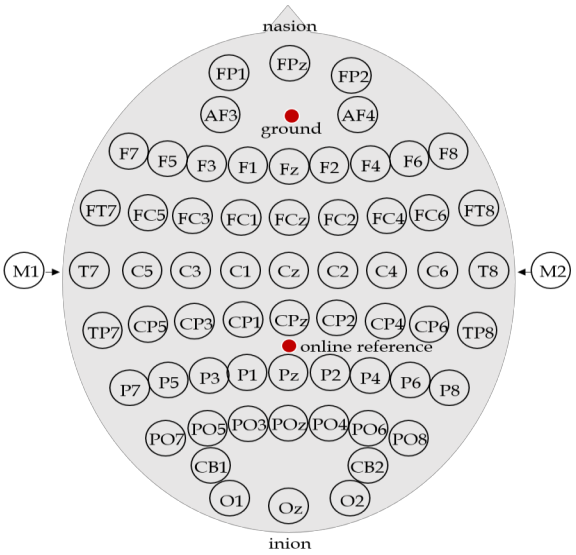


Figure 3.1 *Layout of electrode recording sites across the scalp.*

Electrodes were referenced to an additional electrode located between Cz and CPz during recording and two additional reference electrodes were placed on the mastoids for later off-line re-referencing to recreate an averaged mastoid reference. An additional midline electrode located between AF3 and AF4 served as the ground electrode. Eye movements were monitored through electrodes above and below the left eye (Vertical EOG) and on the outer canthus of each eye (Horizontal EOG). Electrodes were connected to the scalp by means of a conductive gel. The gel was administered into the space between each electrode and the scalp using a blunt syringe and good connections were ensured by moving hair and gently abrasing the top layer of the skin with the help of the wooden end of a cotton swap.

Impedances were maintained below 5kΩ to ensure a good signal-to-noise ratio. Signals were recorded and amplified using Neuroscan 4.4 Acquire software (Quick-Cap, Neuromedical Supplies: www.neuro.com) and a Synamps^2 amplifier with a gain of 2010. Data was digitised at 250 Hz. The Nyquist Theorem states that for analogue signals to be digitised without loss of information, the sampling rate must be at least twice the highest frequency component in the original signal. A sampling rate of 250 Hz is sufficient for creating a faithful digital representation of any signal of interest but this could be compromised by high frequency noise in the analogue signal which could lead to aliasing. Aliasing describes the creation of false low frequency signals in digitised data which can happen when analogue data is sampled at less than twice the rate of its highest frequency components. To prevent aliasing of such high frequency noise, for instance caused by muscle activity, a low-pass filter was set at 40 Hz. A high-pass filter was also set at 0.1 Hz to minimise low-frequency noise such as can be created by impedance drift.

3.4 Processing

ERP processing generally comprises of two tasks: noise reduction and averaging. Although steps were taken to minimise noise in the recording, such as instructing the participant to sit still, demonstrating the effect of bodily and facial movements on the EEG signal, as well as controlling the testing room temperature to minimise sweating, some noise inevitably remains in the

recorded data. As a first step towards reducing noise in the EEG recording, data was visually inspected. This allows segments containing excessive noise, such as noise arising from participant movement, to be removed.

Any problems with individual channels caused by a bad connection or faulty electrode were also identified this way. Where possible without losing an excessive number of trials, segments of EEG containing such electrode problems were removed. In case of long-lasting or permanent electrode problems, the channel affected was reconstituted using data from surrounding channels.

Another significant source of noise in the EEG recording are eye blink movements. While it is possible to instruct participants to blink only at specified times during the experiment, such an instruction can be distracting from the experimental task and introduce additional noise through participants straining to avoid blinking. Compliance with the instruction can also be variable, reducing the number of blink-free trials. Therefore, in the experiments presented in this thesis, no instructions regarding blinking were given and ocular artefacts were removed during EEG processing instead. This is possible because eye blinks affect EEG in a systematic way. It is therefore possible to determine the contribution of the Electrooculogram (EOG) to the signal recorded at each electrode side using linear regression and remove this contribution from the EEG data. This ocular artefact reduction was completed using the procedure provided as part of the Neuroscan Edit software, concluding the steps taken to reduce noise in the EEG data.

To allow averaging, epochs were created for each trial by including data from 100 ms before to 1900 milliseconds after stimulus onset. Epochs were baseline-corrected to a pre-stimulus baseline lasting from -100 ms to stimulus onset, a period that is assumed to be free of trial specific activity. Epochs in which drift exceeded ±75μV were excluded. Data was then re-referenced to a linked mastoid reference and smoothed using a five point rolling average. Amplitudes in excess of ±100μV were assumed to be noise artefacts, since meaningful signal variations range well below this threshold, and epochs containing these were rejected.

Epochs associated with the same stimulus type were averaged within each participant and task. Averaging trials in this way reduces the influence of random noise on the data and amplifies the effects associated with the stimulus and task of interest. To ensure a good signal-to-noise ratio, participants with fewer than 16 trials per condition were excluded from further processing. Individual participants' averages were combined to produce grand averages for each combination of task and stimulus type.

3.5 Analysis

In the present thesis, ERPs were formed for responses in two types of paradigms, affective processing and affective recognition memory. To quantify ERP differences in affective processing, mean amplitudes of the grand average waveforms were calculated for each affective condition (negative, neutral,

positive) in a 400-1000 millisecond time window. For the affective recognition memory tasks, mean amplitudes were similarly calculated for all combinations of affective condition (negative, neutral, positive) with the two response outcomes of interest (hits and correct rejections) in three time windows: 300-500 milliseconds, 500-800 milliseconds and 800-1500 milliseconds. Time windows were chosen based on a combination of a priori expectations of the timing of ERP effects of interest (discussed in Chapter 3.6 below) and visual inspection of the onset and offset of effects in the data. Kilner (2013) argues that selecting time windows and electrodes of interest by visual inspection alone introduces a bias towards false positives and that such an approach must therefore be avoided. To address this, all time windows chosen for the analyses presented here are those that are established in the literature and visual inspection was used only to confirm that effects fell within these time windows to assure that potential effects with temporal distributions not fitting the a priori time windows were not missed. Effect sizes are reported at the electrode locations typically reported in the literature, as well as, where appropriate, at locations where the effect was maximal. Other approaches are available, such as mass univariate analysis implemented in Matlab (Groppe, Urbach, & Kutas, 2011), which instead of relying on a priori selection of time windows use a large number of statistical tests across time, correcting for multiple comparisons, to identify significant effects. These approaches are useful where little or no a priori information about the location or timing of the effect of interest is available. Since the present research investigated affective modulations of a

series of previously established affective processing and memory effect, the approach detailed above was chosen instead.

Since ERP waveforms are the product of all neural processes engaged by a task that are measurable at the scalp, neural correlates of individual variables of interest can be isolated by comparing ERPs that differ in no other aspect than this variable, such as contrasting ERPs for hits with those for correct rejections which will share activity associated with all aspects of memory retrieval apart from those specific to retrieval success. These contrasts comprise the experimental factor(s) of an ANOVA that also includes topographical factors, allowing conclusions about the electrodes sites at which activity differs between experimental conditions. The topographies of the expected effects of interests differed between the affective processing and affective recognition memory paradigms, therefore the exact topographic factors included in the respective analyses varied slightly between them and are described individually below. In short, the LPP effect expected to arise from differences in affective processing between negative or positive and neutral images is typically maximal at midline electrodes, which is why midline sites were included in the analysis. Two of the recognition memory effects of interest, the left-parietal effect and the late right-frontal effect (see sections 3.6.3 and 3.6.4 below for discussion) are typically lateralised to the left and right hemispheres respectively. To be able to demonstrate this lateralisation, the recognition memory analyses excluded midline sites in favour of an additional hemisphere factor. For both types of effects, electrodes included in the topographical

analysis were chosen to be representative of the whole scalp recording but also to allow for closer examination of any topographical effects by fitting a set of distinct topographical factors, namely in the case of memory effects location (front to back), site (superior to inferior) and hemisphere (left, right) and in the case of affective processing effects location (front to back) and site (left inferior to right inferior). Including all electrodes as individual factors would mask this information about where on the scalp effects are strongest and vastly increase the number of factors necessary.

When comparing topographies of ERP distributions, any interpretation of differences is complicated by the fact that they can arise in two ways: through differences in the neural generators engaged by the two experimental conditions being compared or through the same generators being activated differentially. To be able to determine whether topographical differences between two conditions are qualitative, meaning they are caused by differences in the neural generators engaged, data has to be rescaled to remove purely quantitative topography differences (McCarthy & Wood, 1985). For topographic analyses reported in the present thesis, rescaling was carried out using the Max-Min method proposed by McCarthy and Wood (1985). Amplitude differences between conditions are removed by normalising data using the minimum and maximum mean amplitude within each condition. The minimum value for the condition is subtracted from each individual electrode value and the resulting differences are divided by the difference between the maximum and the minimum value (x_R= x-min/max-min).

Rescaled data was submitted to topographical analysis using ANOVAs that included experimental and topographical factors. Affective processing data was initially analysed using three ANOVAs, with the experimental factor of affective content (negative vs neutral, positive vs neutral and negative vs positive respectively) and the topographical factors of location (frontal, centro-frontal, central, centro-parietal, parietal) and site (left inferior[5], left medial[3], left superior[1], midline [z], right superior [2], right medial [4], right inferior [6]). Affective processing data was available from two experiments using identical paradigms, so data from both experiments was included, adding a between-subjects factor of experiment (Experiment 1, Experiment 3). As between-subject comparisons in Chapters 6 and 7 are performed on data from Experiment 3, the electrodes with the largest effect sizes in this dataset were used to quantify the LPP.

To establish the presence of the expected memory effects, affective recognition memory data was initially analysed separately for each affective condition and time window using a series of ANOVAs with the experimental factor of retrieval success (hits, correct rejections) and the topographical factors of location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right) and site (superior [1,2], medial [3,4], inferior [5,6]), separately for three time windows. The significance of the memory effects in their traditional locations was then tested by comparing mean amplitudes at three electrodes which were chosen a priori based on previous research: Electrode Fz in the 300 to 500 millisecond time window for the early frontal old/new effect, electrode

P3 in the 500 to 800 millisecond time window for the left-parietal old/new effect and electrode F4 in the 800 to 1500 millisecond time window for the late right-frontal old/new effect (see Chapter 3.6 below for previous research on the timing and distribution of these effects). To assess affective modulation of the memory effects, difference scores were created for each affective category by subtracting unscaled amplitudes for correct rejections from those for hits at every electrode site. Difference scores for positive and negative affective pictures were then subjected to ANOVAs with an experimental factor of affective content (negative vs neutral/positive vs neutral) and the previously used topographical factors of location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right) and site (superior [1,2], medial [3,4], inferior [5,6]) in all time windows.

ANOVA assumes sphericity, meaning the equality of variances of the differences between all possible combinations of within-subject conditions. The violation of this assumption of sphericity leads to an increase in type 1 error, i.e. false positive findings, and must therefore be corrected. In ERP analyses, the sphericity assumption is typically violated as a consequence of the layout of electrodes on the scalp, since electrodes in closer proximity to each other share greater co-variance than those further apart. Mauchly's test of sphericity (Mauchly, 1940) assesses such violations of the sphericity assumption and was employed for each ANOVA analysis reported in this thesis, with a significance criterion of p=.05. Where a significant result in Mauchly's test indicated a violation of the assumption of sphericity, degrees of freedom and F values

corrected using the Greenhouse-Geisser correction (Greenhouse & Geisser, 1959) are reported.

3.6 Selected ERP effects

The experiments presented here investigated modulations in four ERP effects specifically: The Late-Positive Potential (LPP) as a marker of affective processing, as well as the early mid-frontal, left-parietal and late right-frontal old-new memory effects. Other memory related ERP effects have been demonstrated, such as the subsequent memory effect, which is arises at study when comparing ERPs in response to subsequently remembered items to those in response to subsequently forgotten items (Sanquist, Rohrbaugh, Syndulko, & Lindsley, 1980), or the late posterior negativity, an electrophysiological correlate of source memory (Cycowicz, 2001). While affective modulations of study processes or item-source binding are of interest in gaining a full understanding of the interactions between affect and memory, they are beyond the scope of the present thesis. Instead, the focus of the experiments presented here is on the affective modulation of ERP correlates of successful recognition at test.

The early mid-frontal, left-parietal and late right-frontal old-new effects are defined below in terms of their location, timing and polarity, as well as the conditions known to elicit each effect. This has been the traditional approach to defining ERP components, however, Luck (2005) argues that the parameters of location, timing and polarity are superficial and variable for various reasons

within the ERP components elicited by the same conditions. Instead he proposed to define an ERP component as the neural activity that is associated with "a specific computational operation" and generated in "a given neuroanatomical module" (Luck, 2005, p. 59). He argues, therefore, that observed ERP effects can differ in location, timing and even polarity and still constitute the same ERP component, as long as they are a result of the same cognitive function and are generated in the same module. He further argues that while it is possible for two distinct cortical areas to perform the same cognitive function, this would likely be a rare occurrence and lead to such obvious differences in ERP patterns that the two components would be easily distinguishable. As such, while the ERP effects discussed here are described in terms of their location, timing, polarity and eliciting condition, slight variations from the any of the first three parameters would not be seen as evidence of a separate ERP component.

3.6.1 The Late-Positive Potential (LPP) effect

The LPP is a positive going deflection, maximal over centro-parietal electrodes, starting around 400 milliseconds after stimulus onset and lasting several hundred milliseconds (Pastor et al., 2008). While the term "LPP" is often used to describe the positive going shift in ERP signals at this time and location in general, it is more meaningful to discuss the LPP effect, that is the increase of (positive-going) LPP amplitudes in response to experimental as compared to

control conditions. The LPP effect is generally seen as a marker of emotional processing, although its precise eliciting conditions are still not fully understood.

Because of its similarity in timing and topography to the P3a and P3b components that have long been studied using the oddball paradigm (Squires, Squires, & Hillyard, 1975) in the attention literature, it could be assumed that LPP effects arise from the intrinsic "oddball" properties of affective stimuli, which present with much lower frequencies than neutral stimuli in everyday life. But modified "affective oddball" paradigms, in which affective stimuli are low frequency targets presented among high frequency neutral stimuli, show that the underlying mechanisms are more complicated. For example, using this affective oddball task, Ito, Larsen, Smith and Caccioppo (1998b) showed increased LPPs for infrequent affective compared to frequent neutral pictures, as would be expected in an oddball paradigm. However, they also found a negativity bias, with increased LPP effects for negative compared to positive pictures, despite their matched arousal levels and frequencies of presentation. Using the same paradigm, Wood and Kisley (2006) replicated this negativity bias in younger adults but found no evidence for increased LPP effects in response to negative compared to positive pictures in older adults. Additionally, LPP effects for both affective categories were reduced in older participants, suggesting that the differential processing of affective stimuli, whatever its precise nature, declines with increasing age. Further evidence comes from Delplanque, Silvert, Hot, Rigoulot and Sequeira (2006), who

showed that when the ERPs in response to an affective oddball task are separated into P3a and P3b components, differential effects of stimulus valence and arousal are found. Delplanque et al. (2006) found a negativity bias in the P3a component, proposed to indicate an involuntary switch of attention from the primary task, with larger effects for negative than for positive pictures. For the P3b component, thought to reflect a refreshing of the mental model of the environment (Johnson, McCarthy, Muller, Brudner, & Johnson, 2015), negative and positive pictures elicited effects with differing topographies. This could point to differing neural generators of the effects, although unfortunately no analyses of re-scaled data were reported, meaning that these differences could arise from differences in relative generator strength.

To reconcile evidence of affective modulation of the neural correlates of the oddball task discussed in the attention literature with evidence of affective modulation of the neural correlates of context-free passive picture viewing discussed in the affective literature, Schupp et al. (2000) devised a paradigm in which negative, neutral and positive pictures were presented in random order for passive viewing, followed by a valence rating task as is common in the affective literature, but in blocks of six pictures at a time with the fast presentation rate and brief exposure (here: 1.5s) typical of oddball paradigms. They showed increased LPPs for both negative and positive compared to neutral pictures in a 350 to 750 millisecond time window at frontal, central and parietal electrodes. LPP effects were more pronounced for more highly arousing stimuli. As this paradigm shares many of the parameters of the

oddball task but does not establish a local context in contrast with the affective content of stimuli, Schupp et al. (2000) concluded that the LPP is sensitive, at least in part, to the intrinsic affective properties of the pictures presented.

Pastor et al. (2008) sought to add further evidence in support of the view that affective LPP modulations are not dependent on context, meaning that affective stimuli do not elicit larger LPPs merely by virtue of their relative rarity. They show that LPPs for both negative and positive pictures are unaffected by whether stimuli are presented in a blocked or mixed design. However, crucially, they also report larger LPPs in response to neutral pictures in blocked compared to mixed presentation. This suggests that the LPP effect (the difference between affective and neutral pictures) may be smaller in the blocked than in the mixed condition. Since no affective-neutral differences were reported, it is impossible to decide whether these results constitute evidence for or against the context independence of affective LPP effects proposed by Schupp et al. (2000).

Moran, Jendrusina and Moser (2013) report that the LPP shows good consistency within participants and is robust at comparatively low trial numbers. They found that LPP differences waves varied little once more than 12 trials contributed to the average. While it seems clear that the LPP effect increases with the arousal associated with stimuli (e.g., see Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000; Schupp et al., 2000), some studies find effects of valence when arousal is matched (e.g., see Ito, Larsen, Smith, &

Cacioppo, 1998a; Wood & Kisley, 2006) while others do not (e.g., see Schupp et al., 2000; Hajcak & Olvet, 2008).

Complicating the search for the exact eliciting conditions of the LPP effect is the fact that the definition of its exact parameters in the literature lacks consistency. While the labels "P3a/P3b" and "LPP" originating in different research traditions are often used interchangeably, different researchers also vary in the temporal and topographical definition of the "LPPs" they report. Hajcak and Olvet (2008) demonstrated that increased positivities in response to affective compared to neutral pictures can persist for 800 and 1000 milliseconds after stimulus offset for positive and negative pictures respectively. Despite this finding, most researchers refer to a time window usually starting around 400 milliseconds after stimulus onset and typically lasting around 400 milliseconds when discussing LPPs (e.g. Bianchin & Angrilli, 2012: 400-800ms; Pastor et al., 2008: 400-700ms; Schupp et al., 2000: 350-750ms). Others however use much later time windows to quantify the LPP effect (e.g. Dunning & Hajcak, 2009: 1-2s, 2-3s, 4-5s and 5-6s), creating potential confusion about the nature of the electrophysiological effects being discussed.

Although the association between the LPP effect and processes of attention is widely accepted (Hajcak, MacNamara, & Olvet, 2010), it is a proposed relationship that is difficult to test using LPP eliciting tasks in isolation, because the argument is often circular. Affective stimuli are assumed to be intrinsically more attention-grabbing than neutral stimuli, therefore their electrophysiological correlate – the LPP – is seen as a marker of attention.

Conversely, stimuli that elicit larger LPPs are concluded to preferentially engage attention. While there are obvious parallels between the electrophysiological correlates of attention and affective processing, it seems clear that additional behavioural tasks are needed to try to dissociate the two.

As Brown, van Steenbergen, Band, de Rover and Nieuwenhuis (2012) point out, although the eliciting conditions for the LPP have been relatively extensively studied, its functional significance is poorly understood. They offer two possible functional interpretations of the LPP: The enhanced perception hypothesis, which posits that the LPP reflects more efficient processing of affective stimuli, and the global inhibition hypothesis, which posits that the LPP is a correlate of reduced sensitivity to other visual stimuli in the presence of an affective stimulus. Brown et al. (2012) varied LPP effect size by presenting participants with either neutral or negative IAPS pictures and measured perceptual sensitivity following presentation of these affective pictures with an orientation discrimination task using Gabor patches, sine wave gratings commonly used in perception research. The authors found no difference in perceptual sensitivity following larger compared to smaller LPP amplitudes. They did, however, show a reduction in visual excitability, as measured by the P1/N1 component elicited by a stimulus in trials were the stimulus elicited larger LPPs. Brown et al. (2012) argue that this presents preliminary evidence in favour of the global inhibition hypothesis. It has to be noted, however, that Brown et al. (2012) did not find a significant correlation between LPP and P1/N1 amplitudes. So while there is some evidence for a global inhibition

function over an enhanced perception function of the LPP, the evidence to date is far from conclusive and more research is needed to establish the exact functional significance of the LPP effect.

3.6.2 The early mid-frontal effect

The early mid-frontal effect (sometimes referred to as the FN400 effect) is a positive going old-new memory effect that is typically maximal between 300 and 500 milliseconds post stimulus onset and over mid-frontal electrodes around electrode Fz. Dual-process theorists see it as a marker of familiarity, with familiar items being associated with more positive going mid-frontal waveforms in the 300-500 milliseconds time-window. Rugg and colleagues first suggested an association between familiarity and the early mid-frontal effect in a letter to Nature in 1998 (Rugg, Mark, Walla, & Schloerscheidt, 1998a). They pointed out, however, that the early mid-frontal effect is "less easily characterized" than other old-new effects discussed. This is inherent in the concept of familiarity, as successfully recognised old items may vary in whether they are recollected or not but will always be associated with some degree of familiarity in healthy participants. Since producing recollection without familiarity is therefore not practical, behavioural paradigms have sought instead to vary the degree of familiarity produced by old and new items. Hintzman, Curran and Oppy (1992) showed that frequency judgements of new items similar to studied old items were either zero (effectively a "new"

response) or increased with the number of repetitions of the similar old items during study. Since similar items are new items, no recognition can take place and frequency judgements must be based on familiarity.

Using a similar paradigm, Curran (2000) showed that early (300-500 milliseconds) superior anterior activity varied with familiarity. Participants studied a list of singular and plural words and then categorised a test list into "old", "similar" (study words presented with changed plurality, i.e. words which were presented in the singular at study and in the plural at test or vice versa) or "new" words. Similar words were assumed to elicit familiarity but no recollection and were shown to be associated with more positive anterior superior activity similar to that for old words, compared to activity associated with new words. Furthermore, Curran and Cleary (2003)) showed the same pattern for line drawings of common objects, which were shown in reversed orientation in the "similar" condition.

One important question regarding the early mid-frontal familiarity effect is whether it is sensitive to familiarity manipulations based on perceptual similarity or those based on conceptual similarity or both. By changing stimulus plurality and orientation respectively, the experiments described above created new items that were both perceptually and conceptually similar to studied items.

To manipulate perceptual similarity only, Curran, Tanaka and Weiskopf (2002) created families of abstract shapes referred to as "blobs". Each blob was

computer-generated to be a distortion of one of 12 prototypes, thus creating 12 blob families. Perceptual similarity was high within blob families but low between families. Curran et al.'s (2002) finding that the early mid-frontal effect was modulated by family membership, with new blobs from the same families as previously studied blobs being associated with more positive going waveforms than blobs from new families. In other words, the mid-frontal effect was stronger for purely perceptually similar items than for new items.

Conversely, Nessler, Mecklinger and Penney (2001) used new word stimuli, referred to as "lures" that were purely conceptually similar to studied words by selecting both study items and lures from the same semantic categories, as well as new items from different categories. They found a positive-going old/new effect in frontal locations in the 300-500 milliseconds period that was present for both studied words and lures compared to new words, thus providing support for the idea that the early mid-frontal effect is modulated by familiarity based on conceptual similarity. Further evidence of this familiarity modulation comes from their finding that waveforms in the 300-500 milliseconds are more positive going in response to lures that are classed as "old" (assumed to reflect familiarity, albeit false familiarity) than in response to lures that are classed as "new".

Yonelinas (2002), in his review of investigations of recollection and familiarity, concluded that familiarity can be functionally dissociated from perceptual implicit memory but shows similarities to conceptual implicit memory. While Nessler et al.'s (2001) findings confirm that the early mid-frontal effect is

sensitive to manipulations of conceptual implicit memory, Curran et al.'s (2002) blob study suggests that it is also sensitive to manipulations of perceptual implicit memory.

While the experiments discussed above rely on manipulations assumed to modulate familiarity, another approach to studying the electrophysiological correlates of familiarity is to assess familiarity through participant self-report. The often employed Remember/Know paradigm (Tulving, 1985) asks participants to divide items judged as "old" into those that are "remembered", i.e. those for which study context information is available, and those that are merely "familiar", for which such information cannot be accessed. Items judged as "familiar" are typically associated with increased early frontal activity compared to new items (e.g., see Curran & Cleary, 2003; Curran, 2004; Duarte, Ranganath, Winward, Hayward, & Knight, 2004).

It is, however, important to note that there are inherent difficulties associated with self-report measures, such as variability in task comprehension or compliance. For example, McCabe, Geraci, Boman, Sensenig and Rhodes (2011), showed that when asked to verbalise their thoughts during a word recognition task, these thoughts typically included recollections from the study phase where participants made "recalled" judgements (87%), used synonymously with the more common "remember" judgement. But thoughts about "know" judgements also included such recollections to a higher degree than expected (33%). Although this casts some doubt on the validity of "know" judgements specifically and the Remember/Know procedure in general, McCabe et al.'s

2011 validation procedure itself is of course based on subjective self-report and it is possible that participants failed to verbalise details they really recalled. Conversely, because "think aloud" explanations of why a "remember" or "know" judgement was made where given after the complete block of old/new decisions, additional detail may have been available to participants that they did not have access to at the point of the recognition and recall/know judgements.

3.6.3 The left-parietal effect

The left-parietal old-new memory effect is typically maximal between 500 and 800 milliseconds and at left parietal electrode locations around electrode P3. The more positive going waveforms in response to old compared to new items in this location and time-window are thought to be a marker of item recollection (see Allan, Wilding, & Rugg, 1998 and Curran, Tepe, & Piatt, 2006 for review).

Evidence for the association between the left-parietal effect and recollection primarily comes from studies using one of three types of paradigms: Assessment of the degree of recollection through either subjective self-report, typically in form of the Remember/Know judgements described above, or source memory tasks and manipulation of the degree of recollection through manipulation of depth of encoding.

Using the Remember/Know paradigm, Smith (1993) found more positive going waveforms associated with words that elicited "remember" judgements than both those for "know" judgements and new words in a 550-700 millisecond time window. The difference was largest at left-parietal locations. In a similar study, Curran (2004) also reports larger left posterior/superior positivity for "remembered" words compared to "known" words in a 400-800 millisecond time window.

Similarly, Duzel, Yonelinas, Mangun, Heinze and Tulving (1997) showed a positivity associated with "remembered" compared to new words that was left-lateralised over temporoparietal electrodes in a slightly longer time window from 600 to 1000 milliseconds. They found no significant waveform difference in this time window between words that were correctly judged to be remembered (hits) and words incorrectly judged to be remembered (false alarms), leading the authors to suggest that rather than being a marker of recollection, the left-parietal effect is in fact a marker of autonoetic activity, the act of mentally placing oneself in the past.

Probably due to the difficulty in getting sufficient false alarm trial numbers for producing good quality ERPs, most electrophysiological studies aimed at dissociating the effects associated with familiarity and recollection compare activity during successful recognition (hits) with activity for correctly identified new items (correct rejections), making it impossible to decide between the recollection and autonoetic activity hypotheses. Electrophysiological studies of false or illusory memory typically do not distinguish between familiarity and

recollection, or do so by drawing inferences from ERP effects found. A 2007 study by Geng et al. (2007) did show a left-parietal effect between 500 and 700 milliseconds that was larger for successful recognition than false recognition (false alarms). The effects for false recognition did not differ from that for correct rejection. In contrast to Duzel et al.'s (2007) results, this pattern of activity suggests that the left-parietal effect does not merely reflect autonoetic activity but differentiates between successful recognition and memory illusion.

Nessler et al. (2001) also reported a larger left-parietal effect for true compared to false recognition of words. Additionally, they showed that this differentiation could be shown for participants with low false alarm rates only, while participants with high false alarm rates had equivalent ERP effects associated with true and false recognition. Together, these results suggest that the left-parietal effect is sensitive to both differences in autonoetic activity and recollection and sensitivity to the latter component is associated with better differentiation between old and new items.

Rugg, Schloerscheidt and Mark (1998b) compared the electrophysiological correlates of recollection of words when recollection was assessed by source judgements versus the Remember/Know task. Trials with correct source judgement or "remember" responses respectively were defined as recollected and contrasted with "new" responses. When comparing the scalp topographies of the two resulting old/new effects, which had been re-scaled to remove the influence of magnitude differences, the authors found no significant difference between them. They concluded that source judgement and Remember/Know

assessments of recollection do not differ neurally or functionally. In a conceptually similar study, Duarte et al. (2004) investigated the electrophysiological correlates of familiarity and recollection of pictures, using both the Remember/Know paradigm and a source judgement task, during which the encoding instruction for the remembered item had to be identified. Unfortunately, the authors only state that ERPs were equivalent when sorted according to Remember/Know responses and source judgements but do not report statistics on this relationship.

A different approach was taken by Rugg, Cox, Doyle and Wells (1995), who used a combination of a source memory task and confidence judgements to identify successful recollection of words. A word was defined as recollected when it was correctly identified as "old" with high confidence and its study context was correctly identified with high confidence. They showed that low frequency words were more accurately recognised and the words' study context was more likely to be accurately retrieved than high frequency words. The authors attribute this pattern to low frequency words eliciting higher relative levels of recollection than high frequency words. A left-parietal old/new effect between 400 and 800 milliseconds was only significant for low frequency words, leading the authors to conclude that the left-parietal effect is not only a marker of recollection but is also sensitive to the amount of recollected information available in a graded fashion. Wilding (2000) added further evidence to this hypothesis by including two source judgement tasks in a word recognition paradigm and showing that the size of the left-parietal

old/new effect co-varied with the number of correct source judgements, two correct judgements associated with larger magnitudes than one correct judgement and both of these associated with larger magnitudes than correct rejections.

Murray, Howie and Donaldson (2015) expanded on this quality of recollection approach by using a continuous measurement of source judgement accuracy. Words were presented with location cues during study. Location cues were distributed randomly on a circle. During retrieval, participants were asked to mark the location of the previously presented location cue for each word. Source judgement precision was defined by the distance between the original location cue and the participants' response on the circle. They showed larger left-parietal old/new effects between 500 and 800 milliseconds post stimulus onset for trials in which source judgement precision was high compared to trials in which it was low, while these effects were absent in trials in which source judgement precision was at chance level. They conclude that the left-parietal effect indexes recollection, which is characterised as being both thresholded and graded. Recollection is shown to be thresholded behaviourally by the fact that the distance from target does not increase continuously from 0˚ (perfect precision) to 180˚ (lowest precision) but reaches a plateau after which any location is guessed with equal probability. The grading of both source judgement accuracy and the left-parietal effect above a certain threshold indicate that when recollection does occur, it is of variable quality.

Rather than measuring different levels of recollection at the point of recognition, a third type of experiment aims to actively manipulate recollection rates by varying levels of processing at encoding (see Chapter 1 for a discussion of this relationship). For example, Rugg et al. (1998a) varied the encoding task for words within participant by using two different encoding cues preceding study items, one indicating the instruction to judge whether the first and last letter in the word are in alphabetical order (shallow processing) and one indicating the instruction to verbally form a sentence containing the study word. They found a left-parietal old/new effect which varied with depth of processing.

Since most research into the left-parietal effect has used word stimuli, the important question arises as to whether it is material specific. Curran and Cleary (2003) and Curran and Doyle (2011) both found a left-parietal old/new effect in response to pictures of line drawings. Ranganath and Paller (2000) compared correct responses in a specific picture memory test in which a size judgement had to be made (driven by recollection) with hits in a general old/new decision (assumed to include both familiarity-only and recollection trials) and found widespread increased positivity for correct specific responses in frontal, temporal and parietal sites between 600 and 800 milliseconds, an effect that was larger in the left hemisphere in parietal locations only. Similarly, Duarte et al. (2004) reported an old/new effect in response to pictures that was bilateral in parietal locations between 450 and 800 milliseconds.

Comparing old/new effects for words (names) and faces, MacKenzie and Donaldson (2009) reported the typical 300-500 milliseconds mid-frontal and 500-700 milliseconds left-parietal effects for words. Memory for faces, in contrast, was associated with an anterior old/new effect between 500 and 700 milliseconds and a late right-frontal old/new effect between 700 and 900 milliseconds, while there was no evidence of the early mid-frontal and left-parietal effects commonly found using word stimuli.

To compare the electrophysiological response to the three most commonly used stimulus materials directly, Galli and Otten (2011) employed a source judgment task that paired three types of visually presented stimuli – pictures of objects, words and faces – with auditorily presented locations. At test, an item was defined as recalled if it was recognised and its associated location was successfully identified. They found when different stimulus types were presented using a blocked design at study, scalp topography in a 500 to 700 millisecond time window at test differed between stimulus types. Only words showed the typical left-parietal effect while old/new effects in response to pictures and faces had a much more widespread scalp distribution which included effects at left-parietal sites but also at more anterior sites compared to the word old/new effect.

In sum, a large body of evidence consistently shows a left-parietal old/new effect for words, onsetting around 400-600 milliseconds and lasting between 200 and 400 milliseconds that is associated with successful recollection of a study item and varies with the quality of this recollection. Some studies show

an equivalent left-parietally distributed effect in this time window associated with recollection of pictures of objects but overall the distribution of recollection-related activity for picture stimuli appears to be less left-lateralised and more wide-spread and anterior than that for words.

3.6.4 The late right-frontal effect

The late right-frontal effect is a positive going old-new effect maximal at right-frontal locations around electrode F4. It typically onsets around 500-800 milliseconds post stimulus onset and lasts several hundred milliseconds. It was first described by Wilding and Rugg (1996), who found a right-frontal positivity for recollected compared to new words onsetting at 400 milliseconds and lasting for the remainder of the recording period 1434ms post stimulus onset. They suggested that this late right-frontal effect reflects post-retrieval processes involved in the retrieval of contextual information. To investigate the functional role of the late right-frontal effect, Wilding and Rugg (1997) used a task in which words are presented auditorily in either a male or female voice at study and then presented visually at test and defined as targets and non-targets by the gender of presentation voice at study. While both targets and non-targets, being recognised as old words, were associated with left-parietal old/new effects, only targets were associated with a late right-frontal effect. The authors conclude that the late right-frontal effect is an electrophysiological

marker of non-obligatory processes following retrieval success which can be influenced by retrieval strategy.

Curran, Schacter, Johnson and Spinks (2001) showed increased positive right-frontal activity between 1000 and 1500 milliseconds in response to target and lure words compared to new items in good performers only, while the effect was absent in poor performers. This is consistent with the view that the late right-frontal effect reflects post-retrieval processes, as the engagement of such processes should lead to better task performance. Both good and poor performers showed left-parietal old/new effects between 400 and 800 milliseconds, adding support to the notion that the two effects are dissociable. Apparently contrary to Curran et al.'s (2001) finding that the late right-frontal effect is absent in poor performers, Wolk et al. (2009) show that it is more pronounced in poorer performing older participants. Wolk et al. (2009) also found that it was generally increased in older participants compared to younger participants, while both the early mid-frontal and left-parietal old/new effects were decreased. One possible explanation for the apparent inconsistency between these findings and Curran et al.'s (2001) results for poor performers lies in Wolk et al.'s (2009) conclusion that older participants preferentially engage post-retrieval processes in an attempt to compensate for steadily declining memory performance. Younger participants on the other hand, like those in Curran et al.'s (2001) study, may not have developed these compensation skills to the same degree.

Although the exact nature of the processes underlying the late right-frontal effect has proved difficult to discern, the studies above converge on an interpretation of the late right-frontal effect as a marker of post-retrieval component of recollection. Donaldson and Rugg (1999) also showed a late onsetting right-frontal positivity in associative recall from around 1400 milliseconds. But a more recent paper by Hayama, Johnson and Rugg (2008) suggests that rather than being specific to successful memory retrieval, the late right-frontal effect is a neural correlate of generic monitoring processes. Evidence for this conclusion comes from their finding of a right-frontal positivity in response to correct responses in both a source judgement task but also a semantic decision task only. In a second experiment, participants made semantic judgements on either old or new items at test and exhibited right-frontal effects in response to whichever category of items required these judgements. While these findings suggest a memory-independent role of the late right-frontal effect, it is important to note that in contrast to previous studies that have typically used visually or auditorily presented word stimuli, Hayama et al.'s (2008) study used pictures of nameable objects. It is therefore possible that the findings are stimulus dependent, analogous to the material-specific differences found in left-parietal old/new effects.

Chapter 4: General Methods

4.1 Participants

Participants were recruited through the University of Stirling's online sign-up system (psychweb.stir.ac.uk). Participants in all experiments were given the opportunity to self-exclude if they did not meet all of the following criteria: Right-handedness, being a native English speaker, aged between 18 and 25 years, having normal (or corrected to normal) sight, having no current diagnosis or history of any psychiatric or neurological disorders and no current or history of illegal drugs use. Ethical approval for all experiments was obtained from the University of Stirling Department of Psychology's Ethics Committee. Participants received a reimbursement of £5 per hour and undergraduate students of psychology at the University of Stirling were given the option of receiving a combination of monetary reimbursement and up to two course credits per session.

4.2 Stimuli

The focus of the present research is on processing of visual information, more specifically pictures of everyday scenes. The large trial numbers, and consequently large stimulus sets, needed to obtain good quality ERP data, along with the time restraints inherent in a PhD project, necessitated the use of

an existing stimulus set. At the time of designing these experiments, the only sufficiently large, openly available such set was the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2008). The IAPS is a set of affective pictures associated with standard ratings for valence and arousal on a 9-point scale, with lower valence scores identifying more negative items and, intuitively, lower arousal scores indicating less arousing items. It should be noted that since the conclusion of data collection, two more large affective picture sets have become available: The Geneva Affective Picture Database (GAPED) published in 2011 (Dan-Glauser & Scherer, 2011) and the Nencki Affective Picture System (NAPS) in 2014 (Marchewka, Zurawski, Jednorog, & Grabowska, 2014). The GAPED comprises of 730 pictures and includes positive pictures of animal and human babies and nature scenes, neutral pictures, mainly of inanimate objects and negative pictures of one of four content categories: spiders, snakes, violations of moral norms and violations of legal norms. This narrow selection of picture contents poses a problem for studies comparing different affective categories, because pictures are not matched for physical attributes across affective categories and content types vary systematically. Interpreting any behavioural or neural differences in the processing of the different categories as effects of differences in affective content would be difficult, given the presence of likely confounds such as humans appearing in affective but not neutral pictures or differences in complexity of the scenes depicted between affective categories. The NAPS, which is a set of 1356 pictures addresses some of these confounds by providing

not only standard ratings for valence, arousal and approach-avoidance for each picture but also additional information about the picture content, which falls into one of the five categories of people, faces, animals, objects or landscapes, and its physical attributes such as luminance, contrast and entropy. This allows for greater control of possible confounds of perceptual and conceptual processing across affective categories. However, since picture contents are not matched exactly across affective categories, a relatively large variation in physical and conceptual features remains.

As indicated above, at the time of stimulus selection, the IAPS was chosen as the best available stimulus resource of affective pictures. IAPS pictures were selected by their standard ratings to fit into one of three categories: High arousing negative, low arousing neutral or high arousing positive pictures. To avoid confounds of complexity with the emotionality of stimuli, "simple" pictures (such as a single object in front of a homogenous background) and abstract shapes were not included. Close-ups of faces were also excluded from the stimulus set as they could not be balanced across all three emotion categories. To avoid the confound of sexuality on any gender differences, pictures with sexual content, e.g. male or female nudes, were also excluded. The complete stimulus set was then split into two sub-sets matched for valence and arousal within each emotion category, with equal numbers of stimuli in each category.

In Experiment 1, 222 IAPS pictures were used, 74 per affective category. The mean standard ratings for the three emotion categories were are shown in

Table 4.1. High arousing negative and high arousing positive pictures were matched for arousal, which was higher than mean arousal for neutral pictures.

Affective Category	IAPS valence	IAPS arousal
High arousing negative	3.20 (0.86)	5.24 (0.82)
Low arousing neutral	5.06 (0.26)	3.19 (0.44)
High arousing positive	6.84 (0.62)	5.24 (0.80)

Table 4.1: *IAPS standard ratings [Mean (SD)] for Stimulus Set A, used in Experiment 1.*

In Experiments 2 and 3, 288 IAPS pictures were used, 96 per emotion category. Table 4.2 shows standard valence and arousal ratings for this set. High arousing negative and high arousing positive pictures were again matched for arousal and arousal was higher for positive and negative than for neutral pictures.

Affective Category	IAPS valence	IAPS arousal
High arousing negative	2.57 (0.44)	5.78 (0.55)
Low arousing neutral	5.03 (0.28)	3.26 (0.52)
High arousing positive	7.16 (0.42)	5.83 (0.59)

Table 4.2: *IAPS standard ratings [Mean (SD)] for the Stimulus Set B used in Experiments 2 and 3.*

Despite these standard ratings being used to categorise stimuli, it is important to note that they were obtained over the course of 13 years and from US participants. To assess whether the UK participants in these experiments agreed with the standard ratings provided by Lang et al. (2008), participants' own arousal and valence ratings were collected for all stimuli. These participant ratings will be presented in the following chapters, where data from experiments using IAPS pictures is discussed. The relationship between IAPS standard ratings and participant ratings in the present study is discussed in detail in Chapter 5.1 below.

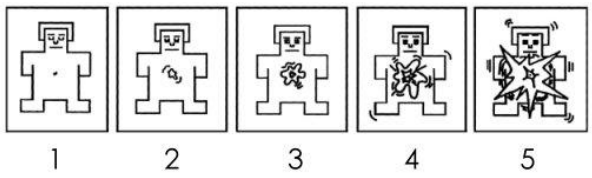
In all experimental tasks, picture stimuli were presented on a black background on a screen, at a size of 9cm by 11.25cm, resulting in approximate visual angles of 5.1˚ by 6.4˚ when viewed from a 100cm distance as instructed.

4.3 Experimental tasks

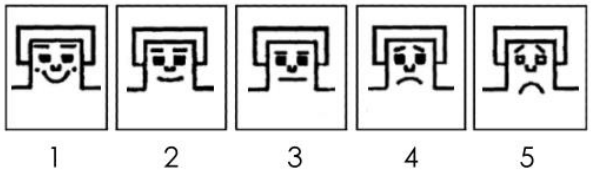
Experimental tasks were presented on a 15" computer monitor, positioned on a desk about one meter in front of the participant, in a darkened room. E-prime 1.1 software (Psychology Software Tools Inc: www.pstnet.com) was used to present tasks and record responses obtained through a Psychology Software Tools serial response box.

4.3.1 Affective processing task

Participants completed an affective processing task which also doubled as the study phase for the subsequent surprise affective recognition memory test. At the beginning of the task, participants were instructed to view each picture presented on the screen and, when prompted, to rate them for their arousal (described as "how exciting or agitating" they found the picture) and valence ("how positive or negative"). They were shown an example of the modified Self-Assessment Manikins (Bradley & Lang, 1994; see Figure 4.1 below) for arousal and for valence ratings and given the opportunity to ask any questions.



a)



b)

Figure 4.1 *Modified version of the Self-Assessment Manikin for a) arousal and b) valence*

Participants were asked to fixate their eyes on the fixation cross while it was on the screen and then look directly at each picture when it was shown and try not to move their eyes. They were asked to sit as relaxed as possible and try to avoid movements.

Each trial started with a fixation cross presented in white at the centre of a black screen. In Experiments 1 and 2, the fixation cross was presented for 500ms. In Experiment 3, this was extended to 1000ms to minimise the chance of an overlap of any signal onset effects in response to the presentation of the fixation cross with stimulus specific effects in the EEG. After the fixation cross, an affective picture was presented for 2000ms, followed by the modified SAM for arousal which remained on the screen until a response was made. This was followed by the modified SAM for valence, also presented until a response was recorded. Experiments 2 and 3, containing more stimuli, included an opportunity to take a self-terminated break every 50 trials, lasting a maximum of two minutes.

4.3.2 Affective recognition memory test

Participants completed a surprise memory test of the pictures presented during the affective processing task. In Experiment 1, there was a 20 minute study-test interval. In Experiment 3, for reasons discussed in detail in Chapter 6.1, the study-test interval was increased to one week. Participants were instructed that they would be seeing a series of pictures, some of which they saw during the

earlier affective processing task and some which would be new to them. They were asked to indicate for each picture whether it was new or old and if they responded old, whether they remembered the picture or just knew it was old. The latter was further explained by the following instructions:

> "Choose REMEMBER if you have a memory of seeing the image on the screen or remember something you thought of when you saw it.
>
> Choose KNOW if you have a feeling that you did see the image before because it looks familiar but you do not have a clear memory of the event."

Participants were then verbally asked if they had understood the instructions and to provide an example of when they would say they "remembered" and when they would say they "knew". If necessary, the distinction was further explained verbally.

At test, each trial again started with the presentation of a fixation cross for 500ms (Experiments 1 and 2) or 1000ms (Experiment 3) respectively, followed by either an old or a new picture for 2000ms. After this, participants were prompted to press either the "1" or "5" key on the serial response box to indicate whether the picture was new or old. A reminder of which button was associated with which response (e.g. "Old=1 or New=5?") was presented. The pairings of buttons with responses was counterbalanced between participants. The prompt remained on the screen until a response was made. In cases where an "old" response was made, a remember-or-know prompt appeared, again using buttons 1 and 5 counterbalanced between participants and again being

terminated by the participant's response. Experiment 3 again included the option of a self-terminated break of a maximum of 2 minutes, every 50 trials.

4.3.3 Attentional disengagement task

For the attentional disengagement task, participants were instructed that they would be seeing affective pictures and asked to rate them for their arousal value. Participants were also told that one of two probes ("x" or "+") would appear at some point during each trial, either above or below the picture, and asked to react as quickly as possible to the probe by pressing 1 for "x" or 5 for "+" on the serial response box. They were reminded to look at the picture while it was on the screen, as they would be asked to rate it later on.

Each trial started with a fixation cross presented for 500ms, followed by an affective picture. After a randomly varying interval of either 500ms or 750ms, one of the two probes appeared either above or below the picture and both the picture and probe remained until a response was made. Then the modified SAM for arousal ratings was presented until the participant responded. There were 144 trials in total, split equally between both probe timings and probe types, as well as the three affective categories.

4.4 Procedure

4.4.1 General procedure

All ERP participants were tested in the Psychological Imaging Laboratory (PIL) at the University of Stirling in the 2009 to 2011 time period. Experiment 2 was a computer based behavioural study and was completed by three to four participants at a time in an adjacent behavioural testing room. Upon arrival, ERP participants were given the standard PIL ERP information sheet and the opportunity to ask any questions and written consent to EEG recording was obtained. Because of its potentially upsetting nature, all participants received detailed information about the stimulus material, consisting initially of a written description of the stimuli and procedure, and then, with verbal consent, of six example stimuli covering the whole range of valence and arousal categories used in the study. After this, participants were given the opportunity to ask any questions and then gave informed written consent. In Experiment 3, information about the genotyping procedure was given separately, in written form, and separate written consent for this procedure was obtained.

ERP participants were fitted with appropriately sized EEG caps and electrodes were filled with conductive gel. Participants were then seated in front of a screen in the experimental room, where impedances were reduced to below 5kΩ by moving hair and gently abrasing the skin with the wooden end of a cotton swap. Participants were asked to express any discomfort felt and short breaks were taken where appropriate. The complete fitting procedure took between 30 minutes and

one hour. Before starting the experimental tasks, participants were shown their EEG on the screen in front of them and instructed to carry out a series of movements (blinking, foot tapping and jaw clenching) to demonstrate the effect of movements on EEG data quality and emphasise the importance of sitting still and relaxed.

Each experiment started with a practice block to familiarise participants with the task and allow for any questions to be answered before data recording commenced. Upon completion of the experiment, participants were fully debriefed about the purpose of the experiment and given the opportunity to ask any questions relating to it. EEG participants had EEG caps removed and were given the opportunity to wash and dry their hair before leaving. All participants received either financial compensation at £5 per hour, or a combination of this rate and up to two course credits. Note that Experiments 1 to 3 include a number of neuropsychological measures beyond those discussed in this thesis. The results and implications of these additional measures exceed the scope of this thesis and will be reported elsewhere.

4.4.2 Experiment 1: Affective memory

Participants completed a computerised version of the Profile of Mood States (McNair, Lorr, & Droppleman, 1971)), before completing the Affective Processing Task described above. This served as the implicit study phase for a later surprise memory test and consisted of 111 trials, with 37 IAPS pictures per affective category. Participants were then given a 20 minute break, during

which they were offered a drink of water but instructed to keep movements to a minimum to maintain good electrode connections. After 20 minutes, participants completed computerised versions of the NEO Five Factor Inventory (NEO-FFI; Costa & McRae, 1985), the National Adult Reading Test (NART; Nelson & Willison, 1991) and the Schizotypal Personality Questionnaire (SPQ; Raine, 1991), followed by a surprise Affective Recognition Test, as described above. Finally, participants completed computerised versions of the Beck Depression Inventory (BDI; Beck, 1961) and Beck Anxiety Inventory (BAI; Beck & Steer, 1990).

4.4.3 Experiment 2: Time-course of affective memory

Experiment 2 consisted of three separate experimental sessions but no EEG was recorded. After consent was obtained at the start of the first session, participants completed a computerised version of the Profile of Mood States, followed by the Affective Processing Task consisting of 144 trials, i.e. 48 pictures per affective category. After a 5 minute break, participants then completed the first of three Affective Recognition Tests, consisting of 96 trials each, which concluded the first experimental session.

Participants returned for a second session at the same time one day later and a third session at the same time one week after the first. These follow up sessions started with the completion of the Profile of Mood States, followed by the Affective Processing Task as above, with each session using a different subset

of old and new stimuli so stimuli did not repeat across the memory tests. Additionally, participants completed a surprise five minute pen-and-paper recall test after one of the three experimental sessions. Timing of the recall test was pseudo randomised to ensure equal numbers of participants in each timing group and a fourth group of participants did not complete the recall test to serve as a control.

4.4.4 Experiment 3: Individual differences in affective memory

After EEG preparation, participants completed computerised trait and state versions of the State-Trait Anxiety Inventory (Spielberger, Gorsuch, Lushene, & Vagg, 1983) and the Profile of Mood States. The Affective Processing Task described above again served as an implicit study phase, comprising here of 144 trials. Self-terminated breaks of a maximum of two minutes were offered every 50 trials to prevent fatigue. The experimental session concluded after participant completed computerised versions of the NEO Five Factor Inventory, the Beck Depression Inventory and the Schizotypal Personality Questionnaire.

Participants returned for a second experimental session exactly one week after the first and were prepared for EEG recording as before. They completed the computerised state version of the State-Trait Anxiety Inventory and a computerised Profile of Mood States. A surprise Affective Recognition Test followed, consisting of 288 trials and again self-terminated breaks of no more

than two minutes were offered after every 50 trials. This concluded the experiment.

4.4.5 Experiment 4: Affective modulation of attention

To maximally utilise resources, Experiment 4 was run immediately following the Affective Recognition Test in Experiment 3. Participants were given a 5 minute break and offered a drink. Impedances were checked during this time and lowered where necessary by applying and moving into place conductive gel to ensure best possible data quality. Participants then received instructions for the Attentional Disengagement Task on the screen and were given the opportunity to ask any questions before starting the task. On completion of the task, the EEG cap was removed and participants were debriefed, paid and given the opportunity to wash their hair, as described above.

4.5 Behavioural measures

4.5.1 Hit rate

The hit rate is the probability that old items are correctly labelled as "old" and is the most direct measure of recognition memory performance. It is calculated by merely dividing the number of items correctly identified as old by the total number of old items. However, it is not a clean measure of recognition success as both trials in which an old item is correctly identified and trials in which the

participant correctly guesses that an item is old contribute to the overall hit rate. This means that a participant with only moderate recognition success but a bias towards guessing "old" for uncertain items can have a higher hit rate than a participant with higher recognition success but a bias towards guessing "new" for uncertain items. Clearer conclusions about recognition memory performance can be drawn from the discrimination index measure described below.

4.5.2 Discrimination index Pr

The discrimination index Pr is a measure of the probability that an item will be correctly classified as old or new (Snodgrass & Corwin, 1988). It assumes a two-high threshold model of recognition memory in which items have to pass one of two signal strength thresholds in order to be correctly classified, one for an "old" response and another for a "new" response (see detailed discussion in Chapter 1.1.3). An item that does not pass either threshold creates an uncertain state and leads to a guess response which can produce either a hit, a false alarm, a miss or a correct rejection. Items which pass the "old" threshold and are correctly remembered as old and items from an uncertain state that are correctly guessed to be old both contribute to the overall Hit rate (H). Since they are pure guesses not relying on any memory signal, correct "old" guesses are assumed to be made with equal probability as incorrect "old" guesses, or false alarms. The False Alarm rate (FA) can therefore be used to estimate the

rate of correct "old" guesses. In other words, the hit rate is made up of Pr, the probability of correctly identifying an old item, and the false alarm rate. Pr can therefore be estimated by subtracting the false alarm rate from the hit rate (Pr=H-FA). Pr estimates recognition memory performance independently of response bias.

4.5.3 Response bias Br

Response bias is defined as the probability to class an item as old in the absence of memory signal that passes either the "old" or the "new" threshold, i.e. in an uncertain state. "Liberal" response bias describes the tendency to class an item as "old" when in a state of uncertainty, "conservative" response bias describes the tendency to class the same item as "new". A liberal response bias increases the false alarm rate because items that fail to pass the "new" threshold (with a probability of 1-Pr) are more likely to be classed as "old" (along with items that fail to pass the "old" threshold, but then result in a correct "old" guess). The false alarm rate is therefore composed of the product of 1-Pr and Br. Solved for Br, it follows that response bias can be calculated by dividing FA by 1-Pr. Neutral response bias would be indicated by a value of 0.5, while higher values indicate a more liberal bias and values below 0.5 indicate a more conservative bias.

4.5.4 Remember rate

To estimate the proportion of "old" responses that relied on recollection of the stimulus, as opposed to "old" responses relying on familiarity with the stimulus presented at test, the remember-know procedure detailed above (see 4.3.2) was employed. Remember rates are given as the number of "remember" responses divided by the total number of correct "old" responses for each stimulus category. Where dual process theory is explicitly investigated, typically both an estimate of recollection R and an estimate of familiarity F are reported. The recollection estimate R is calculated as it is here and the familiarity estimate F calculated by subtracting the familiarity associated with new items Fn from the familiarity associated with correctly identified old items Fo. Fn is estimated by the proportion of false alarms, while Fo is estimated by the proportion of hits minus R, divided by 1 – R (Martin et al., 2011). However, since the dissociation of familiarity and recollection is not the focus of the present thesis, only remember rates are given where they contribute to the understanding of the data presented.

4.6 Genotyping

Each participant provided a 2ml saliva sample for genotyping. This was collected using Oragene DNA (OG-500) vials (DNA Genotek Inc: www.dnagenotek.com) and stored at room temperature until sent to the Welcome Trust Clinical Research Facility in Edinburgh for processing. There,

Oragene Purifier OG-L2P-5 was used for DNA extraction and Picogreen dye for quantification. An applied Biosystems 7900HT Fast Real-Time PCR system (Applied Biosystems: www.appliebiosystems.com) was used for SNP genotyping using the Taqman SNP assay rs6265 (BDNF). Samples were also assessed using the following Taqman SNP assays, analyses of which will be reported elsewhere: rs17070145 (kidney and brain expressed protein gene; KIBRA), rs7412 (Apolipoprotein E gene; APOE), rs429358 (APOE), rs4680 (Catechol-*O*-methyltransferase gene; COMT), rs263249 (Adenylyl cyclase type 8 gene; ADCY8), rs8074995 (Protein kinase C alpha gene; PRKCA), rs3730386 (cAMP-dependent protein kinase catalytic subunit gamma gene; PRKACG) and rs6994992 (Neuregulin 1 gene, NRG1).

Chapter 5:

Electrophysiological Correlates of Affective Cognition I - Affective Processing

This chapter describes the overall affective modulation of task performance in stimulus processing and attention. Affective content of pictures is shown to influence participants' ratings of picture valence and arousal, the late-positive potential (LPP) and attentional disengagement from the stimulus. Relationships between these measures are discussed, particularly in the light of the LPP often being described as an electrophysiological correlate of attention or an indicator of differences in arousal. Later chapters investigate how the affective cognition effects presented here are influenced by individual difference factors of gender (Chapter 7) and genotype (Chapter 8).

5.1 Affective ratings of stimulus material

5.1.1 Introduction

All experiments reported in this thesis rely on the basic assumption that the groups of stimuli used differ in affective content, eliciting distinct affective responses which will affect cognitive processing of these stimuli. Stimulus sets for all experiments were chosen by their IAPS standard ratings to include equal numbers of stimuli in each of three categories: low arousing neutral, high

arousing positive and high arousing negative. IAPS standard ratings for arousal were matched between the positive and negative stimulus sets to allow conclusions separating the effects of valence and arousal. The fundamental assumption that the participants' in these experiments experience of the chosen IAPS stimuli would correspond to IAPS standard ratings was checked, separately for each experiment, by asking all participants to rate all picture stimuli presented for their associated valence and arousal levels. Specifically, it was hypothesised that in terms of valence, pictures included in the "negative" subset of stimuli should be rated by participants as more negative than those included in the "neutral" subset, which should in turn be rated as more negative than the pictures in the "positive" stimulus subset. Secondly, since the negative and positive stimulus subsets were selected to be matched for arousal by their IAPS standard ratings, it was hypothesised that participants would rate negative and positive stimuli as equally arousing and as significantly more arousing than neutral stimuli.

5.1.2 Methods

The study phase of three affective memory experiments (Experiments 1, 2 and 3) comprised of the Affective Processing Task described in detail in chapter 4. A set of 222 IAPS pictures (set A) was rated for arousal and valence by 24 participants (mean age 21.0 years, 12 female) in Experiment 1. A second set of stimuli (set B), comprising of 288 IAPS pictures was rated in the same way by

46 participants (mean age 20.3 years, 23 female) in Experiment 2 and by 65 participants (mean age 20.1 years, 32 female) in Experiment 3.

5.1.3 Results

Participants' valence ratings converged with the IAPS standard ratings according to which stimuli had been selected, meaning stimuli in the positive category were rated as more positive than those in the neutral category, which were in turn rated as more positive than stimuli in the negative set. In all three experiments, valence ratings for stimuli in the "positive" set were significantly lower (indicating a more "positive" response) than those for neutral stimuli [Experiment 1: $t(23) = 10.3$, $p<.001$; Experiment 2: $t(45) = 9.50$, $p<.001$; Experiment 3: $t(63) = 20.6$, $p<.001$]. Ratings for "negative" stimuli were significantly higher, i.e. more "negative" [Experiment 1: $t(23) = 13.3$, $p<.001$; Experiment 2: $t(45)=18.0$, $p<.001$; Experiment 3: $t(63)=25.1$, $p<.001$]. Valence categorisation based on IAPS standard ratings was therefore successful.

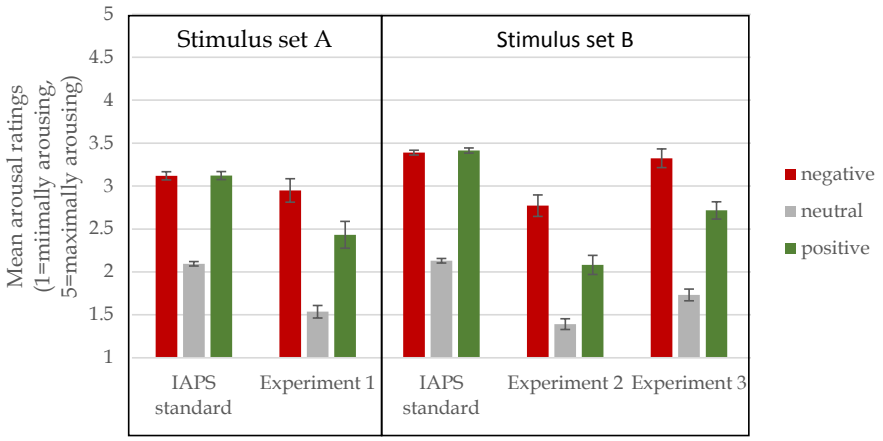


Figure 5.1 *Mean IAPS standard arousal ratings (rescaled to the 5-point scale used in the present experiments) and participants' own arousal ratings. Mean IAPS standard ratings for arousal are matched between negative and positive pictures in both stimulus sets A and B. Despite this, arousal ratings from all experiments reported here are consistently lower for positive than for negative pictures. Error bars show standard errors.*

Participants' reported arousal levels in response to the three picture categories, however, consistently showed a pattern differing from that in the original standard ratings according to which stimuli had been selected (see Figure 5.1). According to IAPS standard ratings, the selected negative and positive pictures were equally highly arousing, while neutral pictures were significantly lower in arousal. By contrast, arousal ratings obtained from the present participant groups were consistently higher for negative pictures than for positive pictures. This difference in arousal ratings between negative and positive pictures was significant in all three experiments [Experiment 1: $t(23) = 6.94$, $p<.001$; Experiment 2: $t(45) = 5.58$, $p<.001$; Experiment 3: $t(63) = 6.33$, $p<.001$], while neutral pictures, as expected, attracted significantly lower arousal ratings than

both negative [Experiment 1: $t(23) = 16.9$, $p<.001$; Experiment 2: $t(45) = 13.4$, $p<.001$; Experiment 3: $t(63) = 18.9$, $p<.001$] and positive pictures [Experiment 1: $t(23) = 8.85$, $p<.001$; Experiment 2: $t(45) = 7.48$, $p<.001$; Experiment 3: $t(63) = 11.9$, $p<.001$].

5.1.4 Discussion

The results presented here are a novel demonstration of a consistent, replicable difference in perception of the pictures between the original IAPS standardisation sample and an experimental sample population, in this case of Scottish university students sampled for the present study in the late 2000s and early 2010s. This divergence could be explained by one of two underlying differences: Either it arises as an artefact of differing experimental procedures or it shows a genuine underlying difference in the affective response elicited by the pictures in the two samples.

Although the present study and the IAPS standardisation studies both used the same instrument, the SAM, to obtain ratings, there were differences in presentation time which may have affected the results. Lang et al.'s (2008) participants viewed each picture for 6000ms, before rating it for valence, arousal and a third dimension of "dominance", in this order. In the experiments reported here, pictures were presented for 2000ms only and the arousal rating was obtained first. It is conceivable that their preceding categorisation of pictures in the positive category as positive, and therefore emotional, may have

influenced standardisation participants' subsequent arousal judgements, artificially inflating their interpretation of the level of arousal they felt in response to the picture. Given the biological significance of threat cues, a component in many of the highly arousing negative IAPS pictures in form of depictions of violence or injury, it is also conceivable that such stimuli evoke faster acting affective processes compared to positive stimuli and that these produce a negative affect reaction that is immediate but abates quickly with further processing. Shorter presentation times instantly followed by an arousal judgement may then tap into the early maximum levels of arousal, while longer presentation times and an intervening valence judgement may leave time for arousal to subside. Further behavioural research could clarify whether there is merit to either of these hypotheses.

Alternatively, the difference in rating patterns observed could have arisen not from procedural differences but from actual differences in the affect elicited by the stimuli in the two sample groups. The IAPS standard ratings on which stimulus selection was based were collected over a period of 13 years, between 1995 and 2008, from a number of participant samples. Very little is published about the characteristics of these participants but the fact that the IAPS was developed at the University of Florida along with the verbatim instructions published in the technical manual (Lang et al., 2008), which include a request to not discuss the experiment "until after the end of the semester", strongly suggests that they were U.S. university students. Participants in the present study mostly drawn from the undergraduate student population of the

University of Stirling in Scotland, between 2008 and 2011. This separation in time and space between the two sample groups may be associated with a cultural difference that may account for a real difference in levels of arousal elicited by stimuli in the positive category between the underlying populations. Some stimuli are intrinsically culture specific. For instance, depictions of American sporting success (for example picture 8540: "Athletes"), which are unlikely to produce the same levels of arousal in Scottish participants as they do in U.S. participants. But there may also be cultural differences in the perception and expression of positive arousal. Of course, these are just hypotheses on the origin of the observed difference and only further research could clarify the causes. If the IAPS stimulus set is to continue to be used in studies of affective processing internationally, an important first step in such future research would be to conduct up-to-date inter-cultural standardisation experiments in order to confirm or exclude cultural differences in the perception of IAPS pictures. If such differences are found, sub-sampling from the original IAPS set may allow for the creation of a new, smaller stimulus set which is free of cultural biases. Similarly, comparisons of different age groups and socio-economic backgrounds are necessary to confirm whether IAPS standard ratings are accurate across these factors.

But regardless of its source, it is important to note that there is a consistent difference between the normative arousal ratings of the IAPS and the arousal ratings collected in these experiments. This has important practical implications for any research relying on the IAPS stimulus set, as it emphasises the

importance of collecting sample specific valence and arousal ratings wherever possible and certainly where conclusions about the influence of these dimensions on other variables are to be drawn.

5.2 Affective modulation of the Late-Positive Potential (LPP)

5.2.1 Introduction

As discussed in chapter 3, the ERP effect most commonly investigated in studies of affective processing in recent years is the affective modulation of the Late-Positive Potential (LPP). More and more research is beginning to illuminate the features of the LPP and its relation to affective cognition in detail. This is one factor that makes the LPP ideal as an electrophysiological marker of affective processing in investigations of individual differences in affective cognition (Chapters 7 and 8). Another vital factor is the LPP's reliability and robustness, even in the face of low trial numbers (Moran, Jendrusina, & Moser, 2013).

Despite its popularity, there are aspects of the LPP that are little researched or understood. Firstly, its topographic properties are often neglected or left altogether unexamined and secondly, there is conflicting evidence regarding the role of stimulus valence in the elicitation of the LPP.

As Woodman (2010) notes, an ERP component is defined by four features: its polarity, timing, eliciting conditions and scalp distribution. The LPP is usually

described as a positive going modulation, starting at around 400ms post stimulus onset and lasting several hundred milliseconds, elicited by affective stimulus content and widespread, maximal at centro-parietal midline electrodes. This centro-parietal distribution, however, is often assumed without being explicitly examined or confirmed (e.g., see Brown, van Steenbergen, Band, de Rover, & Nieuwenhuis, 2012; Moran et al., 2013; Palomba, Angrilli, & Mini, 1997; Pastor et al., 2008). Studies that only report a small number of "traditional" LPP electrodes, most commonly on the midline, cannot confirm the assumed topography. Crucially, while scalp distribution cannot reveal the neural origins of an ERP component, it can provide evidence of neural generators differing between effects where they do. As such, it is important to report scalp distributions of ERP effects elicited by a variety of conditions or by stimuli or conditions that are assumed to be equivalent to previously shown manipulations. In the LPP literature, this is often overlooked.

An ongoing area of contradiction in the literature is the respective influence of valence and arousal associated with picture stimuli on the LPP. Many studies find equivalent effects of positive and negative pictures (e.g., see Keil et al., 2002; Sabatinelli, Lang, Keil, & Bradley, 2006; Schupp et al., 2000), suggesting that affective arousal is the relevant dimension in affective LPP modulation. Others, however, find a negativity bias, a larger modulation of the LPP for negative than for positive pictures of matched arousal (Ito, Larsen, Smith, & Caccioppo, 1998; Wood & Kisley, 2006), while Cuthbert, Schupp, Bradley, Birbaumer and Lang (2000) found largest LPPs in response to positive over

negative pictures. As the comparison of IAPS standard ratings and participants' own ratings above shows (see Chapter 5.1), these contradicting results could be a consequence of underlying differences in actual perceived arousal associated with negative and positive stimuli, as often these are not reported. Wood and Kisley's (2006) results point to a second possibility. While they find a negativity bias for younger adults, they report no evidence of differences between the effects of negative and positive pictures in older adults, pointing to individual differences as a possible cause for differences in LPP enhancement patterns. Chapters 7 and 8 will discuss individual differences in the LPP as a correlate of affective processing in detail.

Here, LPP effects across all participants are reported to establish that the commonly reported affective enhancement could be replicated as well as to clarify the influence of picture valence and arousal on the LPP.

5.2.2 Methods

EEG was recorded while participants completed the affective processing task in Experiments 1 and 3. The task involved looking at individual IAPS pictures on a screen for 2000ms in anticipation of rating the pictures for arousal and valence. The affective processing task is described in full detail in Chapter 4. As noted above (see 5.1.2), 24 participants (mean age 21.0 years, 12 female) completed the task in Experiment 1 and 65 participants (mean age 20.1 years, 32 female) in Experiment 3. Average ERPs in response to affective processing were

formed separately from an average number of 29.8 negative, 30.2 positive and 29.7 neutral trials per participant in Experiment 1 and from an average number of 33.3 negative, 34.6 positive and 34.3 neutral trials per participant in Experiment 3.

For topographic analysis, data from both Experiment 1 and Experiment 3 was subjected to a series of ANOVAs with within-subject factors of affective content (negative, neutral, positive), location (frontal, centro-frontal, central, centro-parietal, parietal) and site (left inferior[5], left medial[3], left superior[1], midline [z], right superior [2], right medial [4], right inferior [6]) and the between-subjects factor of experiment (1, 3). Figure 5.2 indicates the electrode sites included in this analysis. To assess whether any quantitative topographical differences observed also represent qualitative differences, i.e. whether there is evidence of involvement of different neural generators, data was rescaled using McCarty and Wood's (1985) Min-Max method (see Chapter 4 for discussion) and the above analysis repeated. The LPP effect is quantified by the mean amplitude difference at electrode Cz.

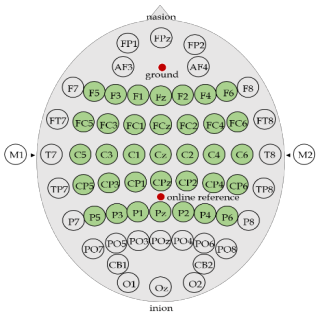


Figure 5.2 *Electrodes included in the topographical analysis of the LPP effect.*

5.2.3 Results

5.2.3.1 Positive affect modulation of the LPP

Visual inspection of waveforms (see Figures 5.3 and 5.4) confirmed an effect during the often reported 400ms to 1000ms LPP time window. Positive pictures elicited more positive going waveforms in this time window over superior centro-parietal electrode sites in both Experiments 1 and 3, although the difference was more pronounced in Experiment 3.

Mean amplitudes for the 400 to 1000ms time window were subjected to ANOVA with two levels of affective content, positive and neutral, which was designed to explore the LPP effect in response to positive pictures. There was a significant affective content by location by site interaction [$F(3.21, 280)=4.40$, $p=.004$], due to the positive-going amplitude difference between the positive and neutral condition being more left-sided in parietal locations only. The fact that this interaction was also significant in rescaled data [$F(3.3, 287)=4.86$, $p=.002$] suggests the topographical difference between the two scalp distributions is caused by differences in neural generators, rather than merely being an artefact of magnitude differences.

The only significant effect of experiment was an interaction with affective content [$F(1, 87)=14.9$, $p<.001$], reflecting a difference in LPP magnitude in response to positive pictures across experiments. The absence of significant interactions involving experiment and either location or site suggests that there are no topographical differences between the LPP effects elicited by positive

pictures in the two experiments. Figures 5.3 and 5.4 show grand average waveforms for positive and neutral pictures at representative electrode sites across the scalp, from Experiments 1 and 3 respectively. Mean amplitudes were significantly more positive in response to positive than in response to neutral pictures at electrode Cz in both Experiment 1 [$t(23)=3.70$, $p=.001$] and Experiment 3 [$t(64)=9.73$, $p<.001$].

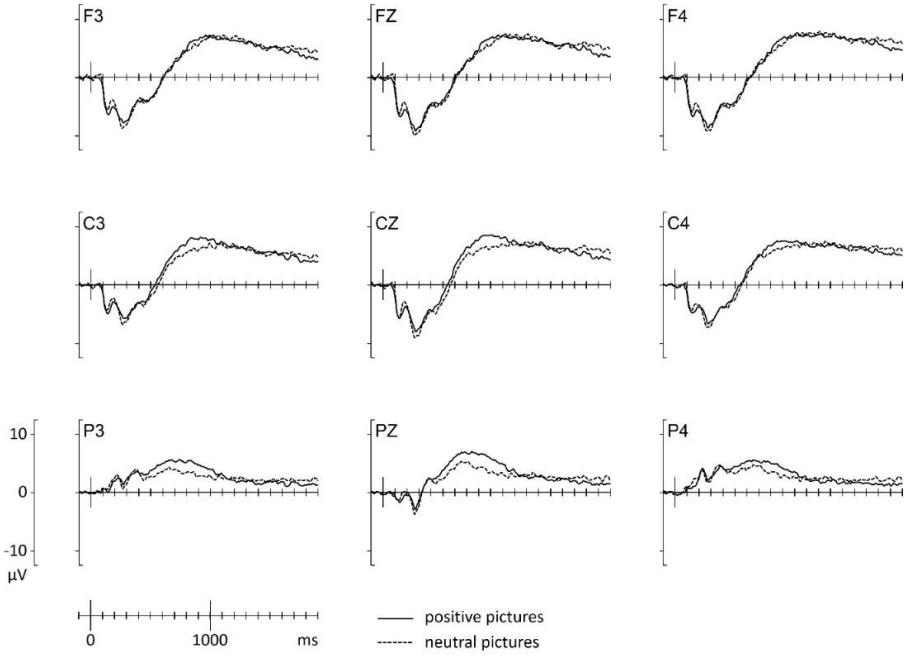


Figure 5.3 *Grand average ERP waveforms for the processing of positive compared to neutral pictures in Experiment 1.*

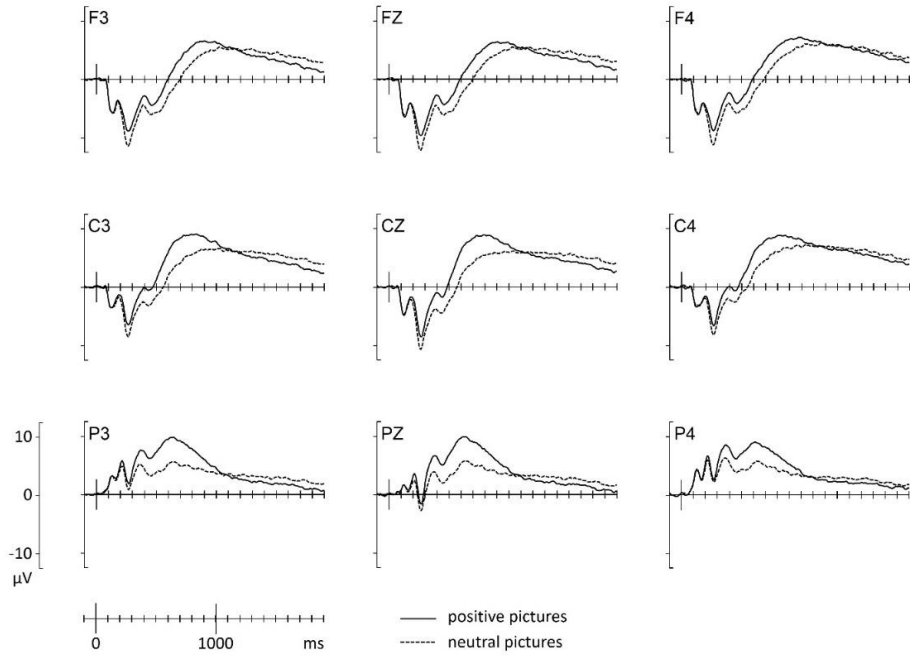


Figure 5.4 *Grand average ERP waveforms for the processing of positive compared to neutral pictures in Experiment 3.*

5.2.3.2 Negative affect modulation of the LPP

The same 400-1000ms LPP time window was chosen for the negative affect condition, confirmed by visual inspection of waveforms. ANOVA with levels of affective content being negative and neutral again revealed a significant affective content by location by site interaction [$F(3.54, 308)=3.38$, $p=.013$], caused by a stronger left lateralisation of the LPP effect in posterior locations. This interaction was also significant in the analysis of rescaled data [$F(3.63, 315)=3.95$, $p=.005$] pointing to a qualitative difference in topographies.

The experiment factor was not significant in any interaction involving affective content, showing that there was no significant topographical or amplitude difference in LPP effects in response to negative pictures between experiments. Figures 5.5 and 5.6 show grand average waveforms for negative and neutral pictures at representative electrode sites across the scalp, from Experiments 1 and 3 respectively. Mean amplitudes were significantly more positive in response to negative than in response to neutral pictures at electrode Cz in both Experiment 1 [$t(23)=3.62$, $p=.001$] and Experiment 3 [$t(64)=5.54$, $p<.001$].

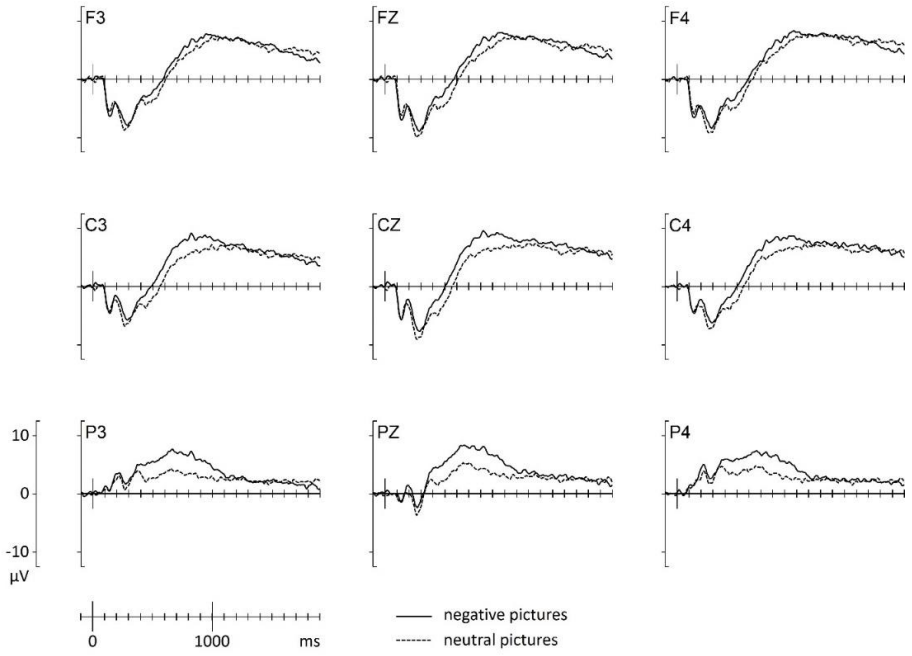


Figure 5.5 *Grand average ERP waveforms for the processing of negative compared to neutral pictures in Experiment 1.*

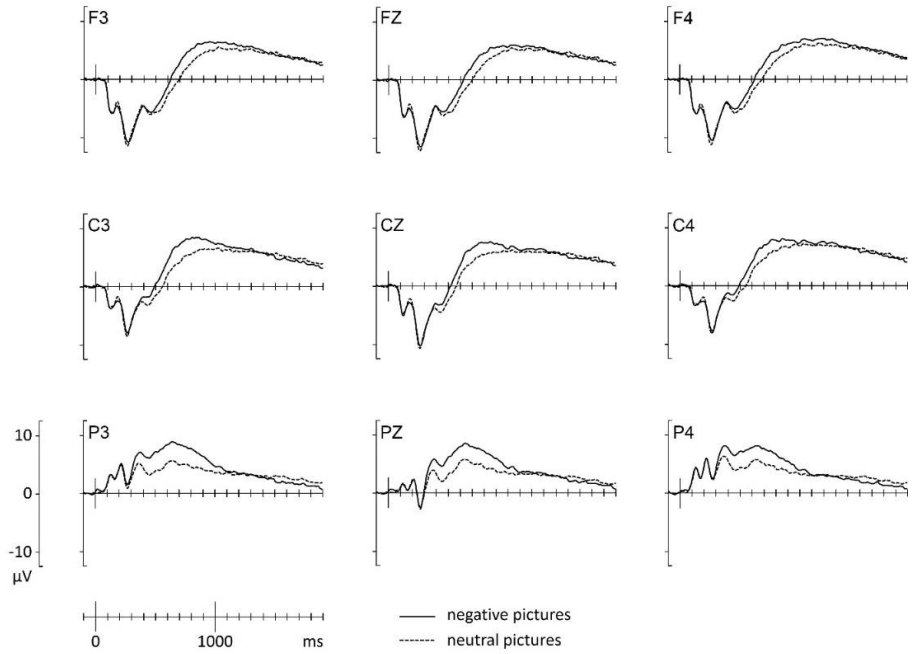


Figure 5.6 *Grand average ERP waveforms for the processing of negative compared to neutral pictures in Experiment 3.*

5.2.3.3 Comparison of positive and negative affect modulations of the LPP

To investigate LPP effect modulations by valence, mean amplitude differences between the affective conditions (negative, positive) and the neutral condition were calculated for both experiments and subjected to ANOVA with factors affective content (negative, positive), location, site and experiment, as above. Affective content interacted with site and experiment [$F(1.96, 171)=3.91$, $p=.023$], stemming from greater differences between the negative and positive LPP effects at midline electrodes in combination with a reversal of the polarity of the effect difference (Experiment 1: negative LPP effect > positive LPP effect; Experiment 2: positive LPP effect > negative LPP effect). The same interaction

was present in rescaled data [F(1.96, 171)=3.99, p=.021] suggesting a qualitative difference. T-tests comparing LPP effect sizes at electrode Cz showed a larger LPP effect for negative than for positive pictures in Experiment 1 which narrowly missed significance [t(23)=1.92, p=.067] and a significantly larger LPP effect for positive than for negative pictures in Experiment 2 [t(64)=4.20, p<.001].

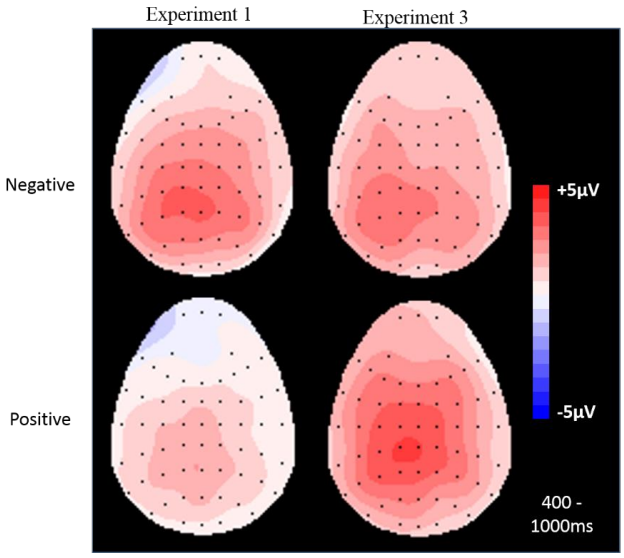


Figure 5.7 *Scalp maps of amplitude difference from neutral condition in the 400-1000ms time window. LPP effects in response to negative pictures are more left parietal, while LPP effects in response to positive pictures show the more central distribution typically reported for LPPs.*

5.2.4 Discussion

Increased LPPs could be demonstrated in both experiments for both negative and positive compared to neutral pictures. While the effects were significant, and strong, at the commonly reported centro-parietal midline electrode sites, the distribution of the effects were slightly left sided for both affective conditions.

The comparison between the modulation of the LPP by negative and positive affective pictures respectively proved interesting in light of conflicting results in previously published findings. Both experiments reported here employed the same paradigm and procedure, differing only in the size of the stimulus sets used. More importantly, participants from both experiments reported the same pattern of arousal in response to the three affective picture categories, with arousal levels in response to negative pictures significantly higher than to positive pictures and neutral pictures reported to be the least arousing (see Figure 5.1 above). Despite the stimulus sets eliciting the same pattern of arousal, LPP modulation was stronger for negative pictures in Experiment 1 but positive pictures in Experiment 3. Taken on its own, results from Experiment 1 would have suggested that arousal not valence is the crucial factor in the affective modulation of the LPP. However, the different pattern found in Experiment 3 shows that the relationship between perceived stimulus arousal and valence and the affective LPP modulation is more complex. In Experiment 3, positive stimuli, which were rated as only moderately arousing and were associated with only moderate effects in Experiment 1, produced the

strongest LPP enhancement. This directly contradicts findings that LPP enhancement is positively associated with arousal. An enhancement of the LPP effect for positive pictures caused by stimulus set size looks implausible, especially since participants' ratings remained constant. In the absence of any other differences between the experiments, the mostly likely cause of the difference must then lie in the differences between participants groups. As gender ratios were held constant between experiments, the differences in LPP enhancement patterns observed here are not a function of gender differences in affective processing. It is conceivable however, that other individual differences influence affective processing and that such differences underlie the fact that a negativity bias in LPP enhancement was shown in Experiment 1 while a positivity bias was shown in Experiment 3. Chapter 8 discusses the possibility of genetic differences in affective processing.

The differences between the two experiments reported here in the respective size of LPP modulation by positive and negative picture content, has important implications for the design and reporting of future studies of affective modulations of the LPP. They highlight the importance of replication of patterns of affective modulation across a number of samples if any universally applicable conclusions are to be drawn, as well as the need for future research into the factors influencing the existence of positivity versus negativity biases. Establishing whether consistent, at least over the short- to medium-term, biases can be shown reliably for individual participants would enable future studies

to compare negativity bias to positivity bias groups and explore potential individual differences governing such biases.

In a clinical setting, if such consistent biases can be demonstrated using the LPP as an electrophysiological marker of affective processing, LPP paradigms could become an important objective assessment tool in the treatment of conditions linked to negativity bias such as anxiety or depression, which would avoid the subjective factors associated with self-report.

5.3 Affective modulation of attentional disengagement

5.3.1 Introduction

The LPP is often described as a measure of sustained attention, the argument being that it is the attention capturing properties of emotional stimuli that modulate LPP mean amplitudes (Schupp, Flaisch, Stockburger, & Junghoefer, 2006).

The evolutionary argument for an attention capturing effect of affective stimuli is obvious. Negative stimuli, such as the roar of a wild animal or an image of a person showing aggression, commonly indicate a potentially dangerous situation, often a threat to safety or health. Attending these stimuli preferentially therefore carries a survival advantage, as it enables quicker assessment of the situation and fight or flight reactions where appropriate. Positive stimuli, on the other hand, are often associated with potential increases

in health, wellbeing and safety. Their preferential processing enables quicker reactions which leads to an advantage in the competition for resources.

Most behavioural evidence for preferential attention to affective stimuli comes from affective versions of two classic attention paradigms: The emotional pictures dot-probe task (MacLeod, Mathews, & Tata, 1986) and the emotional Stroop task (Gotlib & McCann, 1984). The emotional pictures dot-probe task works on the premise that when two pictures are presented simultaneously and followed a probe in one of the picture locations, probe detection will be quicker when the probe is presented in the location of the preferentially attended picture. Proponents of the emotional Stroop task propose that when words presented in different colours have affective content, colour naming will be slowed compared to words of neutral content, as attention to the affective content interferes with the primary colour naming task.

Generally, these paradigms are employed to show attentional biases in clinical populations, such as participants who are clinically anxious or depressed. Williams, Mathews and MacLeod (1996) reviewed the use of the emotional Stroop task is research of attentional bias in psychopathology and reported a wide range of demonstrations of the effect in clinical and sub-clinical samples including patients with clinical anxiety, clinical depression, post-traumatic stress disorder, obsessive-compulsive disorder and high trait anxiety. Notably, only four of the 53 studies reviewed also found emotional Stroop effects in control groups. So if, as the evolutionary line of reasoning suggests, there are affective biases in the general population, the emotional Stroop seems to lack

power to show these. Additionally, Larsen, Mercer and Balota (2006) question the emotional Stroop's construct validity by showing that in 32 reviewed emotional Stroop studies, affective words were significantly longer, less frequently used and had smaller orthographic neighbourhoods. They argue that slower colour naming can be explained by slower word recognition resulting from these distinct lexical features. McKenna and Sharma (2004) distinguish between fast and slow components of the emotional Stroop, fast effects acting automatically at the single trial level and slow effects spanning several trials. By comparing the typically used blocked presentation format with mixed presentation, they showed that fast effects play a negligible role and conclude that the emotional Stroop effect reflects slowing of attentional disengagement from affective stimuli.

To assess attentional disengagement from affective and neutral pictures, a novel task was designed in which participants had to detect probes presented above or below a picture that remained on the screen.

The pattern of LPP effects found in the same participants who completed this attentional disengagement task did not match the pattern of the self-reported arousal in response to the stimuli (arousal ratings: negative > positive > neutral; LPP mean amplitudes: positive > negative > neutral). Therefore, the pattern of attentional disengagement results can give further insights into the nature of the LPP.

It was hypothesised that affective pictures would preferentially capture attention over neutral pictures, and thus reaction times to probes presented with affective pictures would be longer than to probes presented with neutral pictures. If attentional disengagement is slowed by affective arousal, then attentional disengagement should be slower from negative than from positive pictures, since participants rated negative pictures as more arousing than positive pictures (see Chapter 5.1). This would suggest that the increase in the LPP is driven by processes other than merely attention to affective stimuli. If, on the other hand, the LPP is an electrophysiological correlate of attention, then attentional disengagement should be slowest from positive pictures, followed by negative and then neutral pictures. It would follow that attention is captured by affective stimulus features beyond arousal.

5.3.2 Methods

64 participants completed the attentional disengagement task described in detail in Chapter 4. Nine participants whose overall mean accuracy was less than 0.7 on this task were excluded from the analysis, leaving 55 datasets (mean age 20.1 years, 27 participants female).

Only reaction times associated with correct responses were included. A lower cut-off for reaction times was not set, as the fastest response recorded, 338ms after stimulus onset, was within the limits of what can be presumed to be a genuine response to the stimulus. Reaction times above 3 standard deviations

above the sample mean (2188ms) were considered outliers and removed from the dataset.

5.3.3 Results

As figure 5.7 illustrates, reaction times were longest in response to negative pictures, followed by reaction times in response to positive pictures. Shortest mean reaction times were recorded in trials where participants had to disengage from neutral pictures. A repeated-measures ANOVA showed a significant main effect of affective picture content on mean reaction times [$F(2,108)=5.03$, $p=.008$]. Follow-up t-tests revealed this to be driven by a significant difference between reaction times to probes presented with negative compared to neutral pictures [$t(54)=3.13$, $p=.003$]. Reaction times were longest for probes presented with negative pictures and shortest for probes presented with neutral pictures. The differences in reaction times between the positive compared to the neutral condition [$t(54)=1.60$, $p=.115$] and between the negative and the positive condition [$t(54)=1.60$, $p=.116$] failed to reach significance.

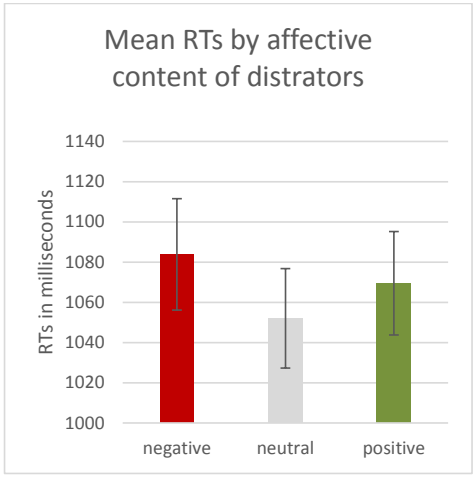


Figure 5.7 *Reaction times were longest in the negative condition (M=1084ms, SD=205ms), followed by reaction times in the positive condition (M=1069, SD=191ms). Participants reacted fastest to probes presented with neutral pictures (M=1052ms, SD=183ms).*

5.3.4 Discussion

Reaction times were significantly longer for probes presented with negative pictures than for those presented with neutral pictures. Although, in line with predictions, reaction times to probes presented with positive pictures lay between those in the negative and neutral conditions, no other difference reached significance. This is likely due to a lack of power in light of high intra and inter participant variance, a hypothesis supported by relatively low p-values for these differences (negative-positive: p=.116 and positive-neutral: p= .115). It is plausible that future research could show significant differences between all three affective categories, given sufficient trial and participant numbers. The pattern of results is consistent with participants' arousal ratings in response to the affective pictures, which were significantly higher for

negative than for positive and for positive than for neutral affective content (see Chapter 5.1). Despite the negative-positive and positive-neutral RT differences' failure to reach significance in the attentional disengagement data, the pattern of results supports the view that increased arousal slows attentional disengagement. This is in line with Vogt, De Houwer, Koster, Van Damme and Crombez's (2008) findings from an affective spatial cuing task, where targets presented in one of two locations were preceded by either valid (same location) or invalid (opposite location) cues, selected from one of four categories: highly arousing positive, highly arousing negative, low arousing positive or low arousing negative IAPS pictures. They found no effects of valence but an increase in the cue validity effect (shorter RTs in valid cue trials) for highly arousing compared to low arousing pictures. The present data presents a novel demonstration of the slowing of attentional disengagement with increasing affective arousal using a simultaneous target paradigm. Future studies employing larger trial and participant numbers for increased power, as well as a wider range of arousal levels associated with affective stimuli, are necessary to establish whether the relationship between affective arousal and slowing of attentional disengagement is linear and whether there are differences in this relationship driven by stimulus valence.

A better understanding of the factors affecting attentional disengagement has important practical applications in a number of areas requiring both the focussing attention and flexible switching between different focuses of attention, especially where affective factors are likely to come into play, such as

in road safety, police and security work or professional sports. Research could then establish whether participants can be trained to improve their attention switching times in affectively arousing situations using attentional disengagement paradigms similar to the one employed here.

5.4 General Discussion

This Chapter sought to establish the influence of affective stimulus content on subjective picture ratings, the LPP and performance in an attentional disengagement task, as well as the interplay between these measures. Conflicting with IAPS standard ratings, according to which negative and positive stimuli were matched for arousal, participants rated negative stimuli as significantly more arousing than positive stimuli in all three experiments that included the rating task. Performance on the attentional disengagement task was consistent with the view that attention is sustained longer for more arousing stimuli, as reaction times were longest in response to negative, followed by positive and then neutral items. Both of these results are not consistent with an attention view of the LPP. The LPP increase for negative pictures, which were rated as most arousing and produced the only significant slowing of attentional disengagement, was significant but was surpassed by the increase for positive pictures, rated as less arousing than negative pictures and producing less and non-significant slowing of attentional disengagement. Therefore, differences in attention alone cannot account for differences in LPPs

in response to pictures of different affective content. The LPP is commonly used as an index for sustained attention towards affective stimuli (e.g., see Hajcak & Olvet, 2008; Weinberg & Hajcak, 2011) but the results presented here suggest that this cannot be the full story. Dunning and Hajcak (2009) and Hajcak, MacNamara, Foti, Ferri, and Keil (2013) showed that the LPP was reduced when attention was directed to a non-arousing region of negative pictures, lending support to the hypothesis that attention to affective content is a necessary prerequisite of the affective LPP increase. But findings presented here show that attention on its own is not sufficient for explaining this increase. It has been shown that additionally to bottom-up processes which are driven by stimulus properties likes arousal, top-down processes like reappraisal of stimulus content (Hajcak & Nieuwenhuis, 2006), neutral rather than negative description prior to stimulus presentation (Foti & Hajcak, 2008) and voluntary suppression (Moser, Hajcak, Bukay, & Simons, 2006). These processes could account for varying results showing negativity biases like the one observed in Experiment 1 in some circumstances and positivity biases like the one observed in Experiment 3 in others. However, like bottom-up processes resulting from differences in stimulus arousal, these top-down processes are also understood to modulate the LPP via changes in attention to stimuli, as part of Desimone and Duncan's (1995) biased competition model of visual attention.

The findings presented here point strongly to an eliciting condition for increases in the LPP over and above stimulus arousal and sustained attention. However, while stimulus arousal was assessed immediately following each

stimulus presentation during LPP data collection, attentional disengagement was assessed in a separate experiment, one week later. Since arousal, LPP and attention data was collected from the same participant sample and arousal and attentional disengagement pattern are consistent with each other, it is unlikely that top-down processes differed between experiment sessions. Nevertheless, this could be clarified by future research incorporating both the picture processing (LPP) and attentional disengagement tasks in close temporal proximity. Given a replication of the mismatch between attentional disengagement and LPP results, more research will be needed to establish the conditions under which affective LPP increases can and cannot be explained by differences in attention. Specifically, studies with larger trial numbers are needed to establish, whether the LPP increase is linked to an increase in affective arousal within one or both valence categories and whether slowed attentional disengagement is associated with LPP increases in some circumstances or merely a spurious co-occurrence driven by different underlying factors.

The present findings do clearly demonstrate, however, that the LPP cannot be used as a universal electrophysiological index of sustained attention and that studies presenting it as such need to provide corroborating evidence in the form of behavioural or other functional neuroimaging indexes of attention.

Chapter 6: Electrophysiological Correlates of Affective Cognition II - Affective Memory

6.1 Time-course of affective memory effects

6.1.1 Introduction

Experiment 1, comprising of the affective processing task followed after a 20 minute delay by an affective memory task (both are described in detail in chapter 4), failed to find any affective modulation of recognition memory evident in either behaviour or electrophysiological data. Given an ample sample size of 24 participants and 111 "old" stimuli (37 high-arousing negative, 37 high-arousing positive and 37 low-arousing neutral), it is unlikely that the absence of significant effects can be explained solely by lack of power. It could, however, be a result of the way in which affective content modulates memory, if indeed it does. As discussed in Chapter 1, there are three distinct stages during which memory may be affected: Encoding, consolidation, retention and retrieval. If the affective content of a stimulus simply enhanced retrieval of that stimulus, such an effect should be seen after any length of study-test interval. If, on the other hand, the affective content of the stimulus affects stimulus consolidation or retention, through differences at the encoding stage, then effects on memory performance may only become apparent with increasing study-test intervals.

A classic study by Kleinsmith and Kaplan (1963) showed that in a paired associates learning task, recall was improved for high-arousal word pairs only after an interval of one week, while recall was actually worse for high-arousal pairs than for neutral pairs when tested immediately after study, with a study-test interval of only 2 minutes. Walker and Tarte (1963) replicated their result. More recently, Pierce and Kensinger (2011) found no effect of affective word content on immediate associative recognition performance, but enhanced accuracy for negative intact word pairs with a study-test interval of one week. Sharot and Phelps (2004) also reported that recognition of peripherally presented neutral words declined over time. Recognition of arousing words was the same after one week delay as it was when tested immediately after study.

Sharot and Yonelinas (2008) demonstrated similar effects of study-test delay on memory for negative affective pictures. They found no significant differences in item recognition between affective and neutral items after a five minute delay and no significant effects on remember/know ratios or source judgement. After 24 hours, recognition for affective pictures was significantly better and the proportion of "remembered" items was significantly higher for affective items than for neutral items. While Sharot and Yonelinas (2008) reported that the affective memory enhancement effect is not present for negative pictures when memory is tested immediately after encoding, Chainay, Michael, Vert-pré, Landré and Plasson (2012) showed that affective memory enhancement can be demonstrated for positive, but not negative or neutral, pictures, if encoding was

incidental rather than intentional. Unfortunately, this study did not include a longer study-test interval to allow conclusions about the relative development of affective memory enhancement for negative and positive pictures over time.

To further illuminate the development of affective memory effects for pictures over time and the impact of picture valence on this development, a paradigm including three study-test delays was designed. It was hypothesised that enhancement of memory performance for negative pictures would not be present at immediate recognition test but develop over time. It was further hypothesised that memory enhancement for positive over neutral pictures should increase over time. As encoding was incidental in this experiment, an immediate effect was expected for positive pictures, based on Chainay et al.'s (2012) earlier results.

6.1.2 Methods

56 participants completed the affective processing task described in chapter 4 on a set of 288 IAPS pictures. Eight participants did not complete one or more of the subsequent test phases, leaving complete data sets from 48 participants (mean age 20.3 years, 24 female) for analysis. All of these participants completed affective recognition tests on different subsets of stimuli after 5 minutes, 1 day and 1 week delay. Discrimination index Pr (Pr=hit rate-false alarm rate) and response bias Br (Br=false alarm rate/[1-Pr]) were calculated and subjected to repeated-measures ANOVA with factors of affective content

(positive vs neutral and negative vs neutral respectively) and test delay (immediate, 1 day, 1 week).

6.1.3 Results

As discussed in Chapter 5.1 and shown in Figure 6.1, despite the negative and positive affective picture sets being matched for arousal according to their IAPS standard ratings, participants in this study rated negative images as significantly more arousing than positive pictures [$t(45) = 5.58$, $p<.001$]. In line with the classification by standard ratings, participants also rated positive pictures as significantly more arousing than neutral pictures [$t(45) = 7.48$, $p<.001$]. Valence ratings for negative pictures were significantly higher than those for neutral pictures [$t(45)=18.0$, $p<.001$] and valence ratings for positive pictures were significantly lower than those for neutral pictures [$t(45) = 9.50$, $p<.001$], confirming the classification by IAPS standard ratings.

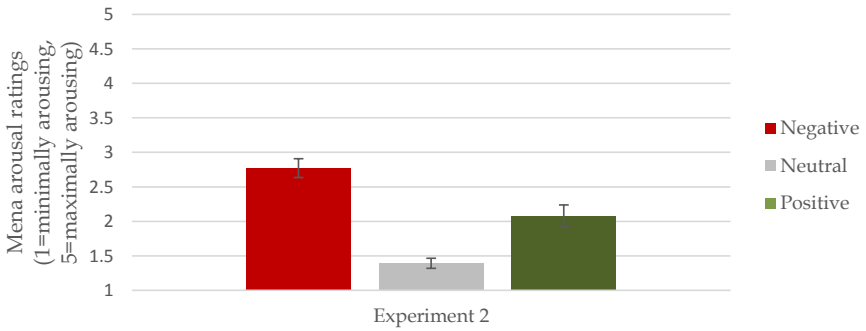


Figure 6.1 *Arousal ratings for negative pictures were significantly higher than those for positive pictures and arousal ratings for positive pictures were significantly higher than those for neutral pictures.*

As Table 6.1 indicates, hit rates decreased over time in all affective categories, while false alarm rates increased, leading to decreasing discrimination accuracy over time. Response bias became more conservative over time for positive and neutral pictures but was most liberal at one day study-test delay for negative pictures. At the "immediate" recognition test after five minutes delay, discrimination was highest for neutral, followed by negative and then positive pictures. After one day delay, discrimination was highest for negative, followed by neutral and then positive pictures, while after one week, discrimination was still highest for negative pictures but higher for positive than for neutral pictures. Response bias was consistently more liberal for affective than for neutral pictures and more liberal for negative than for positive pictures, across all three study-test delays.

		Study-test delay					
		5 mins		1 day		1 week	
Picture valence	Negative	Hit rate	0.949 (0.007)	Hit rate	0.876 (0.022)	Hit rate	0.737 (0.026)
		FA rate	0.073 (0.012)	FA rate	0.125 (0.027)	FA rate	0.126 (0.022)
		Pr	0.876 (0.014)	Pr	0.751 (0.042)	Pr	0.611 (0.028)
		Br	0.435 (0.059)	Br	0.472 (0.053)	Br	0.327 (0.046)
	Neutral	Hit rate	0.936 (0.011)	Hit rate	0.801 (0.027)	Hit rate	0.570 (0.028)
		FA rate	0.048 (0.011)	FA rate	0.089 (0.026)	FA rate	0.091 (0.020)
		Pr	0.888 (0.015)	Pr	0.712 (0.044)	Pr	0.479 (0.031)
		Br	0.275 (0.056)	Br	0.219 (0.044)	Br	0.176 (0.031)
	Positive	Hit rate	0.919 (0.015)	Hit rate	0.783 (0.026)	Hit rate	0.637 (0.027)
		FA rate	0.089 (0.014)	FA rate	0.141 (0.026)	FA rate	0.138 (0.022)
		Pr	0.831 (0.021)	Pr	0.642 (0.040)	Pr	0.499 (0.030)
		Br	0.414 (0.055)	Br	0.362 (0.050)	Br	0.271 (0.035)

Table 6.1 *Means and standard errors (in brackets) for hit rate, false alarm (FA) rate, discrimination index Pr and response bias Br by picture valence and study-test delay.*

6.1.3.1 Time-course of positive affective memory

6.1.3.1.1 Discrimination index Pr

There was a significant interaction in Pr between affective stimulus content and test delay [F(2,94)=4.73, p=.011]. As above, this was due to a sharper decline of Pr in response to neutral pictures over time, when compared to positive pictures. However, Pr for neutral pictures was significantly higher than for positive pictures at immediate test [t(47)=3.52, p=.001] and after 1 day [t(47)=2.91, p=.006], with no significant difference after 1 week (see Figure 6.2).

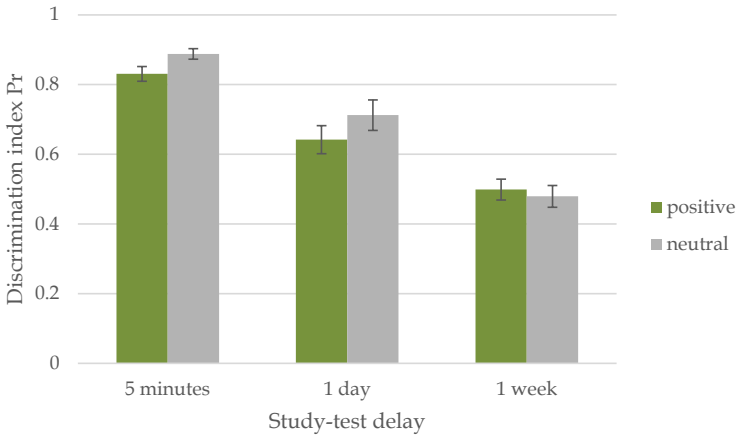


Figure 6.2 *Discrimination index Pr was significantly higher for neutral than for positive pictures at one minute and one day study-test delay but decreased to the same level as Pr for positive pictures after one week. Error bars show standard errors.*

6.1.3.1.2 Response bias Br

There was no significant interaction between affective stimulus content and test delay on response bias. Instead, there was a significant main effect of affective stimulus content [F(1,47)=23.4, p<.001], with Br being higher for positive than for neutral pictures, indicating a less conservative bias (see Figure 6.3). The main effect of test delay was also significant [F(1.57,73.60=4.26, p=.026], reflecting an increasingly conservative response bias over time.

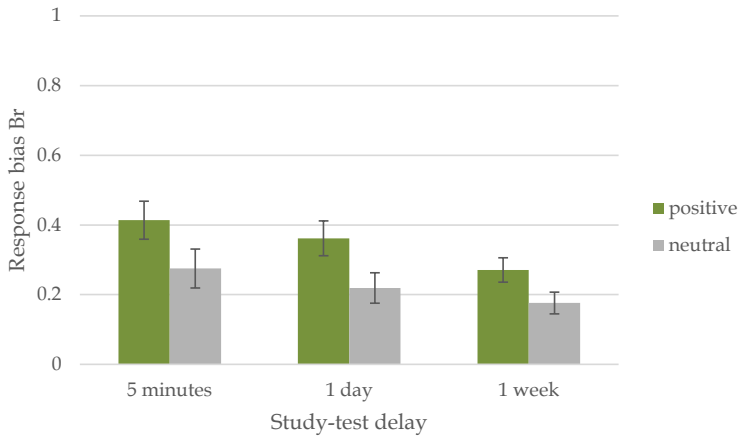


Figure 6.3 *Response bias Br is more liberal for positive than for neutral pictures at all test times and becomes increasingly conservative for both positive and neutral pictures over time. Error bars show standard errors.*

6.1.3.2 Time-course of negative affective memory

6.1.3.2.1 Discrimination index Pr

Pr showed an analogous interaction between affective stimulus content and test delay [$F(1.71,80.2)=10.7$, $p<.001$], however the difference in Pr between negative and neutral pictures failed to reach significance until 1 week delay [$t(47)=4.71$, $p<.001$], see Figure 6.4.

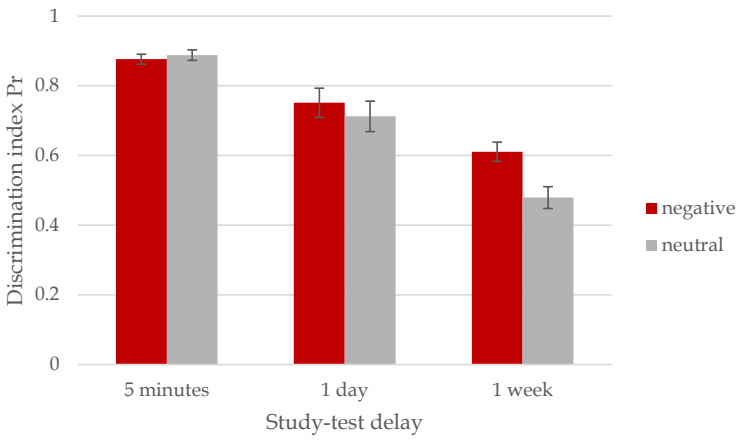


Figure 6.4 *Discrimination index Pr differed significantly by affective picture content only after one week delay, with Pr being higher for negative than for positive pictures. Error bars show standard errors.*

6.1.3.2.2 Response bias Br

There was no significant interaction between affective stimulus content and test delay in response bias but there were significant main effects of affective

stimulus content [F(1,47)=37.8, p<.001] and test delay [F(1.88,88.1)=3.61, p=.034]. This reflects a more conservative response bias for neutral than for negative pictures and an overall decline in Br over time as Figure 6.5 illustrates.

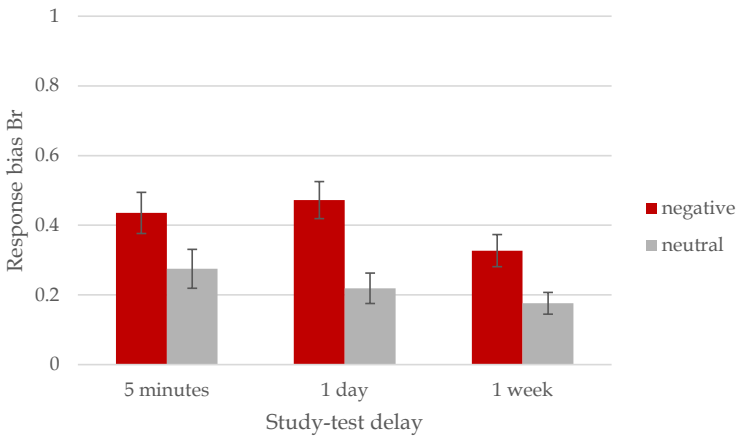


Figure 6.5 *Response bias was more liberal for negative than for neutral pictures but became more conservative for both picture categories over time. Error bars show standard errors.*

6.1.3.3 Valence effects on development of affective memory over time

Three within-subject ANOVAs with factors of picture valence (negative, positive) and test delay (5 minutes, 1 day, 1 week) were performed on the differences for affective from neutral pictures in Pr and Br respectively to assess whether observed differences in the development of these measures over time between the two affective valences were statistically significant.

6.1.3.3.1 Discrimination index Pr

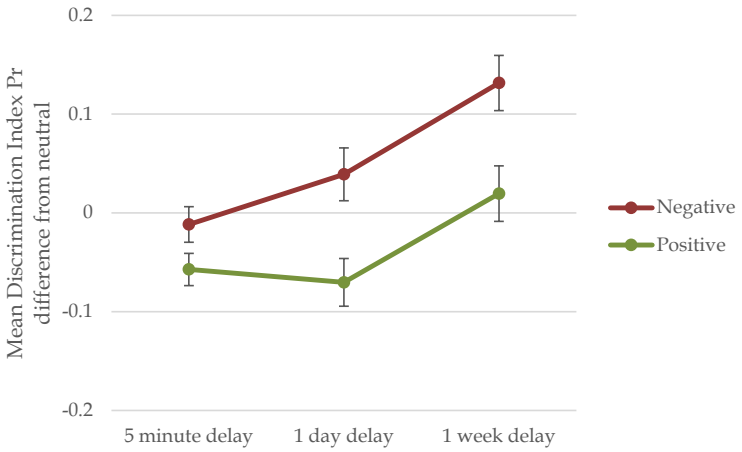


Figure 6.6 *Pr difference from neutral increases over time for both negative and positive pictures. The apparent increase in the difference between negative and positive difference scores over time failed to reach significance. Error bars show standard errors.*

Figure 6.6 shows a valence effect on the difference in discrimination index Pr for affective minus neutral pictures, with negative pictures producing the bigger Pr difference from neutral and the valence effect seemingly increasing over time. The content valence by test delay term failed to reach significance however, and only significant main effects of content valence [$F(1, 47)=26.29$, $p<.001$] and test delay [$F(2, 94)=13.91$, $p<.001$] were found.

6.1.3.3.2 Response bias Br

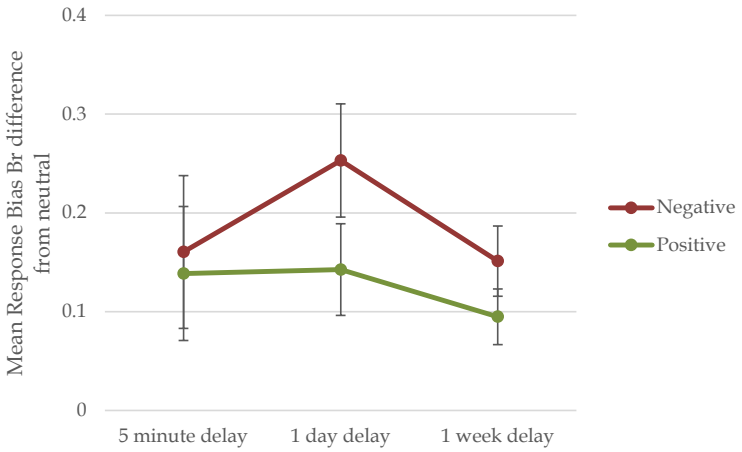


Figure 6.7 *There was no significant interaction between valence and test delay on Response Bias Br difference from neutral. Error bars show standard errors.*

Response bias differences from neutral appeared to be somewhat larger for negative than for positive pictures, a difference that was most pronounced after one day test delay (see Figure 6.7). ANOVA did not return a significant content valence by test delay interaction and there was also no significant main effect of test delay. Despite the visually observed difference between the Br difference scores for negative and positive pictures, the main effect of content valence narrowly missed significance [t(1)=3.85, p=.056].

6.1.4 Discussion

Memory enhancement was expected to be immediate and to increase over time for positive pictures, while memory enhancement for negative pictures was expected to only be demonstrable after longer delays.

Response bias was significantly more liberal for affective as compared to neutral pictures but became more conservative over time for all picture categories. The analysis of difference scores from the neutral baseline revealed no difference between Br for negative and positive pictures. As a consequence of consistently increasing conservativism in response bias across all three stimulus categories, performance on discrimination index Pr was actually poorer for positive than for neutral pictures after five minutes and one day delay and showed no difference between positive and neutral pictures after one week. For negative pictures, Pr did not differ from neutral pictures until one week post study, at which point it became significantly higher. Analysis of the differences from neutral revealed main effects of content valence and test delay, showing that the difference in Pr between negative and neutral pictures was consistently higher than the Pr difference between positive and neutral and that these difference scores increased with time for both valences.

The pattern seen for positive pictures is in contrast with Chainay et al.'s (2012) results in that these authors showed immediate enhancement of recognition memory for positive pictures over negative and neutral pictures, while here, recognition performance as measured by discrimination index Pr was actually

significantly worse for positive than for neutral pictures at five minute and one week delay. In Chainay et al.'s (2012) paradigm, the last study phase was immediately followed by a recognition memory test, while the minimum study-test interval employed here was five minutes. It is possible that affective enhancement of recognition memory by positive stimulus valence follows a U-shape, with very short lived immediate memory benefits for positive over neutral stimuli which give way to effects on consolidation that produce slower developing, more long-term benefits.

A recently published study by Wang (2014) employed a similar paradigm to the one reported here, with study-test delays of five minutes, one day and one week respectively. Two noteworthy differences between the present paradigm and Wang (2014) are his use of the non-parametric measure A' (see Snodgrass, Levy-Berger, & Haydon, 1985) to quantify recognition memory performance and the fact that he compares study-test intervals between rather than within participants. Consistent with present data, he showed a significant affective content by test delay interaction. Unfortunately, Wang (2014) did not statistically compare either hit rates or A' between affective content categories at each study-test delay. The reported means, however, not only contradict an immediate memory enhancement for positive pictures but are generally lower for affective than for neutral pictures for both measures, hit rate and A', and at all three study-test intervals. Compared across all study-test intervals, Wang (2014) showed recognition accuracy for positive pictures to be significantly lower than for negative and neutral

pictures did not differ significantly. A probable explanation for this lack of evidence for affective enhancement of recognition memory is the ceiling effect likely to be caused by the very high hit rates (all ≥ 0.85) and very low false alarm rates (all ≤ 0.90) reported throughout. The fact that recognition accuracy does not significantly decline over time for positive pictures, while it does for both neutral and negative pictures lends some support to the idea of "sparing" of affective memory over time, for negative valence at least.

This "sparing" can more clearly be seen in the difference data presented above, where differences from the neutral condition in Pr increase over time for both negative and positive pictures. Pr is spared over time for affective pictures when compared to neutral pictures. The difference from neutral is larger for negative than for positive pictures but increases in parallel over time.

The lack of affective memory enhancement at five minutes after encoding in the present data, along with the development of affective memory enhancement over time, is strong evidence that while encoding effects may exist, they cannot sufficiently explain memory advantages for affective material. Instead, the time dependence of affective memory effects is evidence for mechanisms that work on memory consolidation or retention.

Two types of accounts have been proposed to explain how affective content influences memory consolidation: modulatory emotional consolidation accounts (McGaugh, 2004; Sharot, Verfaellie, & Yonelinas, 2007) and, most recently, an emotional binding account (Yonelinas & Ritchey, 2015). Both types

of model place crucial importance on the role of the amygdala in affective memory but they differ in the mechanisms being proposed. As the name suggests, modulatory emotional consolidation accounts see the amygdala's significance in affective memory consolidation in a modulatory function only. Arousing stimuli lead to amygdala activation, more specifically activation of the basolateral complex of the amygdala (BLA). The BLA, through its many projections to other brain areas, modulates the consolidation of different types of memories in these other regions (McGaugh, 2004). Although their consolidation is modulated by the amygdala, episodic memories are stored in the MLT and the amygdala plays no ongoing role in the binding of a memory to its affective content. The fact that memory advantages for affective stimuli develop over time is accounted for by the idea that amygdala modulation of the memory trace happens after initial encoding and takes some time to be completed. In contrast, Yonelinas and Ritchey's (2015) emotional binding account proposes that the amygdala's role in affective memory consists of binding the memory and its affective content and storing the resulting item-emotion binding, while non-affective item-context bindings are stored in the hippocampus. The amygdala's role in affective memory is therefore ongoing. The development of a memory advantage for affective stimuli over time is explained by the higher rate of neurogenesis and cell death in the hippocampus, relative to the amygdala. Yonelinas and Ritchey (2015) argue that the higher rate of neurogenesis can lead to interference, while increased cell death will speed forgetting. Together, these processes would lead to

memories stored in the hippocampus being more vulnerable to forgetting than memories stored in the amygdala, with its relatively lower rates of cell turnover.

Yonelinas and Ritchey (2015) cite findings that affective content improves recollection but not familiarity of an item (Anderson, Yamaguchi, Grabski, & Lacka, 2006; Atienza & Cantero, 2008; Dewhurst & Parry, 2000; Dolcos, LaBar, & Cabeza, 2005; McCullough & Yonelinas, 2013; Pierce & Kensinger, 2011; Ritchey, Dolcos, & Cabeza, 2008; Sharot et al., 2007; Sharot & Yonelinas, 2008; Yonelinas, Parks, Koen, & Jorgenson, 2011) as further support for recollectable item-emotion bindings being stored relatively more robust to decay in the amygdala, while familiarity for any item is supported by the perirhinal cortex and therefore does not show effects of affect.

The emotion-binding account of affective memory would predict a steady decline in memory performance over time for all types of stimuli which is steeper for neutral compared to affective items. Modulatory accounts on the other hand would predict an increase in the rate of decline of memory performance for affective pictures after consolidation is completed. Benefits of affective content that act on consolidation would initially offset some or all of the performance decline for affective items, leading to a slower decrease compared to neutral items or even an increase in memory performance while consolidation takes place. After completed consolidation, memory performance for both affective and non-affective stimuli should decline in parallel, at the same rate. The experiment presented here did not include a sufficient number

of study-test intervals to decide between these two alternatives but future research including a greater number of trials and recognition test delays could provide valuable further insight.

6.2 Affective memory and its electrophysiological correlates

6.2.1 Introduction

As Chapter 2 discusses in more detail, affective enhancement of memory is well documented in the literature (see LaBar & Cabeza, 2006 for review). Several studies have also investigated its electrophysiological correlates using word, face and general picture stimuli. An early study by Maratos, Allan and Rugg (2000) reports much higher false alarm rates in response to negative compared to neutral words and correspondingly, a lower average discrimination index Pr for negative than neutral words. There was no affective modulation of an early frontal old/new effect between 300 and 500 milliseconds, thought to index familiarity. A left-parietal old/new effect between 500 and 800 milliseconds was less pronounced for negative than for neutral words. A later right-frontal old/new effect between 800 and 1000 milliseconds, while present for neutral words, could not be shown for negative words at all. The difference in left-parietal old/new effects was caused by higher amplitudes in response to negative new items than in response to neutral new items. The authors interpreted this as evidence for retrieval of false episodic memories for negative words, which had to be assessed before negative words could be classified as

"new", thus also explaining the longer reaction times reported for negative compared to neutral correct rejections. Reaction times for hits on the other hand were faster for negative than for neutral words, along with a more liberal response bias Br for negative than for neutral words.

Windmann and Kutas' (2001) findings are in contrast with Maratos et al.'s (2000) results in that no affective modulation of old/new effects could be shown when comparing ERPs for hits and correct rejections. Instead, Windmann and Kutas (2001) report an affective modulation of the difference between waveforms in response to hits and false alarms, with neutral words showing an old/new effect in frontal sites between 300 and 500 milliseconds post stimulus onset which is absent from the negative word condition. The absence of this early frontal effect was again attributable to more positive-going waveforms for negative compared to neutral new items. This electrophysiological finding responds to the behavioural finding of a more liberal response bias for negative than for neutral words, providing further support for the affective modulation of response bias.

In contrast to the two studies discussed above, Inaba, Nomura, & Ohira (2005) did find evidence of an affective modulation of both an early frontal old/new effect between 150 and 300 milliseconds and a left-parietal old/new effect between 400 and 700 milliseconds. Contrary to previous findings, discriminability (measured by d') was significantly different between all three affective categories (negative, neutral and positive), being highest for negative words and lowest for neutral words. The size of the left-parietal old/new effect

mapped onto this pattern, with negative words eliciting significantly larger old/new differences than both other word categories and positive words eliciting significantly larger old/new differences than neutral words. The early frontal old/new effect was increased for both positive and negative words but did not differ between these categories, suggesting an all-or-nothing effect of affective content on the electrophysiological correlate of familiarity.

As they only compared negative and neutral stimuli, one question the studies of Maratos et al. (2000) and Windmann and Kutas (2001) cannot answer, is whether the reported affective modulations arise as a result of differences in the affective arousal elicited by the two stimulus categories or whether they are specific to stimuli of negative valence. While Inaba et al. (2005) do compare both negative and positive affective stimuli to neutral baseline stimuli, unfortunately no arousal values are reported and therefore, again, the relative effects of arousal and valence cannot be discerned. To investigate the individual influence of these two affective dimensions on affective processing, Gianotti et al. (2008) created two stimulus sets, one of words and another of pictures taken from the IAPS (Lang, Bradley, & Cuthbert, 2008), with four groups of stimuli each: high arousing negative, high arousing positive, low arousing negative and low arousing positive. Consequently, data from a passive viewing task could be split by either valence or arousal for analysis, while controlling the second dimension. ERP microstate analysis revealed evidence for effects of valence from 118 milliseconds post stimulus onset for words and from 142 milliseconds post stimulus onset for pictures. Effects of arousal emerged later,

at 260 milliseconds and 302 milliseconds respectively for words and pictures. This finding supports the hypothesis that the processing of valence and arousal information is implemented separately on a neural level and further suggests that valence information is available for integration with other functions, such as recognition memory, before arousal information is available. However, electrophysiological correlates of the effects of both dimensions can be demonstrated by the typical onset of the early frontal old/new effect around 300 milliseconds, for both words and pictures.

Besides words, most research into the effects of affective content on recognition memory has used picture stimuli. Studies using face stimuli differing in emotional expression have been reported and while Johansson, Mecklinger and Treese (2004) found no affective modulation of the electrophysiological correlates of memory, Graham and Cabeza (2001) reported differences in the lateralisation of a late frontal old/new effect between happy and neutral faces. But due to the specialised nature of faces as stimuli in recognition memory research (see MacKenzie & Donaldson, 2009) and the use of IAPS stimuli in the research presented in Chapters 5 through 8, discussion of affective modulations of face memory and its electrophysiological correlates is beyond the scope of the present thesis.

Van Strien, Strekalova and Gootjes (2009) compared the effects of affective content of negative, neutral and positive IAPS pictures on the electrophysiological correlates of recognition memory in a continuous memory task in female participants. Stimuli were presented a total of two times in the

same continuous random presentation block and participants indicated after each stimulus whether it was presented for the first or second time. Van Strien et al. (2009) showed an early fronto-central old/new effect from 200 to 400 milliseconds post stimulus onset and a right-centroparietal old/new effect from 400 to 600 milliseconds. They argue that the right lateralisation of the centroparietal effect may be a consequence of using picture stimuli rather than the word stimuli normally associated with left-parietal old/new effects. A late (750-1000ms) frontal old/new effect was also shown. Picture valence modulated only the early fronto-central effect which was more frontally distributed for negative than for positive pictures. Picture arousal modulated only the late frontal old/new effect, with mean amplitudes being higher for old than for new low arousing pictures but this pattern being reversed for high arousing pictures. The author's conclusions that valence modulates fast recognition processes while arousal modulates slower processes of sustained encoding of new pictures is consistent with Gianotti et al.'s (2008) finding that valence information is accessible earlier than arousal information.

Van Strien (2008), using the same continuous memory paradigm, showed that affective content modulated the parietal and late frontal old/new effects only in younger participants, while older participants showed an affective modulation of the early frontal old/new effect. This suggests an affective enhancement of recollection and post-retrieval processes in younger adults that gives way to affective enhancement of familiarity with age.

The nature of the continuous memory task, in which each stimulus has to be simultaneously classified as "old" or "new" and encoded for potential future recognition, makes it impossible to fully dissociate memory effects from further encoding attempts. Using a study-test paradigm more commonly employed in studies of recognition memory, however, Weymar, Löw, Melzig and Hamm (2009) showed a pattern of affective modulation consistent with that found by Van Strien (2008). Participants completed a passive viewing task on negative, neutral and positive pictures and after an interval of one week returned to make old/new decisions for each picture followed by confidence ratings for "old" responses. Hit rates were highest for negative, followed by positive and then neutral pictures. Response bias was also highest for negative, followed by positive and then neutral pictures but despite this, Pr followed the same pattern. They found that a frontal and parietal old/new effect were unaffected by affective content between 300 and 500 milliseconds post stimulus onset. They also report a widespread centro-parietal old/new effect between 500 and 800 milliseconds which varied with response confidence, suggesting that it is a marker of recollection driven memory retrieval. This centro-parietal effect was larger for both negative and positive pictures than it was for neutral pictures, suggesting greater engagement of recollection by the affective pictures.

In sum, the existent literature on the affective modulation of recognition memory is far from cohesive. For word stimuli, one study found no affective modulation of the ERP difference between Hits and Correct Rejections (Windmann & Kutas, 2001), a second found a decrease in left-parietal and late

right-frontal old/new effects for negative stimuli (Maratos et al., 2000) and a third found an increase in the early mid-frontal old/new effect for affective words generally, while the left-parietal old/new effect increase was more pronounced for negative than for positive words. For pictures, two experiments using a continuous memory task consistently found a positive affective modulation of the left-parietal old/new effect (Van Strien, 2008) but evidence for similar modulations of the early frontal and late right-frontal old/new effects was only found by one of the studies but not the other respectively. A recognition memory study using a one week study-test interval reported an increased left-parietal old/new effect for affective over neutral stimuli, while an earlier fronto-parietal old/new effect was unchanged by affective content. It is unclear whether the reported effects are driven by arousal or valence associated with affective stimuli but the evidence points to the conclusion that the answer to this question will be complicated and depend on the specific correlate of recognition memory in question.

There has also been relatively little interest in the question of whether the memory effects seen for affective stimuli are qualitatively different from those for neutral stimuli. This has important theoretical implications. Chapter 6 above introduced two competing explanations for the slow-developing nature of the behavioural affective memory effect. Modulatory emotional consolidation accounts (McGaugh, 2004; Sharot et al., 2007) posit that while the amygdala is involved in the preferential consolidation of affective over neutral stimuli, both types of stimuli are stored in the same location in the medial temporal lobe. By

contrast, Yonelina and Ritchey's (2015) emotional binding account proposes that, for affective stimuli, emotion-stimulus bindings are stored in the amygdala. Thus, modulatory emotional consolidation predicts quantitative but not qualitative ERP effect differences at the point of retrieval, while emotional binding predicts a qualitative topographical difference also.

As later chapters will investigate the effects of gender and genotype on the affective modulation of recognition memory and its electrophysiological correlates, this chapter seeks to establish the initial affective modulation. Additionally, it will be investigated whether any differences in the electrophysiological correlates of recognition memory of affective and non-affective pictures present quantitative variations only, suggesting the differential activation of the same underlying neural systems, or whether these differences are of qualitative nature, pointing to the involvement of different neural generators.

6.2.2 Methods

56 participants (mean age 20.0 years, 28 female) completed an affective processing task (described in detail in Chapter 4.3.1) and followed by an affective recognition memory test (see Chapter 4.3.2) after one week delay. During the memory test, participants made old/new decisions for 288 IAPS pictures (Lang et al., 2008): 96 low arousing neutral, 96 high arousing negative and 96 moderately arousing positive pictures. Chapter 5.1 discussed the

difference in arousal levels associated with the two affective categories. Half of the pictures in each category were old, i.e. had been presented at study one week prior. Where participants gave an "old" response, they were required to make a remember/know judgement.

For behavioural data, discrimination index Pr and response bias Br were calculated (see Chapter 4.5 for details) and analysed using ANOVA with the factor affective content (negative, neutral, positive) along with remember rate. Paired comparisons were used to follow up any significant interactions.

ERP averages were formed separately for hits and correct rejections in each of the three affective categories (negative, neutral, positive). The following mean number of trials contributed to ERP averages: an average of 27.2 and 32.6 trials to negative hit and correct rejection averages respectively, an average of 23.9 and 33.8 trials to neutral hit and correct rejection averages respectively and an average of 23.7 and 32.0 to positive hit and correct rejection averages respectively.

To establish whether the expected memory effects were present, data from neutral trials was analysed first, then memory effects for positive and negative pictures were investigated separately. Data in each affective content categories was subjected to ANOVA with within-subject factors of retrieval success (hits, correct rejections), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right) and site (superior [1,2], medial [3,4], inferior [5,6]), separately for three time windows. The time windows were set as 300 to

500ms to assess the presence of an early mid-frontal old/new effect, 500 to 800ms to assess the presence of a left-parietal old/new effect and 800 to 1500ms to assess the presence of a late right-frontal old/new effect (see Chapter 3 for a discussion of these effects).

To assess differences between the memory effects in affective and neutral conditions, difference scores were created by subtracting mean amplitudes in response to correctly identified new pictures (correct rejections) from amplitudes in response to correctly identified old pictures (hits) at every electrode site. Amplitudes greater than zero in the difference wave indicate a positive going memory effect, amplitudes below zero show a negative going memory effect. Difference scores for negative and positive pictures were compared to those for neutral pictures to assess the effect of affective picture content on memory effects. Negative and positive memory effects were also compared. To this end, difference scores were subjected to separate ANOVAs with the factors affective content (negative, positive, neutral), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right) and site (superior [1,2], medial [3,4], inferior [5,6]) in all time windows. The electrode sites included in this analysis are indicated in Figure 6.8 below. Where significant interactions between affective content and any of the topographical factors were found, the analysis was repeated on rescaled data to assess whether these interactions reflect qualitative or merely quantitative differences in old/new effect topographies.

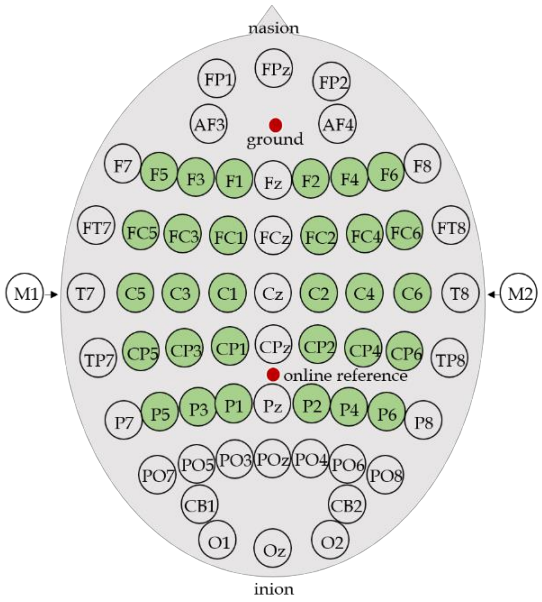


Figure 6.8 *Electrode sites included in the topographical analysis of affective memory effects.*

6.2.3 Behavioural results

6.2.3.1 Affective modulation of discrimination index Pr and response bias Br

	Picture Valence		
	Negative	Neutral	Positive
Hit rate	0.723 (0.019)	0.640 (0.019)	0.622 (0.020)
FA rate	0.098 (0.011)	0.074 (0.009)	0.119 (0.014)
Pr	0.623 (0.018)	0.565 (0.016)	0.501 (0.016)
Br	0.278 (0.027)	0.188 (0.022)	0.251 (0.026)
Remember rate	0.581 (0.025)	0.477 (0.027)	0.492 (0.026)

Table 6.2 *Means and standard errors (in brackets) for hit rate, false alarm (FA) rate, discrimination index Pr, response bias Br and remember rate by picture valence.*

As Figure 6.9 illustrates, discrimination index Pr was largest for negative items, followed by neutral items and then positive items (see also Table 6.2). ANOVA with the factor affective content (negative, neutral, positive) showed a significant main effect of the same on Pr [$F(1.68, 106.4)=39.3$, $p<.001$].

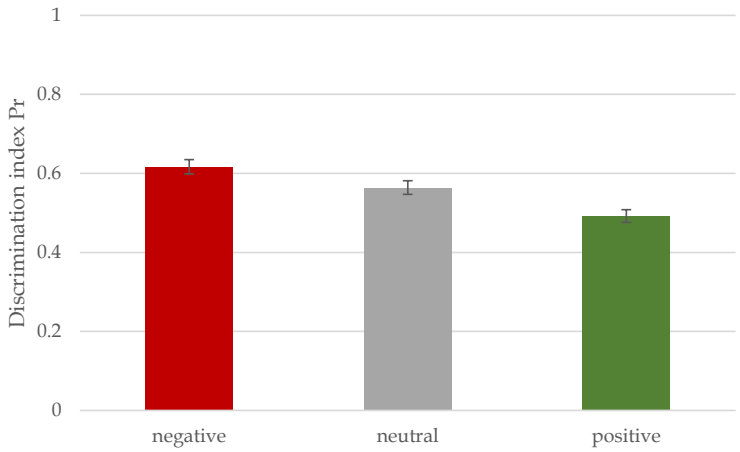


Figure 6.9 *Discrimination index Pr was significantly higher for negative than for both neutral and positive pictures and significantly lower for positive than for both negative and neutral pictures. Error bars show standard errors.*

Planned comparisons of Pr in the three affective content conditions showed that negative Pr was significantly higher than both neutral [$t(55)=3.91$, $p<.001$] and positive Pr [$t(55)=7.84$, $p<.001$] and positive Pr was also significantly lower than neutral Pr [$t(55)=-6.17$, $p<.001$].

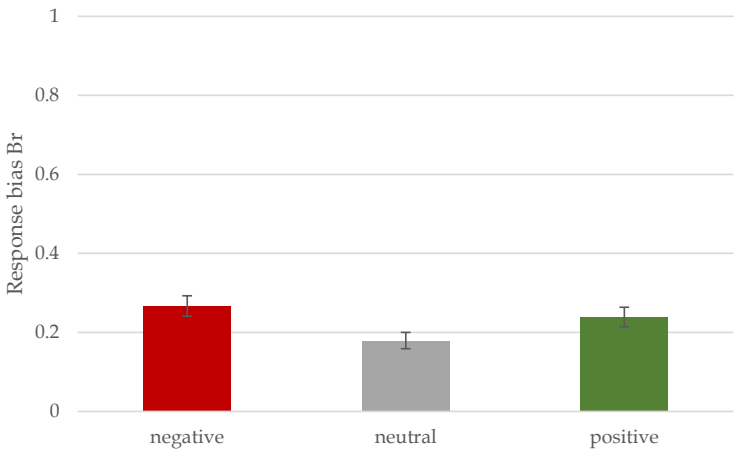


Figure 6.10 *Response bias Br was higher (more liberal) for affective than for neutral pictures. Br for both negative and positive pictures differed significantly from Br for neutral pictures but not from each other. Error bars show standard errors.*

Figure 6.10 shows response bias Br in the three affective content conditions. Here, both sets of highly arousing pictures, negative and positive, were associated with higher Br values than neutral pictures, indicating a more liberal response bias (see also Table 6.2). One-factor ANOVA confirmed a main effect of affective picture content on Br [$F(2, 110)=11.1$, $p<.001$] and planned comparisons showed significant Br differences between negative and neutral [$t(55)=4.08$, $p<.001$] and between positive and neutral [$t(55)=3.27$, $p<.001$] but not between negative and neutral items [$t(55)=1.52$, $p=.135$].

6.2.3.2 Affective modulation of remember rates

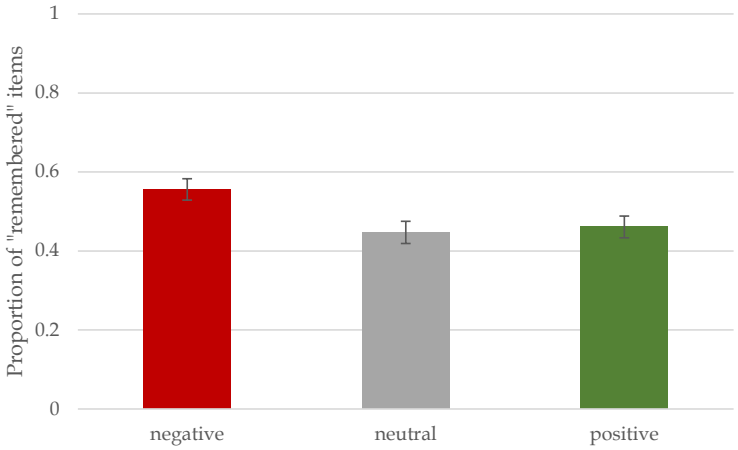


Figure 6.11 *The proportion of correctly identified old negative items rated as "remembered" was significantly higher than the proportions of "remembered" items in correctly identified neutral or positive items. Error bars show standard errors.*

Figure 6.11 shows the proportions of correctly identified old items that were labelled as "remembered". As the graph shows, the rate of "remembered" items was highest in the negative condition and slightly higher in the positive than in the neutral condition (see Table 6.2 for means and standard errors). One-factor ANOVA confirmed a main effect of affective picture content on the remember rate [$F(2, 110)=15.38$, $p<.001$]. Planned comparisons showed that this was driven by a significantly higher proportion of "remember" responses in the negative condition than in the positive [$t(55)5.08$, $p<.001$] and in the neutral condition [$t(55)=4.70$, $p<.001$], while the neutral and positive conditions did not significantly differ [$t(55)=0.75$, $p=.455$].

6.2.4 Electrophysiological results

Figures 6.12 to 6.16 below show comparisons of mean amplitudes in response to all hits compared to correct rejections in the three affective picture categories across three time windows of interest: The 300-500ms time window typically associated with an early frontal positivity, the 500-800ms time window usually reported for the left-parietal old/new effect and the 800-1500ms time window often employed to characterise the late right frontal effect. To make distributions of activity comparable between time windows and affective categories, Figure 6.12 shows scalp maps of mean amplitudes for hits minus those for correct rejections. Average waveforms for hits in contrast with correct rejections are shown below, separately for neutral (Figure 6.13), positive (Figure 6.14) and negative pictures (Figure 6.15).

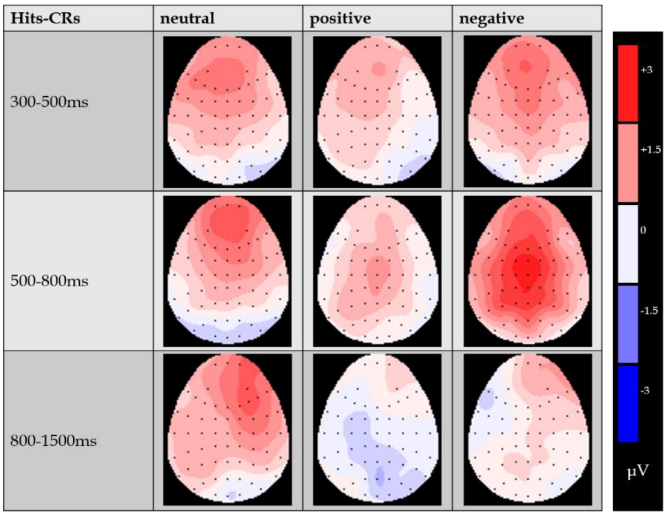


Figure 6.12 *Scalp distributions showing mean amplitudes for hits minus mean amplitudes for correct rejections in the 300-500ms (early mid-frontal old/new effect), 500-800ms (left-parietal old/new effect) and 800-1500ms (late right-frontal old/new effect) time windows.*

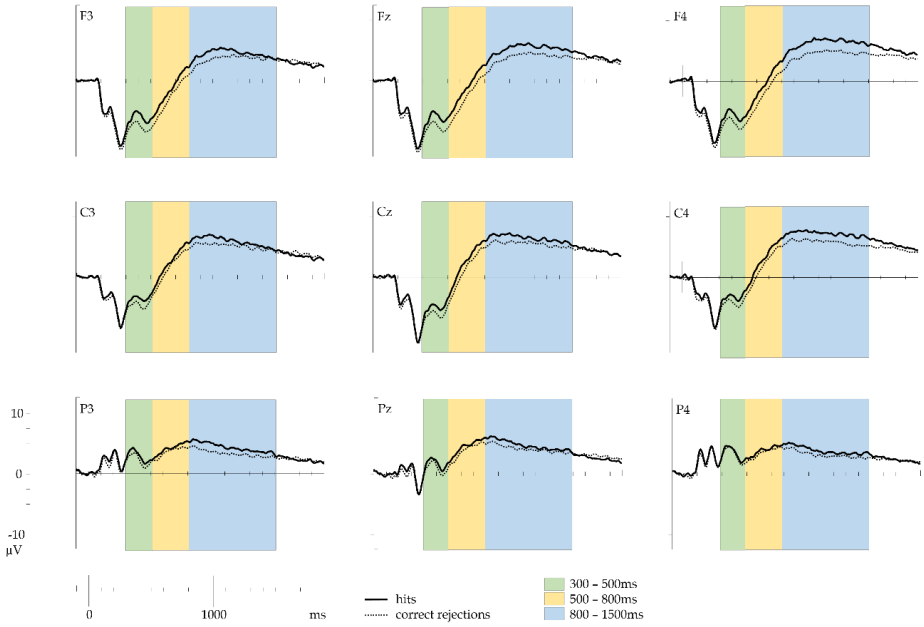


Figure 6.13 *Average waveforms for hits versus correct rejections for neutral pictures.*

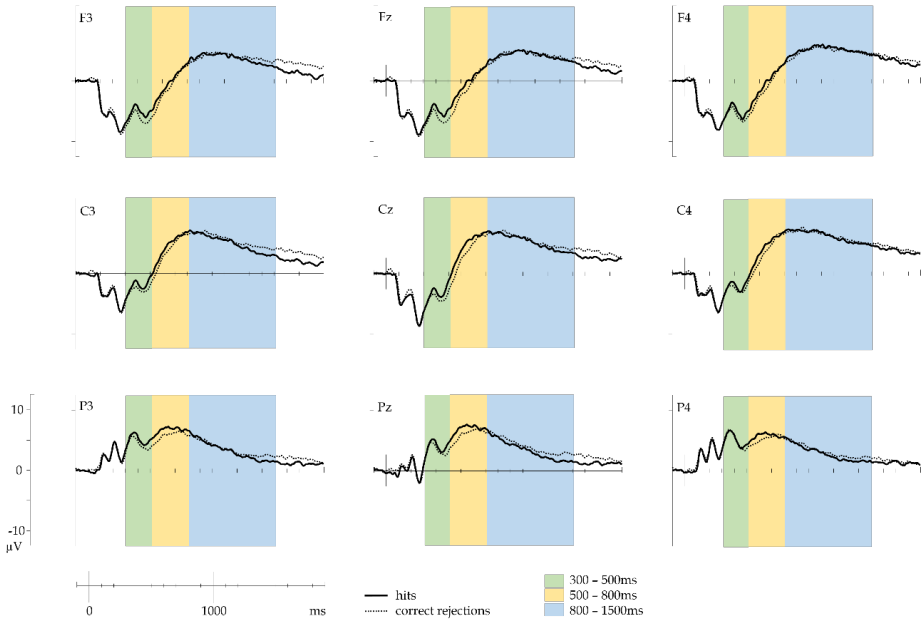


Figure 6.14 *Average waveforms for hits versus correct rejections for positive pictures.*

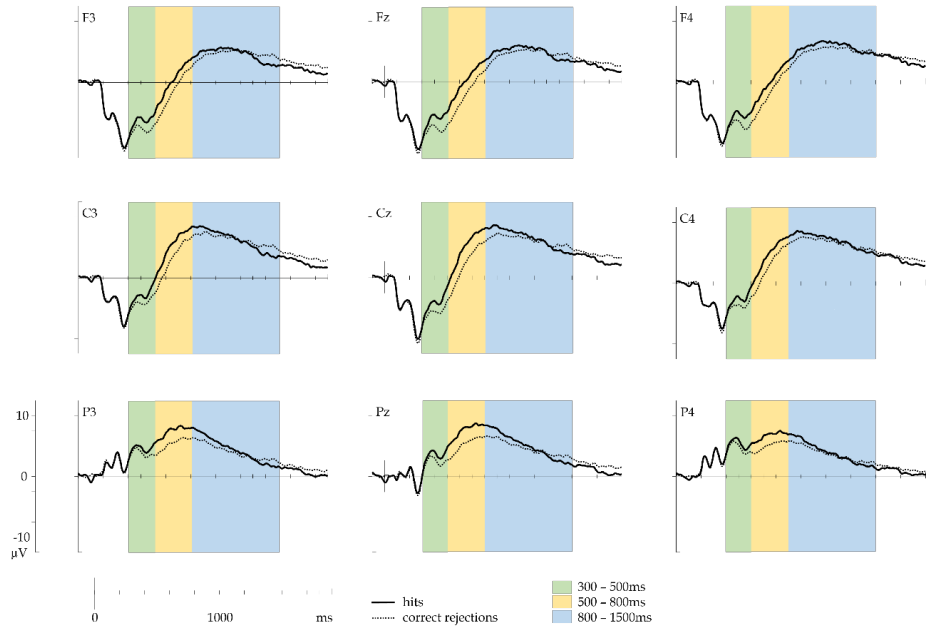


Figure 6.15 *Average waveforms for hits versus correct rejections for negative pictures.*

6.2.4.1 Affective modulation of the old/new effect between 300 and 500ms

6.2.4.1.1 Neutral pictures

Visual inspection of the data from neutral trials showed a mid-frontal old/new effect in the classic 300 to 500ms time window. ANOVA with within-subject factors of retrieval success (hits, correct rejections), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right) and site (superior [1,2], medial [3,4], inferior [5,6]) confirmed a retrieval success by site interaction [$F(1.09, 59.7)=4.21$, $p=.041$], reflecting the fact that the effect was larger over superior sites, and a retrieval success by location interaction

[F(1.15,63.4)=4.96, p=.025], reflecting the frontal distribution of the effect. There were no significant interactions with hemisphere. The frontal and superior distribution of the effect is consistent with that commonly reported for the early mid-frontal positivity and the effect was significant at the representative electrode Fz [t(55)=3.75, p<.001].

6.2.4.1.2 Positive pictures

Data from positive picture trials was analysed in the same way. As Figure 6.14 shows, average waveforms in response to hits were somewhat more positive going than those in response to correct rejections in the 300 to 500ms time window in left and midline fronto-central locations. An ANOVA with within-subject factors of retrieval success (hits, correct rejections), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right) and site (superior [1,2], medial [3,4], inferior [5,6]) showed only a retrieval success by hemisphere by site interaction [F(1.13, 62.20=3.92, p=.047], caused by a superior distribution in the right hemisphere only. Although on visual inspection the memory effect looks frontal, no interaction that includes retrieval success and location reached significance. The memory effect for positive pictures was significant at electrode Fz [t(55)=2.03, p=.048].

6.2.4.1.3 Negative Pictures

Negative hits elicited more positive going waveforms than negative correct rejections in the 300 to 500ms time window across frontal to parietal electrodes (see Figure 6.15) and the difference appeared stronger at more frontal and more superior electrode sites (see Figure 6.12). Memory effects for negative pictures were assessed in the same way as above, revealing a significant interaction of retrieval success with site only [$F(1.12, 61.60=9.64$, $p=.002$). This reflects a superior distribution. Despite a frontal appearance of the effect, such a distribution could not be confirmed statistically. The memory effect for negative pictures was significant at electrode Fz [$t(55)=3.70$, $p<.001$].

6.2.4.1.4 Positive vs neutral comparison

Difference scores (hits – correct rejections) for positive and neutral pictures were calculated. ANOVA with the factors affective content (positive, neutral), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right) and site (superior [1,2], medial [3,4], inferior [5,6]) of these difference scores showed no significant main effect of affective content and no significant interactions of affective content with location, hemisphere or site or any combination of these, meaning the differences between memory effects in the neutral and positive conditions observed above failed to reach statistical significance. The size of the early frontal old/new effect did not differ significantly between positive and neutral pictures.

6.2.4.1.5 Negative vs neutral comparison

Difference scores for negative pictures were also compared to those for neutral pictures using the same ANOVA structure. There was a significant interaction between affective content, location, hemisphere and site [$F(4.11,226)=2.42$, $p=.047$] reflecting a positive going difference in memory effects mainly over right-hemisphere electrodes that increases from frontal to parietal locations and is maximal at right-inferior frontal and midline and right-superior parietal electrode locations. This interaction was also significant in the rescaled data [$F(4.27,2350)=2.61$, $p=.033$], adding evidence that it reflects a qualitative difference between topographies for negative compared to neutral old/new effects in the 300 to 500 millisecond time window. Old/new effect sizes did not significantly differ between negative and neutral pictures at electrode Fz in the 300 to 500 millisecond time window.

6.2.4.1.6 Negative vs positive comparison

A final ANOVA comparing the difference scores from negative and positive trials failed to produce a significant main effect of affective content or any interaction of affective content with any other factor. As well as showing no topographical difference, the size of the early frontal old/new effect did also not differ significantly between negative and positive pictures.

6.2.4.2 Affective modulation of the old/new effect between 500 and 800ms

6.2.4.2.1 Neutral pictures

In the 500 to 800ms time window, hits elicited more positive going waveforms than correct rejections for neutral pictures at midline sites and the effect appeared stronger in frontal than in parietal locations as well as at superior than at inferior sites (see Figures 6.16 and 6.17). ANOVA with within-subject factors of retrieval success (hits, correct rejections), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right) and site (superior [1,2], medial [3,4], inferior [5,6]) of the data from neutral trials in the 500 to 800ms interval failed to show a significant interaction of retrieval success with hemisphere and could therefore not confirm a left-parietal contribution of the memory effect found. Instead, there was a retrieval success by site interaction [$F(1.06,58.4)=7.55$, $p=.007$], reflecting a larger effect over superior sites. Retrieval success also interacted with location [$F(1.23,67.6)=5.98$, $p=.012$], with the effect being largest in frontal locations. Mean amplitude associated with hits did not differ significantly from mean amplitude associated with correct rejections at electrode P3, the site commonly reported to demonstrate a left-parietal old/new effect, in this time window. At electrode Fz, where the effect was maximal, mean amplitude for hits was significantly larger than mean amplitude for correct rejections [$t(55)=3.94$, $p<.001$].

6.2.4.2.2 Positive pictures

Hits in response to positive pictures elicited more positive going waveforms than correct rejections in central midline as well as medial to midline parietal electrode sites (see Figure 6.14). As Figure 6.12 shows, the effect appeared strongest at the central electrode Cz and showed a slight left-sided skew in parietal locations. Data from positive trials in the 500 to 800ms time window was subjected to the same analysis as above and only the interaction of retrieval success with site reached significance [$F(1.06, 58.2)=8.84$, $p=.004$]. Despite a left-parietal appearance of the effect on the scalp map (Figure 6.12), hemisphere and location failed to significantly interact with retrieval success. The old/new effect was maximal centrally, at electrode Cz, where it reached significance [$t(55)=3.00$, $p=.004$]. In contrast with neutral trials however, the memory effect was also significant at electrode P3, the commonly cited maximum of the left-parietal old/new effect [$t(55)=2.95$, $p=.005$].

6.2.4.2.3 Negative pictures

For negative pictures, waveforms in response to hits were markedly more positive going than those in response to correct rejections across the scalp, with the effect appearing strongest at central midline electrodes but present from frontal to parietal and from left inferior to right inferior electrode sites. The analysis above was repeated for mean amplitudes between 500 and 800ms in negative trials. Again, retrieval success interacted significantly only with site

[F(1.06, 58.2)=34.5, p<.001], reflecting the stronger memory effect at superior sites. A left-parietal distribution could not be demonstrated and the old/new effect was again maximal centrally, at electrode Cz, as for positive pictures, where it was significant [t(55)=5.85, p<.001]. The effect was still significant at electrode P3 [t(55)=5.61, p<.001).

6.2.4.2.4 Positive vs neutral comparison

When subjected to ANOVA with the factors affective content (positive, neutral), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right) and site (superior [1,2], medial [3,4], inferior [5,6]), difference scores showed no significant main effect of or interaction with affective content in the 500 to 800ms time window. Taking into account the effect's midline maxima in all three affective conditions, old/new effect sizes were quantified as the average of the old/new difference at three midline electrodes: Fz, FCz and Cz. The size of the old/new effect at this midline cluster did not differ significantly between positive and neutral pictures.

6.2.4.2.5 Negative vs neutral comparison

ANOVA comparing difference scores from negative to those from neutral trials and including the same topographical factors as above revealed a significant affective content by site interaction [F(1.10, 60.2)=5.62, p=.018]. This reflects

larger differences between memory effects at superior sites, with memory effects being larger in response to negative pictures. However, the interaction did not survive rescaling and therefore reflects a quantitative rather than qualitative difference in topographies. Negative pictures evoked significantly larger old/new effects than neutral pictures at electrode P3 [t(55)=2.99, p=.004]. The size of the old/new effect at the midline cluster (Fz, FCz, Cz) was significantly increased for negative compared to neutral pictures [t(55)=2.33, p=.024].

6.2.4.2.6 Negative vs positive comparison

When comparing memory effects in the negative and positive picture conditions using the same ANOVA design, the affective content by site interaction failed to reach significance [F(1.06, 58.4)=2.77, p=.099] but there was a significant main effect of affective content [F(1.00,55.0)=6.78, p=.012] pointing to larger memory effects in response to negative than to positive pictures across all electrode sites. Comparison of old/new effect sizes in the unscaled data at electrode P3 confirmed that negative pictures evoked significantly larger old/new effects than positive pictures in the 500 to 800 millisecond time window [t(55)=2.99, p=.004]. The old/new effect at the midline cluster (Fz, FCz, Cz) was also significantly more pronounced for negative than for positive pictures [t(55)=2.44, p=.018].

6.2.4.3 Affective modulation of the old/new effect between 800 and 1500ms

6.2.4.3.1 Neutral pictures

Neutral pictures elicited more positive going waveforms in the 800 to 1500ms time window across much of the scalp, as Figures 6.16 and 6.17 show. The effect appeared stronger in the right hemisphere in frontal and central locations, while a slight left-sided skew was observed in parietal electrodes. For mean amplitudes between 800 and 1500ms, ANOVA with within-subject factors of retrieval success (hits, correct rejections), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right) and site (superior [1,2], medial [3,4], inferior [5,6]) produced a significant retrieval success by location by hemisphere by site interaction [$F(3.50,192.3)=3.79$, $p=.008$]. This reflects a memory effect that is maximal at frontal medial sites in the right hemisphere and weaker and more evenly spread across locations and sites in the left hemisphere. The effect is maximal at electrode F4 where mean amplitudes associated with hits differed significantly from those associated with correct rejections [$t(55)=5.33$, $p<.001$].

6.2.4.3.2 Positive pictures

Visual inspection reveals only a very weak memory effect for positive pictures in the 800-1500ms time window, with mean amplitudes for correct rejections being larger than those for hits in posterior locations in the right hemisphere

and central locations in the left hemisphere. Despite a more superior appearance of this effect, ANOVA showed only a significant retrieval success by location by hemisphere interaction [$F(1.67, 91.8)=6.21$, $p=.005$]. Hits showed the largest positive going difference from correct rejections at electrode F4, which is considered representative for the right-frontal old/new effect, but the effect was far from significant [$t(55)=0.53$, $p=.601$].

6.2.4.3.3 Negative pictures

Visual inspection of the scalp topography for negative hits compared to negative correct rejection (Figure 6.12) suggests a distribution broadly equivalent to that seen in response to neutral pictures. And indeed, ANOVA with within-subject factors of retrieval success (hits, correct rejections), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right) and site (superior [1,2], medial [3,4], inferior [5,6]) returned a significant retrieval success by location by hemisphere by site interaction [$F(3.59, 197.4)=4.78$, $p=.002$]. The positive-going memory effect is seen largely in the right hemisphere, where it shows a more superior distribution in parietal locations and a more inferior distribution in frontal locations. Although the effect is maximal at electrode F4, it narrowly fails to reach significance [$t(55)=1.74$, $p=.087$].

To establish whether the absence of evidence for a late right-frontal effect for negative pictures was driven by the significantly higher proportion of

remember responses than in the neutral condition, separate mean amplitude differences from correct rejections were calculated for remembered and known pictures at electrode F4 in the 800 to 1500 millisecond time window. ANOVA with the factors of affective content (negative, neutral) and remember/know response returned no significant interaction with or main effect of remember/know response. Therefore old/new effect size did not vary significantly between old decisions based on recollection and those based on familiarity. A significant main effect of affective content [$F(1,55)=4.64$, $p=.036$] reflected the larger old/new effect sizes for neutral pictures as expected.

6.2.4.3.4 Positive vs neutral comparison

The absence in the positive data of the right-frontal memory effect seen in the neutral data drove an effect of affective content in the difference waves (hits – correct rejections) that is maximal in frontal and fronto-central locations in the right hemisphere. ANOVA of the difference scores confirms this with a significant affective content by location by hemisphere interaction [$F(1.65, 90.8)=4.41$, $p=.021$]. In the analysis of the rescaled data, this interaction failed to reach significance, suggesting a quantitative difference in topographies only. As expected, the amplitude difference between hits and correct rejections at electrode F4 in the 800 to 1500 millisecond time window was significantly smaller for positive than for neutral pictures [$t(55)=3.23$, $p=.002$].

6.2.4.3.5 Negative vs neutral comparison

Memory effects for negative pictures were larger than those for neutral pictures at superior parietal electrodes but smaller at inferior frontal electrodes in the left hemisphere and inferior frontal and inferior central electrodes in the right hemisphere. When analysed using ANOVA however, none of the interactions with affective content reached significance and there was only a significant main effect of affective content to report [$F(1.00, 55.0)=6.35$, $p=.015$]. As expected, the amplitude difference between hits and correct rejections at electrode F4 in the 800 to 1500 millisecond time window was significantly smaller for negative than for neutral pictures [$t(55)=3.22$, $p=.002$].

6.2.4.3.6 Negative vs positive comparison

When comparing memory effects in response to negative and positive pictures using ANOVA with the factors affective content (negative, positive), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right) and site (superior [1,2], medial [3,4], inferior [5,6]), neither the main effect of affective content nor any interaction with affective content reached significance.

6.2.5 Discussion

Behaviourally, an affective modulation of all performance measures could be shown. Remember rates were significantly increased for negative compared to

neutral pictures only, while no difference between positive and neutral pictures was found, indicating that a larger degree of recollection of negative pictures helped old negative pictures be identified more frequently than positive or neutral old pictures. Discrimination index Pr was also highest for negative pictures, with differences from both other categories being significant. In contrast to expectation and most previous research, discrimination accuracy was lower for positive than for neutral pictures. This difference was driven by higher numbers of false alarms in response to positive than in response to neutral items, reflected in a significantly more liberal response bias. Response bias for negative pictures was also significantly more liberal compared to neutral pictures and did not differ significantly from positive pictures.

The overall picture emerging from these behavioural patterns is that participants were more likely to class affective pictures as "old", making misses less likely than in the neutral condition. This more liberal response bias, coupled with higher rates of recollection than for other picture categories leads to the improved memory performance for negative pictures. Positive pictures are also associated with a more liberal response bias compared to neutral pictures but did not benefit from higher involvement of recollection in the memory decision.

The analysis presented here focused on three electrophysiological correlates of recognition memory – the early frontal "familiarity" effect, the left-parietal "recollection" effect and the late right-frontal "post-processing" effect – and their affective modulation. Old/new effects in the 300 to 500 millisecond time

window were shown for all three picture types (neutral, negative and positive). For neutral pictures the effect showed a superior and frontal distribution but for both affective categories the effect, while still being larger at superior than inferior sites, was more widespread and despite the visual appearance of a frontal maximum, the location factor did not reach significance. For positive pictures, the absence of an old/new difference in right inferior electrodes also drove a significant hemisphere factor. When comparing the topographies of old/new effects across affective categories statistically, only the difference between negative and neutral pictures reached significance. The fact that the topographic difference remained significant when data was rescaled to remove effects of amplitude differences across conditions points to a qualitative difference in topographies of the old/new effects likely to reflect differences in the underlying neural generators. At electrode Fz, which was used to quantify the early frontal old/new effect, no combination of affective categories produced significant differences. Taken together, these results suggest an equal activation of early familiarity effects across all three affective categories, although additional processes that aid memory performance may be at play for negative items. The more posterior and widespread distribution of the old/new effect for negative pictures compared to neutral ones may indicate an early onset of the wide-spread effect seen in the 500 to 800 time window adding to the frontal "familiarity" effect. It is noteworthy that the distribution of old/new effects for positive pictures, apart from its left-sided skew, seems to fall somewhere between the frontal distribution seen in neutral pictures and the

wider distribution across all locations seen in negative pictures. This impression is supported by the fact that the distribution difference between both positive and neutral and positive and negative pictures failed to reach statistical significance.

The biggest, and only significant, difference in distributions of the old/new effects among the three affective categories is seen between negative and neutral pictures, while the distribution of positive pictures lies somewhere in between, not differing significantly from either other affective category. At this point, it is of interest to note that although negative and positive pictures were chosen by their IAPS standard ratings to be matched for arousal, this manipulation failed and participants actually reported significantly higher levels of arousal for negative than for positive pictures, with neutral pictures attracting significantly lower arousal levels than both other categories (see Chapter 5.1). The differences in distribution of the old/new effects by affective category in the 300 to 500 millisecond time window maps onto these arousal differences, with only the differences between the two categories furthest apart in arousal ratings, negative and neutral, reaching significance. The qualitative topographical difference between old/new effects for negative and neutral items in the 300 to 500 millisecond time window is novel evidence in support of Yonelinas and Ritchey's (2015) emotional binding account of affective recognition memory, which posits that emotion-item bindings are stored separately from neutral items. Modulatory emotional consolidation accounts cannot account for a difference in old/new effect distributions, as affective

memories are retrieved from the same brain regions as neutral memories and any effects of affective content on retrieval attempts would act on all affective items equally and thus not be reflected in old/new effects. In the 500 to 800 millisecond time window, the topographical difference in old/new effect distributions between negative and neutral pictures failed to survive rescaling, so there is no evidence of a qualitative difference here. However, it is important to note that the failure to reject the null hypothesis in this case does not constitute evidence of absence of a difference, especially in light of Haig, Gordon and Hook's (1997) and Ruchkin, Johnson and Friedman's (1999) observation that McCarthy and Wood's (1985) method of rescaling is prone to type II errors.

Between 500 and 800 milliseconds, old/new effects in recognition memory studies typically show a left-parietal distribution which is thought to index recollection processes. In the present data, no such left-parietal distribution could be shown for old/new effects in any of the affective categories. Instead, neutral pictures produced an old/new effect that was more pronounced at more frontal and more superior sites, which seems to be a continuation of the old/new effect found for these stimuli in the earlier 300 to 500 millisecond time window. For neutral pictures, the effect was not significant at electrode P3, the location typically used to quantify the left-parietal effect, so there was no evidence for a left-parietal “recollection” effect. Positive and negative pictures both produced old/new memory effects that were widespread and did not vary in strength from anterior to posterior locations but were largest along the

midline. The left-parietal appearance of the old/new effect for positive words was not associated with a significant hemisphere effect. However, in contrast to neutral pictures, both positive and negative pictures produced significant old/new differences at electrode P3. This allows for two possibilities: Either a traditional left-parietal effect is present for these two picture categories but is obscured by an additional, affect-specific old/new effect or the difference at P3 is produced solely by the widespread superior effects observed. To account for the midline maxima of the old/new effects in all affective categories, a midline cluster of electrodes Fz, FCz and Cz was chosen to quantify the old/new effects observed. The size of the old/new difference in this cluster was significantly increased for negative compared to both neutral and positive pictures. When comparing the old/new effects for positive and neutral pictures, no significant differences in distribution or size could be shown. Negative pictures also elicited a significantly higher proportion of "remember" judgements than either neutral or positive pictures, suggesting a larger degree of recollection for negative stimuli. This suggests the conclusion that despite a lack of evidence for a left-parietal distribution, the widespread midline old/new effect between 500 and 800 milliseconds post stimulus onset shown here is an electrophysiological marker of recollection for picture stimuli. This constitutes novel evidence for a distinct distribution of recollection effect in response to picture scene stimuli, at least in an affective context, analogous to the stimulus type specific distribution of the recollection effect for face stimuli shown by MacKenzie and Donaldson (2007) and MacKenzie and Donaldson (2009).

Since the completion of data collection for the present experiment, two studies have reported ERP old/new effects for affective and neutral picture stimuli, in similar time windows to the present study, with a one week study-test delay. Schaefer, Pottage and Rickart (2011) compared electrophysiological correlates of memory for negative and neutral pictures. They found a frontal old/new effect between 300 and 500 milliseconds, which was significant only for negative "remembered" pictures. A wide-spread old/new effect between 500 and 700 milliseconds after stimulus onset was also driven by a significant old/new difference for negative "remembered" items. The distributions of the 300 – 500 millisecond and 500 – 700 millisecond remember/new effects reported by Schaefer et al. (2011) are broadly consistent with the distributions of the old/new effects presented in this chapter, although their early old/new effect shows an anterior distribution which is absent from the present data.

Weymar, Löw and Hamm (2010) compared recognition memory for negative, positive and neutral pictures after one week and one year delay. In contrast to Schaefer et al. (2011), they report a parietal old/new effect for negative pictures in the early 300 - 500 millisecond time window. A parietal old/new effect between 500 and 800 milliseconds is also reported and its modulation by affective picture content appear consistent with the present data, although no topographical analysis is reported. Weymar et al. (2010) found largest old/new effects in this time window in response to negative items, followed by positive and then neutral items at one week delay. After one year, negative items still

elicited significantly larger old/new effects, but the difference between neutral and positive items was no longer significant.

The present study additionally showed an affective modulation in the late 800 to 1500 millisecond time window. The pattern of effects that emerges here differs from that common to the two earlier time windows. Neutral pictures showed a positive going right-frontal old/new effect, thought to reflect post-retrieval processing, which was significant at electrode F4. The old/new effect for negative pictures, while not differing qualitatively in topography from the effect for neutral pictures, failed to reach statistical significance at electrode F4, where it was maximal. The right-frontal positivity for hits compared to correct rejections was largely absent from the data for positive pictures and the old/new effect was instead characterised by negativity spreading from left-central to right-parietal and occipital sites. The topography of the old/new effect for positive pictures was not significantly different from that for negative pictures. The absence of the late right-frontal old/new effect from the affective picture conditions, contrasting with its presence in the neutral picture condition, contributes to the understanding of its functional significance. It supports Hayama, Johnson and Rugg's (2008) view that the right-frontal effect is not contingent on successful memory retrieval, as previously thought, but reflects more general monitoring or decisional processes.

Based on comparisons of ERP and fMRI studies of its eliciting conditions, the right-frontal old/new effect is thought to reflect activation of the right dorsolateral prefrontal cortex (Rugg, Otten, & Henson, 2002). Using event-

related fMRI, Henson, Rugg and Shallice (1999) showed that right lateral and medial prefrontal cortex activity is sensitive to the relative contributions of familiarity and recollection to old/new decisions. Activity in this area was increased for hits receiving "know" judgements, compared to both "remember" judgements and new items. The authors conclude that this increased activity reflects the evaluation of the retrieval decision relative to the present task, which means that it increases where the old/new decision is made with less certainty, such as in the case of old decisions based on familiarity only. In the present experiment, negative pictures, which failed to elicit a significant late right-frontal old/new effect, were also associated with a higher proportion of "remember" responses than neutral pictures, for which a significant late right-frontal old/new effect was shown. However, a comparison of the old/new effects for "remembered" and "known" items showed no significant differences. The larger involvement of recollection in recognition of negative pictures can therefore not account for the absence of evidence for a late right-frontal old/new effect. Additionally, the effect could also not be demonstrated for positive pictures, which attracted a comparable proportion of "remember" judgements to neutral pictures. In the absence of other differences between the three stimulus types, the modulation of the late right-frontal effect is likely driven by consequences of the difference in affective picture content.

The difference that emerges between both affective categories and neutral pictures in the behavioural data is in response bias. Participants show significantly more liberal response biases when making old/new decisions for

negative and positive compared to neutral pictures. Windmann and Kutas (2001) and Windmann (2002) have previously shown effects of response bias on the subjective old/new effect (comparing "old" with "new" responses irrespective of accuracy, rather than hits with correct rejections) in frontal regions at earlier latencies. Windmann and Kutas (2001) showed that a more liberal response bias for negative compared to neutral words mapped onto a larger prefrontal subjective old/new effect for negative words in two earlier time windows (300-500ms and 500-700ms). Windmann (2002) split their sample into a high bias and a low bias group and confirmed a larger subjective old/new effect in the high bias group at prefrontal sites between 300 and 500 milliseconds. They conclude that the frontal areas underlying these prefrontal subjective old/new effects are involved in lowering the response criterion, thus creating a more liberal response bias. With regards to affective stimuli, Windmann and Kutas (2001) suggest that the more liberal response bias for affective stimuli serves an adaptive function, ensuring that stimuli that are potentially significant for survival are not missed.

The present results replicate Maratos et al.'s (2000) finding that a post-retrieval right-frontal old/new effect between 1100 and 1400 milliseconds post stimulus onset is also modulated by affective content, being significant for neutral words but absent for negative words. The same pattern is presented here in pictures and shown to apply to both negative and positive valence equally. Maratos et al. (2000) interpret the late right-frontal old/new effect as a marker of monitoring of the relevance of retrieved information to the task being

completed. The present study adds the finding that the late right-frontal old/new effect also co-varies with response bias for pictures. That is, both old and new affective pictures are more likely to evoke "old" responses and activate dorsolateral prefrontal cortex areas to similar degrees post-retrieval, while neutral pictures show differential dorsolateral prefrontal cortex activation for correctly identified old and new pictures. In consequence, the size of the right frontal effect differentiates between correctly identified old and new pictures of neutral content but not between correctly identified old and new pictures of affective content. Functionally, the affective modulation of both response bias and the size of the late right-frontal effect can be interpreted in light of the prefrontal involvement in the selection of memories that are currently relevant (Schnider, Treyer, & Buck, 2000). The preferential processing of affective stimuli carries a potential survival advantage, making affective stimuli inherently relevant. This leads to a more liberal response bias, ensuring relevant stimuli are less likely to be missed. It also leads to increased prefrontal cortex activation indexing task relevance, irrespective of retrieval status, which is reflected in a lack of difference in late right-frontal effect sizes. Neutral stimuli by contrast are only task relevant if they have been successfully retrieved, leading to increased late right-frontal amplitudes for old compared to new items.

In sum, the present study demonstrates three distinct old/new effects for picture recognition that are modulated differentially by affective picture content. An early effect between 300 and 500 milliseconds showed a

significantly more superior distribution for negative than for neutral pictures but there was no significant affective modulation of old/new effect size at electrode Fz. The qualitative topographical difference between old/new effects for negative and neutral pictures adds weight to Yonelinas and Ritchey's (2015) emotional binding account of affective recognition memory. In the 500 to 800 millisecond time window, the topographical difference between old/new effects for negative and neutral pictures failed to reach significance in rescaled data but effect sizes at the midline cluster were significantly larger for negative than either neutral or positive pictures, corresponding to a significantly higher remember rate in the negative condition. The widespread midline distribution of these old/new differences is in contrast with the clear left-parietal distribution seen in old/new effects for words associated with recollection but maps onto differences in remember rates in the way expected of an ERP correlate of recollection. Mackenzie and Donaldson (2007; 2009) have previously demonstrated ERP correlates of recollection with an anterior distribution in the case of faces, concluding that the left-parietal distribution of recollection driven old/new effects seen in response to word stimuli does not generalise to all stimulus types and paradigms. The widespread midline distribution of the effect reported here, suggests that differential distributions may arise from picture stimuli more generally and not just face stimuli specifically.

A late right-frontal old/new effect could be demonstrated for neutral pictures only. There was no significant influence of remember rates on the size of the

late right-frontal effect, suggesting affective content itself engages the eliciting processes to different degrees. This is interpreted as a reflection of inherit relevance assigned to affective over neutral stimuli, which leads to both a more liberal response bias and a decline in the late right-frontal effect.

Future replications of the work presented here, with special emphasis on topographical analysis of the results, are necessary to add further weight to the idea that the left-parietal distribution of the recollection effect between 500 and 800ms does not generalise from word to picture scene stimuli. Such replications would establish a gold standard for the distribution of recollection effects elicited by picture scene stimuli in this time window and contribute to the wider understanding of the relationship between stimulus type and recollection effect distribution.

Chapter 7: Gender Differences in Affective Cognition

Of all of the widely held stereotypes of gender differences, a presumed difference in "emotionality" is the most fundamental. Women are seen as more emotionally responsive, while men are assumed to be more stoical (NESBITT, 2000). Variably, these supposed respective attributes are considered assets or shortcomings of one gender or the other. Often they are part of prejudices that continue to support gender inequality, as women are seen as more emotional and in apparent consequence as less rational. But is there a scientific foundation for believing that men and women differ in their affective processing? Do such gender differences, if they exist, have a neural basis? And do such differences in affective processing between the genders lead to differential affective modulation of cognitive function?

The present chapter explores gender differences in the affective cognition tasks presented in Chapters 5 and 6. There was no evidence of a gender effect on attentional disengagement suggesting that affective content captures attention in men and women equally. There was also no evidence of a gender effect on the time-course of affective memory. Gender effects on affective picture processing and affective memory are discussed below.

7.1 Gender differences in affective processing of pictures and the Late-Positive Potential (LPP)

7.1.1 Introduction

The most commonly repeated stereotype, when it comes to differences between the sexes, is that "women are more emotional than men". This statement of course, like most folk wisdom, is very loosely defined. Broadly, it suggests that men show less emotion than women in response to various situations. This, if it was the case, could have two underlying causes: Either women are more emotionally reactive, that is they experience increased levels of affective arousal compared to men, or women are simply more emotionally expressive, that is the affective arousal they do feel is more easily identified by others. To test gender differences in both emotional expressivity and emotional reactivity. Kring and Gordon (1998) showed female and male participants short film clips of happy, sad and fear content. Emotional expressivity was assessed by a panel of trained coders who recorded frequency, intensity and duration of participants' negative and positive expressions during film watching. They found that women were more expressive than men across all film categories. However, the use of this qualitative assessment of emotional expressivity for the purpose of investigating its modulation by gender has one crucial weakness: Coders cannot be blind to each participant's gender. Any gender differences in expressivity observed could therefore have arisen or been exacerbated as a self-fulfilling prophecy based on a social bias for preferentially interpreting women's expressions as indicative of emotion. However, gender

differences in emotional expressivity have also been shown by analysing changes in participants' Electromyograms (EMG) during picture viewing (Bradley, Codispoti, Sabatinelli, & Lang, 2001). For aversive stimuli, women showed significantly larger changes in EMG, indicating changes in facial expression from neutral, than men did. This increased expressivity was accompanied by women rating aversive pictures are significantly more arousing and negative than men. By contrast,(Kring and Gordon (1998) did not find a gender difference in self-reported emotion experience. In a second experiment, Kring and Gordon (1998) showed that expressivity varied with perceived expressivity of participants' close family and strength of gender role, showing that the observed gender difference arises, at least in part, from social learning. Because of these social influences on emotional expressivity, it is reasonable to assume that self-report measures of emotional reactivity can also be socially coloured, by factors such as self-image and social desirability.

Studying brain reactivity to emotional material as a marker of emotional reactivity circumvents such social factors but of course interpretation of neural activity patterns in terms of emotional experience in turn relies on self-report measures. Whittle, Yücel and Allen (2011) reviewed fMRI studies of gender differences in the neural correlates of emotion perception. They report an emerging pattern across studies, of greater activation in males than females in frontal and parietal regions and greater activation in females than males in limbic subcortical and temporal regions. However, a quantitative meta-analysis by Stevens and Hamann (2012) shows that gender differences in neural

correlates of emotional processing vary by valence. In the case of the left amygdala for example, activation was greater for women than for men for negative stimuli but greater for men than for women for positive stimuli. Negative stimuli also produced greater activation for women than for men in the left thalamus, hypothalamus, mammillary bodies, left caudate and medial prefrontal cortex, while positive stimuli were associated with greater activation for men than for women in the bilateral inferior frontal gyrus and right fusiform gyrus. Although not directly addressed by Stevens and Hamann (2012), their results also point to a differential lateralisation of emotion-related neural activation by gender. Specifically, a meta-analysis of the relationship between valence, gender and lateralisation of neural activation in response to emotion by Wager, Phan, Liberzon and Taylor (2003) found that lateralisation of emotion-related activity was more pronounced in males.

Although source localisation in ERP studies is complex and often ambiguous and spatial resolution is not one of the strengths of the ERP method, a difference in lateralisation of the neural generators of electrophysiological correlates of affective processing should nevertheless be reflected in topographical differences between ERP distributions. Based on this, Gasbarri et al. (2007) compared P300 amplitudes between 300 and 500 milliseconds in response to negative, neutral and positive pictures at left and right frontal and parietal sites (electrodes F3, F4, P3, P4) between men and women. There was no gender difference in participants' valence ratings of the pictures, which confirmed their categorisation. They found a gender difference in the

lateralisation of P300 amplitudes for negative pictures, which were larger for women than men in the left hemisphere but larger for men than for women in the right hemisphere. At a surprise memory test after one week, recall was significantly better for negative than for positive or neutral pictures, as well as significantly better for positive than neutral pictures across genders, with no significant gender effects.

The following analyses assess gender differences in participants' valence and arousal ratings of negative, neutral and positive pictures as a self-report measure of affective reactivity, as well as the size and topographies of the LPP effects elicited by negative and positive compared to neutral pictures as an electrophysiological correlate of affective processing. Women were expected to be more extreme in their self-reports of affective experience during picture viewing and show increased LPP effects for affective stimuli compared to men. LPP effects were expected to differ in topography between the genders.

7.1.2 Methods

Behavioural and ERP data from the affective processing task (see Chapter 4.3.1) for the 65 participants in Experiment 3 were split by gender. The task involved looking at individual IAPS pictures on a screen for 2000ms in anticipation of rating the pictures for arousal and valence. The affective processing task is described in full detail in Chapter 4. The 288 IAPS pictures (Lang, Bradley, & Cuthbert, 2008) used as stimuli had been selected by their IAPS standard

ratings to fit three affective categories: high arousing negative, high arousing positive and low arousing neutral. Importantly for the present analysis, sexual content was an exclusion criterion for stimuli, in order to eliminate confounds of sexual orientation and differences in perceived attractiveness of pictures containing male or female nudity between the genders.

Participants' ratings for arousal (on the modified SAM scale: 1=minimal arousal and 5=maximal arousal) and valence (on the modified SAM scale: 1=most positive and 5=most negative) were separately subjected to ANOVA with the within-subjects factor of affective content (negative, neutral, positive) and the between-subjects factor of gender (male, female). Any significant interactions of affective content with gender were further investigated using t-tests.

Mean amplitudes in response to the affective processing task (see Chapter 4.3.1) in the 400-1000ms time were subjected to ANOVA with factors of affective content (negative, positive), location (frontal, fronto-central, central, centro-parietal, parietal), site (left inferior[5], left medial[3], left superior[1], midline [z], right superior [2], right medial [4], right inferior [6]) and the between-subjects factor of gender. To test whether interactions with topographical factors represented differences in neural generators between conditions, the analysis was repeated on rescaled data.

Mean LPP effect sizes (mean amplitude for affective minus mean amplitude for neutral pictures) at electrode Cz were subjected to ANOVA with factors of affective content (negative, positive) and gender (female, male). A significant

interaction was then followed up by t-test comparisons within genders. The significance of the LPP effect at Cz was assessed separately for men and women and negative and neutral pictures by comparing mean amplitudes in response to affective with those in response to neutral pictures using t-tests.

7.1.3 Behavioural results

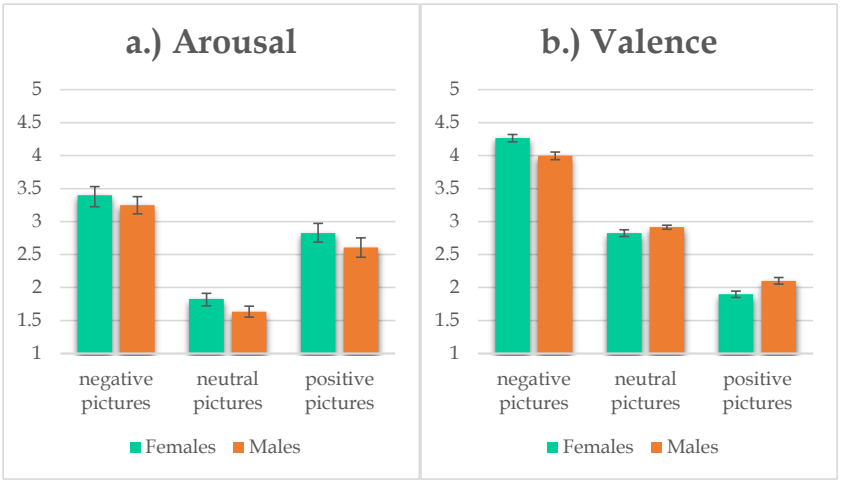


Figure 7.1 *a.) Arousal ratings from female and male participants did not significantly differ within affective categories (1=minimal arousal; 5=maximal arousal). b.) Valence ratings from female participants were higher for negative pictures and lower for positive pictures relative to ratings from male participants (1=most positive; 5=most negative). Valence ratings for neutral pictures did not differ significantly by gender. Error bars show standard errors.*

As Figure 7.1a illustrates, females rated pictures in all three affective categories as slightly more arousing overall than males did. Both genders rated negative pictures as most arousing on average, followed by positive and then neutral pictures. ANOVA of arousal ratings with factors affective content (negative,

neutral, positive) and gender (female, male) showed a significant main effect of affective content [$F(2,124)=165.1$, $p<.011$] but no significant interaction with gender and no main effect of gender on arousal ratings.

Both genders conformed to IAPS standard ratings by rating negative pictures as more negative than either of the two remaining picture set and positive pictures as more positive than either negative or neutral pictures. However, Figure 7.1b shows that female participants were more extreme in their valence ratings compared to male participants, rating negative pictures as more negative and positive pictures as more positive than males. Confirming this, ANOVA of valence ratings with factors affective content (negative, neutral, positive) and gender (female, male) returned a significant affective content by gender interaction [$F(1.70,105)=12.69$, $p<.001$]. Planned comparisons showed the difference in valence ratings to be significant for negative [$t(62)=3.33$, $p=.001$] and positive pictures [$t(62)=-2.94$, $p=.005$], while there was no significant gender difference in valence ratings for neutral pictures.

7.1.4 ERP results: Gender effects on the Late-Positive Potential (LPP)

As the scalp maps of the difference between mean amplitudes for the two affective picture conditions and mean amplitudes for neutral pictures in the 400-1000ms time window (Figure 7.2) show, there are differences in affective modulation of the LPP effect between the genders. Women show a stronger modulation of the LPP by positive than by negative picture content, whereas

this difference between affective categories is much less pronounced in men. The affective modulation of the LPP by negative picture content in the 400-1000ms time window is strongest in left medial sites for both men and women and decreases steadily going left and right. The affective modulation of the LPP by positive picture content is maximal at left superior electrodes in women, whereas it is centrally maximal in men.

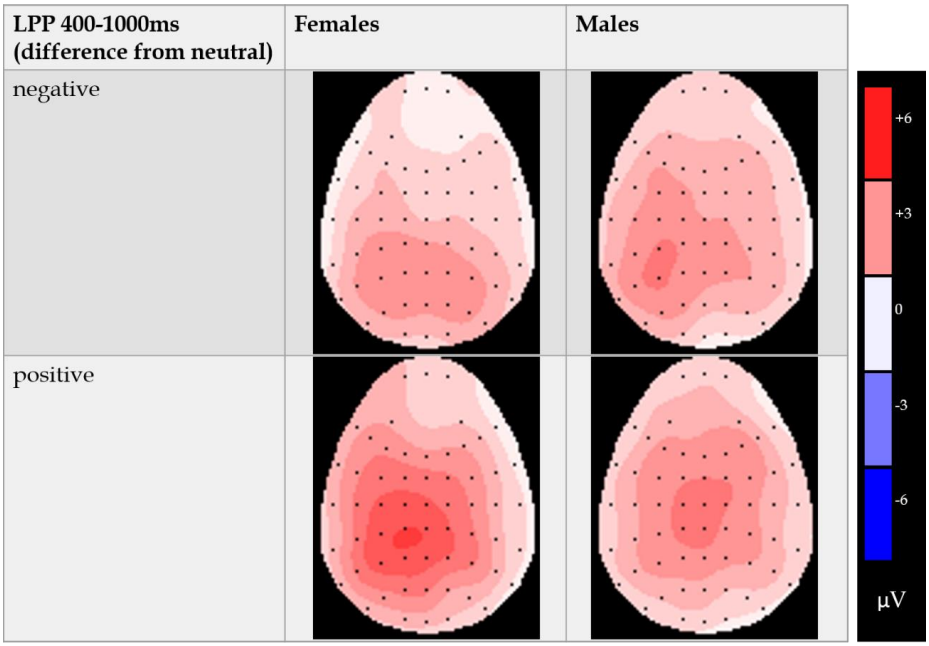


***Figure* 7.2** *Late-positive potential differences from neutral were more pronounced for positive than for negative pictures in women and appear equivalently strong but more left-sided for negative than for positive pictures in men.*

ANOVA with factors of affective content (negative, positive), location (frontal, fronto-central, central, centro-parietal, parietal), site (left inferior[5], left medial[3], left superior[1], midline [z], right superior [2], right medial [4], right inferior [6]) and the between-subjects factor of gender on the difference in mean amplitudes between affective and neutral conditions in the 400-1000ms time window confirmed a significant affective content by site by gender interaction [$F(1.97,124)=5.12$, $p=.008$]. The interaction survived rescaling [$F(1.98,124)=4.93$, $p=.009$], indicating a difference in neural generators. The way in which negative picture content modulated the LPP differently from positive picture content differed between the genders. The interaction with site reflected the fact that negative LPP effects were maximal in left-medial electrodes for both genders but positive LPP effects differed in lateralisation. In women, the LPP for positive pictures was stronger over the left hemisphere, being maximal at left superior electrodes. In men, the LPP effect for positive pictures was strongest at the midline and showed no evidence of lateralisation. The LPP effect for negative pictures, by contrast, was more strongly left-lateralised in men than in women.

At electrode Cz, a mixed factors ANOVA of affective content and gender on LPP effect size returned a significant affective content by gender interaction [$F(1,63)=4.12$, $p=.047$]. As Figure 7.3 illustrates, the LPP effect was significantly larger for positive than for negative pictures in women [$t(31)=4.18$, $p<.001$] but not in men. The LPP effect was significant at electrode Cz for both affective picture categories in women [negative-neutral: $t(31)=3.06$, $p=.005$; positive-

neutral: t(31)=6.14, p<.001] and men [negative-neutral: t(32)=4.78, p<.001; positive-neutral: t(31)=8.80, p<.001].

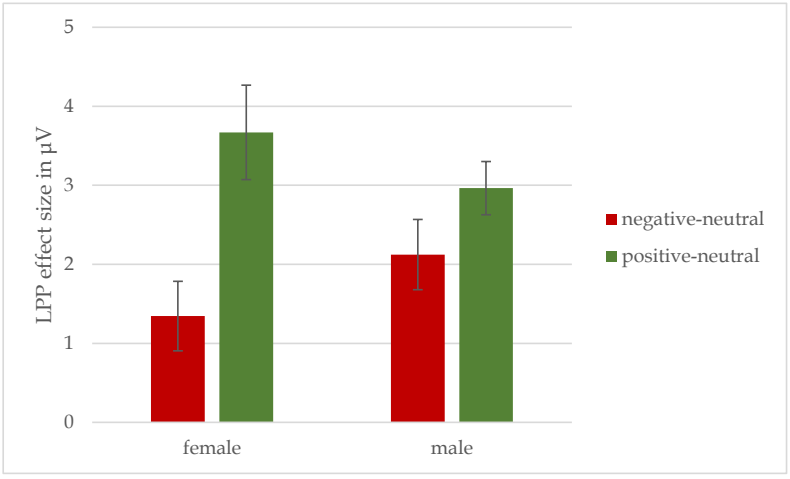


Figure 7.3 *Mean LPP effect size (mean amplitudes for affective – mean amplitudes for neutral pictures) was significantly larger for positive than for negative pictures in women but not in men. Error bars indicate standard errors.*

7.1.5 Discussion

It was hypothesised that women's self-reports of affective experience during picture viewing will be more extreme than men's. Women did report significantly higher arousal in response to pictures but this was consistent across all three affect categories, meaning the relative increase in arousal ratings for negative and positive compared to neutral pictures was consistent between the genders. In their valence ratings, women did give significantly more extreme values for affective compared to non-affective pictures than men.

While there was no gender difference in the valence ratings of neutral pictures, women rated positive pictures as significantly more positive than men did and negative pictures as significantly more negative. This increased behavioural affective reactivity is consistent with some (Bradley et al., 2001; Lang, Greenwald, Bradley, & Hamm, 1993) but not all (Kring & Gordon, 1998) previous findings.

A possible explanation for this discrepancy lies in Kring & Gordon's (1998) observation that expressivity varies with strength of gender role. It is possible that it is not biological sex but rather psychological gender that determines differences in emotional processing. Since the two dimensions are closely linked, comparisons between the sexes can still reveal differences that are produced by gender differences. But since gender is continuous rather than dichotomous, some samples with relatively low gender variability will likely not show these differences when split by sex. Bourne and Maxwell (2010) show the importance of assessing gender by reporting different influences of masculinity on the lateralisation of the neural correlates of facial emotion processing between the sexes. While neural activation was more lateralised with increasing masculinity scores in men, interestingly, it was less lateralised with increasing masculinity in women. Since the terms “sex” and “gender” are often used interchangeably in common usage and the variable, for practical reasons, is usually assessed through self-report, the boundaries between the terms are likely to be blurred. Unless the variable to be recorded is specifically defined and explained as part of the study procedure, it is likely to be

interpreted as biological sex by some participants and psychological gender by others. Of course the overlap between the two, when assessed dichotomously, is overwhelming. More likely to be important for practical purposes is a measure of degree of masculinity/femininity such as the Bem Sex Role Inventory (Bem, 1977) used by Bourne and Maxwell (2010). The present study, like most research in this field, is limited by not having assessed degree of masculinity/femininity. "Gender" was assessed through self-report and although it can therefore not be defined with absolute certainty, the variable is more likely to reflect psychological gender rather than biological sex.

In terms of their electrophysiological responses to affective pictures, women and men were hypothesised to differ in both LPP effect size and topography. There was evidence for topographical differences between LPP effects in men and women. While distributions of LPP effects for both negative and positive pictures showed left-sided maxima in women, men's LPP effects were more strongly left-lateralised for negative pictures but maximal at the midline with no hemisphere difference for positive pictures. This extends Gasbarri et al.'s (2007) findings of hemispheric differences in an earlier time window.

Since the completion of data collection, three studies have reported gender differences in the affective modulation of the LPP. Two of them investigated gender effects on topography. Groen, Wijers, Tucha and Althaus (2013) found an increase in LPPs in response to affective pictures including humans compared to affective pictures of landscapes which was stronger in the left hemisphere. They did not report any effects of gender on LPP topographies.

Bianchin and Angrilli (2012) reported LPP effects for positive and negative pictures that look to be maximal at the midline. They showed a gender by affective picture content interaction at electrode F7, at the periphery of the LPP effect. Here, men showed increased mean amplitudes in response to negative compared to neutral pictures, while women showed increased mean amplitudes for negative compared to positive pictures. They did not report comparisons of LPP effects, i.e. differences between mean amplitudes in response to affective and neutral pictures. A third study by Syrjänen and Wiens (2013) does not include topographical analysis. Consequently, the present study is the first to demonstrate an interaction between gender and LPP effect topographies.

As well as a topographic difference, there was also an interaction between gender and affective content on LPP effect size (mean amplitude difference from the neutral condition) at electrode Cz. While women showed significantly larger LPP effects for positive than for negative stimuli, this difference was not significant for men. Interestingly, this gender difference was reversed in Syrjänen and Wiens' (2013) data. Here, males showed larger LPP effects for positive than for negative pictures, while no differences could be shown for females. This different pattern likely arises from differences in stimulus selection. While the present study explicitly excluded pictures with sexual content, Syrjänen and Wiens' (2013) stimulus set included a large proportion of erotic stimuli. As Bradley, Codispoti, Sabatinelli and Lang (2001) show, men are more reactive to erotic stimuli than women are, making it likely that the

increased LPP effects for positive pictures reported by Syrjänen and Wiens (2013) rely on this sub-type of stimuli. Bianchin and Angrilli (2012) did not compare LPP effect amplitude between differences between negative and positive pictures across the genders. Groen et al. (2013) reported an interaction between affective content and gender on mean amplitudes at electrode P3, which seems to arise from an increase in LPP effect for negative compared to positive pictures in women but not in men, although they only report a significant difference in LPP amplitudes for negative pictures between the genders. This pattern is consistent with previous findings that women are more emotionally reactive to negative stimuli than men (Bradley et al., 2001) but did not arise in the present data. Groen et al.'s (2013) female participants scored significantly higher than male participants on a number of empathy measures, including one assessing personal distress. This is likely to mediate the observed negativity bias in female participants.

In sum, the present study expands previous electrophysiological evidence of gender differences in the processing of negative and positive affective pictures by showing a qualitative topographic difference between LPP effect distributions suggesting that men and women differ in the neural generators involved in the processing of negative and positive affective pictures respectively. The present ERP data suggest a positivity bias in women that is absent in men. However, comparison with other studies shows that positivity and negativity biases are not directly caused by differences in gender but arise from interactions of gender with other variables such as for example erotic

picture content or empathy. Future studies should address the interactions between these factors by employing larger stimulus sets varying not only in affective arousal and valence but also more specific picture content, such as pictures eliciting erotic arousal or empathy, coupled with self-report assessments of the success of these manipulations.

7.2 Gender differences in affective memory and its electrophysiological correlates

7.2.1 Introduction

One important reason for the investigation of gender effects in affective processing is the well-established gender difference in the incidence of mood disorders such as anxiety and major depression. Women are between 70% and 100% more likely to develop clinical depression than men (Kessler, 1993; Weissman, 1977) and the higher incidence of clinical depression in women is consistent across a wide range of international populations (Maier et al., 1999; Weissman, 1996). As Maier et al. (1999) show, this difference is partially socially mediated. When variables of social role such as marital status, number of children and occupational status are matched between genders, the gender difference in depression is reduced by about half. Other consequences of social gender roles, such as a difference in willingness to present for diagnosis and therapy, are also likely to contribute. Gender differences in affective processing, especially when they are associated with structural or functional neural

differences, are also likely to contribute to the gender difference in the incidence of mood disorders and thus their better understanding may contribute to both improved theoretical models of mood disorders and their treatment. Differences in the online processing of affective information as it is encountered (discussed in Chapter 7.1 above) will contribute to differences in people's emotional experience of the world. For example, a negativity bias in processing will lead to the subjective experience of living in a more negative world. This effect is likely to be amplified by potential differences in affective memory.

As part of their assessment of gender differences in overall emotional intensity, Fujita, Diener and Sandvik (1991) reported increased recall of both negative and positive life events in women compared to men. In conjunction with the additional emotional intensity measures of self-report, peer report and daily report, the authors present this as evidence of increased affect of both valences in women compared to men. Seidlitz and Diener (1998) also showed that women recalled significantly more positive and negative life events compared to men in a free recall task, despite not differing in mood at the time of recall. However, when asked to recall their activities during specific time periods in the preceding week, a task designed to increase the recall of neutral relative to affective life events, women also showed a general autobiographical recall advantage. They did not differ from men in their recall of positive and negative historical events or aspects of American life, raising the possibility that women's improved recall for affective autobiographical information arises from

an overall advantage in autobiographical recall. To assess whether an increased focus on emotional information at encoding facilitates greater recall, Bloise and Johnson (2007) presented participants with a script containing both emotional and neutral information and varied instructions to focus on either the protagonists' interpersonal issues or concrete plans. They found that women performed better for emotional items on a surprise recognition test, irrespective of focus, and performed better than men for neutral items in the neutral focus condition. An emotional sensitivity measure mediated the gender difference. Unfortunately, neither Seidlitz and Diener (1998) nor Bloise and Johnson (2007) directly assess gender effects on the affective modulation of memory performance, i.e. effects on the difference between memory performance for affective and neutral information. Interestingly, Dewhurst, Anderson and Knott (2012) also showed increased rates of false memory for emotional words in females relative to males.

If there is a gender difference in the affective modulation of memory, then the nature of this difference can be further illuminated using functional imaging. Using positron emission tomography (PET), Cahill (2004) showed that memory performance was differentially predicted by amygdala activation in response to negative and neutral films in men and women. While left amygdala activation during encoding was associated with subsequent memory performance in women, right amygdala activation was associated with memory performance in men. Canli, Desmond, Zhao and Gabrieli (2002) replicated this finding of gender-specific lateralisation of encoding activity in the amygdala using picture

stimuli and fMRI. In a recognition memory test three weeks after encoding, men and women did not differ in their recognition of low to moderately arousing pictures but showed significantly better recognition of highly arousing negative pictures. There was no gender difference in false alarms. Cahill (2004) replicated Canli et al.'s (2002) results and extended them by the demonstration of a gender-by-hemisphere interaction in amygdala activation during affective memory encoding, which further substantiates the findings in light of the possibility of asymmetry in function being artificially amplified by thresholding differences. The gender difference in lateralisation of amygdala activation during affective memory encoding is therefore well documented. Investigating gender differences in affective autobiographical memory using fMRI, Piefke, Weiss, Markowitsch and Fink (2005) also showed a gender effect on activation during affective memory retrieval. Despite a lack of evidence for behavioural differences in memory performance or reported emotional intensity between men and women, there was an interaction of gender with memory content in right insula activation, which the authors interpret as reflecting a difference in cognitive strategies for the retrieval of autobiographical memories.

Using ERP, Galli, Wolpe and Otten (2011) have also shown that men and women differ in the extent to which anticipatory brain activity before stimulus onset at study predicts later affective memory performance. They showed an influence of right-lateralised anticipatory activity on the encoding of negative pictures in women but not men. At the time of data collection, no direct ERP

evidence of a gender difference in the affective modulation of recognition memory was available, either in the form of differences in subsequent memory effects or old/new memory effects. The present study explores the influence of gender on the affective modulation of recognition memory and its electrophysiological correlates. On the basis of previous findings of overall higher recall of both true and false affective memories in women, it is hypothesised that women will show a stronger increase in hit rates and false alarm rates for affective relative to neutral pictures, meaning they will have a more liberal response bias than men for affective material. Given their recall advantage for affective material, it is further hypothesised that women will have a larger increase in remember rates for affective relative to neutral pictures than men. It is expected that the affective modulation of old/new effects in the 500 to 800 millisecond time window, thought to reflect recollection, will be more pronounced in women than in men. Finally, if response bias increases for affective pictures are larger in women than in men, it is hypothesised that they show a stronger reduction of the late right frontal old/new effect.

7.2.2 Methods

Data from 28 women and 28 men on the affective recognition memory test (see Chapter 6.2) were split by gender. For behavioural analysis, discrimination index Pr, response bias Br and remember rate (calculated by dividing the

number of "remember" responses by the total number of hits for each participant) were subjected to separate ANOVAs with factors of affective content (negative, positive, neutral) and gender (female, male). For ERP analysis, mean amplitude differences for hits minus correct rejections in the three time windows examined in Chapter 6.2 (300-500ms, 500-800ms and 800-1500ms) were separately subjected to ANOVA with the factors affective content (negative, neutral, positive), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right), site (superior [1,2], medial [3,4], inferior [5,6]) and gender (female, male). To assess whether any interactions with topographical factors reflected qualitative or merely quantitative differences, the same analysis was repeated on rescaled data. ANOVAs with factors of affective content (negative, neutral, positive) and retrieval success (hit, correct rejection) were performed separately for each gender and time window. Old/new effects were analysed separately for each affective category for each gender and compared between genders.

7.2.3 Behavioural results

Table 7.1 shows that both men and women achieved highest hit rates and Pr scores for negative, followed by neutral and then positive pictures, while false alarm rates where lowest for neutral pictures, followed by negative and then positive pictures for both genders. Response bias was most liberal for negative pictures and most conservative for neutral pictures for both groups. The

genders did diverge in their patterns of remember rates. While both genders showed highest proportions of remembered items in hits for negative pictures, women showed higher remember rates for neutral than for positive pictures, while men showed a higher proportion of remembered pictures in the positive compared to the neutral condition.

		Picture valence		
		Negative	Neutral	Positive
Females	Hit rate	0.682 (0.028)	0.603 (0.028)	0.569 (0.029)
	FA rate	0.080 (0.011)	0.054 (0.005)	0.088 (0.013)
	Pr	0.600 (0.026)	0.549 (0.027)	0.480 (0.024)
	Br	0.228 (0.036)	0.142 (0.019)	0.189 (0.030)
	Remember rate	0.551 (0.042)	0.483 (0.045)	0.473 (0.041)
Males	Hit rate	0.765 (0.023)	0.678 (0.023)	0.674 (0.024)
	FA rate	0.115 (0.017)	0.094 (0.017)	0.150 (0.023)
	Pr	0.646 (0.024)	0.581 (0.019)	0.522 (0.021)
	Br	0.328 (0.039)	0.235 (0.038)	0.313 (0.040)
	Remember rate	0.611 (0.028)	0.471 (0.031)	0.511 (0.032)

Table 7.1 *Means and standard errors (in brackets) for hit rate, false alarm (FA) rate, discrimination index Pr, response bias Br and remember rate by picture valence for males and females.*

ANOVAs with factors of affective content (negative, positive, neutral) and gender (female, male) on Pr and Br revealed no significant affective content by gender interactions. Men had a significantly more liberal response bias Br [$F(1,51)=5.90$, $p=.019$] than women but did not differ significantly from women in discrimination index Pr. There were no gender differences in the ratio of correctly identified old pictures reported to be "remembered".

Since there was no significant influence of gender on affective modulation, all main effects of affective content were significant [discrimination index: $F(1.69,86.1)=38.4$, $p<.001$; response bias: $F(2,108)=11.0$, $p<.001$; remember rate $F(2,108)=15.6$, $p<.001$] and affective content modulated all behavioural measures equally for males and females. Remember rates were significantly higher for negative pictures than for neutral or positive pictures in both genders. Discrimination index Pr was greatest for negative followed by neutral and then positive pictures for both genders and all participants showed more liberal response biases to negative and positive pictures than to neutral pictures (see Chapter 6.2.3 for detailed analysis).

7.2.4 ERP results

7.2.4.1 Gender differences in the affective modulation of the old/new effect between 300 and 500 milliseconds

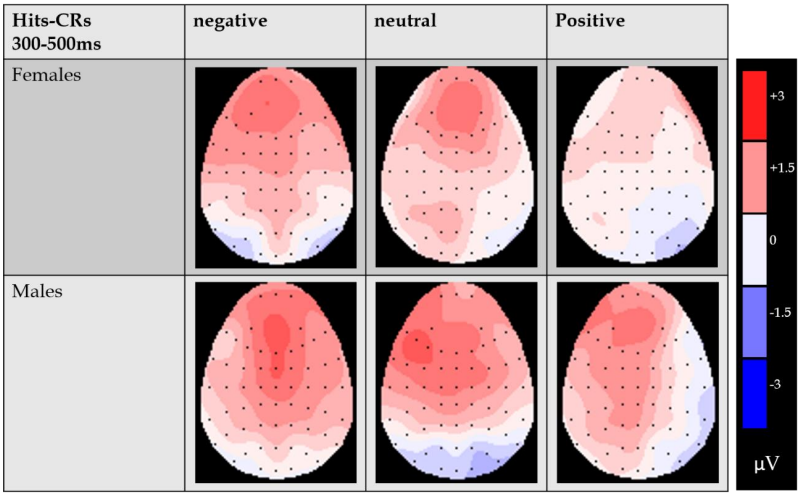


Figure 7.4 *Distributions of memory effects in the 300-500ms time window differed between men and women.*

Visual inspection of the scalp maps of memory effects in the 300-500ms time window (see Figure 7.4) suggest an overall stronger memory effect in males than in females, with the effect being especially weak for positive pictures in females. ANOVA with the factors affective content (negative, neutral, positive), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right), site (superior [1,2], medial [3,4], inferior [5,6]) and gender (female, male) on mean amplitude differences (hits minus correct rejections) in the 300-500ms time window revealed only a marginally significant affective content by location by site by gender interaction [$F(4.44,235)=2.17$, $p=.066$], which reached a similar level of marginal significance when data was rescaled [$F(4.48,237)=2.05$, $p=.080$]. Despite a left-sided appearance of memory effects in response to neutral and positive pictures, the hemisphere factor did not produce significant effects. Separate ANOVAs with factors of affective content (negative, neutral, positive), location (frontal, centro-frontal, central, centro-parietal, parietal) and site (superior [1,2], medial [3,4], inferior [5,6]) for men and women did not show a significant affective content by location by site interaction in women [$p=.233$] or men [$p=.248$] and no significant interactions involving affective content and either of the topographical factors.

In ANOVAs with factors of affective content (negative, neutral, positive) and retrieval success (hit, correct rejection) on mean amplitudes at electrode Fz, the affective content by retrieval success interaction failed to reach significance in both women [$p=.644$] and men [$p=.837$]. The gender difference in old/new

effects at electrode Fz was not significant for any affective content [negative: p=.741; neutral: p=.697; positive: p=.499].

7.2.4.2 Gender differences in the affective modulation of the old/new effect between 500 and 800 milliseconds

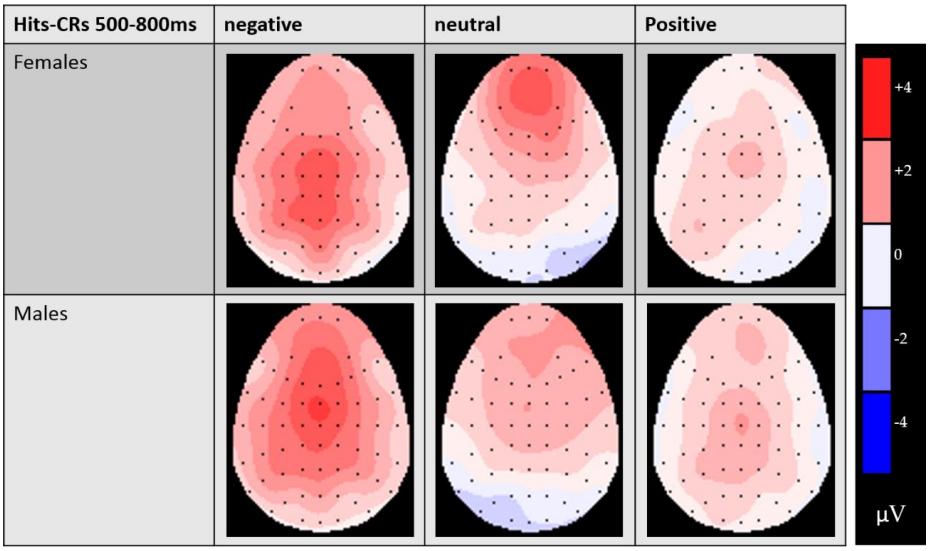


Figure 7.5 *Memory effects in the 500-800ms time window in response to negative, neutral and positive pictures for men and women.*

Figure 7.5 shows the distributions of mean amplitude differences between hits and correct rejections in the 500-800ms time window. Visual inspection of the scalp maps (Figure 7.5) suggests a central memory effect for negative pictures, a frontal memory effect for neutral pictures and a somewhat left-parietal effect for positive pictures only, with no strong differences between the genders.

However, ANOVA with the factors affective content (negative, neutral, positive), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right), site (superior [1,2], medial [3,4], inferior [5,6]) and gender (female, male) on mean amplitude differences (hits minus correct rejections) in the 500-800ms time window returned a significant affective content by location by site by gender interaction [$F(4.17,246)=2.60$, $p=.035$], which is also significant in rescaled data [$F(4.19,222)=2.77$, $p=.026$], driven by a more parietal old/new effect for negative pictures in women than in men. Follow-up ANOVAs with factors of affective content (negative, neutral, positive), location (frontal, centro-frontal, central, centro-parietal, parietal) and site (superior [1,2], medial [3,4], inferior [5,6]) returned no significant affective content by location by site interaction for either men [$p=.145$] or women [$p=.273$] and no significant interactions of affective content with either of the topographical factors.

Separate ANOVAs with factors of affective content (negative, neutral, positive) and retrieval success (hit, correct rejection) on mean amplitudes at the midline cluster (Fz, FCz, Cz) revealed a marginally significant affective content by retrieval success interaction in men [$F(2,52)=3.09$, $p=.054$] but not in women [$p=.240$]. The old/new effect was significant at the midline cluster for negative [$t(27)=3.32$, $p=.003$] and neutral pictures [$t(27)=2.55$, $p=.017$] but not for positive pictures [$p=.103$] in women. In men, the effect was significant for negative [$t(26)=5.40$, $p<.001$] and neutral pictures [$t(26)=2.34$, $p=.027$] and approached significance for positive pictures [$t(26)=2.01$, $p=.055$]. However, the gender

difference in old/new effects at the midline cluster was not significant for any affective content [negative: p=.652; neutral: p=.967; positive: p=.851].

7.2.4.3 Gender differences in the affective modulation of the old/new effect between 800 and 1500 milliseconds

On visual inspection of the memory effects in the 800-1500ms time window (see Figure 7.6), a late right-frontal effect seems to be present in all affective content categories in men but only for neutral pictures in women.

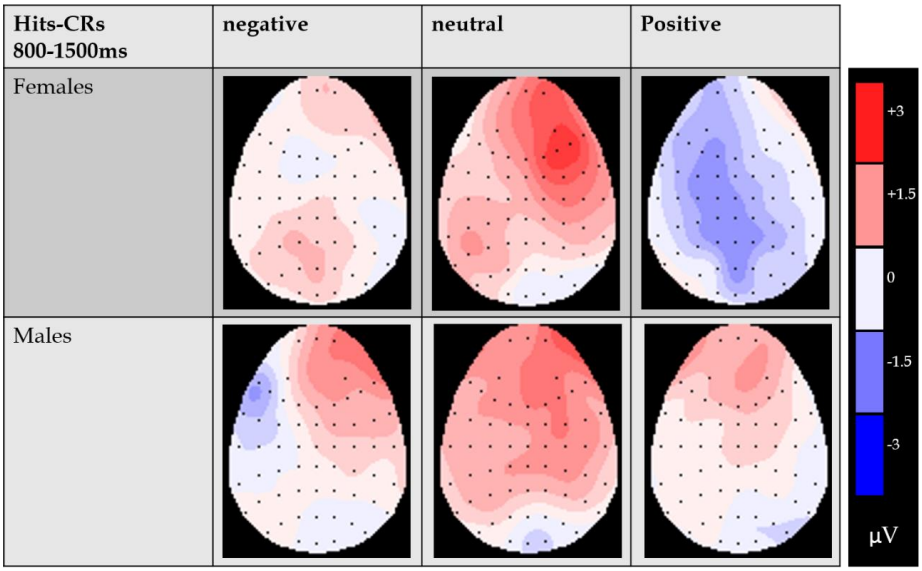


Figure 7.6 *The right-frontal memory effect in the 800-1500ms can be demonstrated for negative and neutral pictures in men. Women showed evidence of a positive going right-frontal effect only in response to neutral pictures.*

ANOVA with factors affective content (negative, neutral, positive), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right), site (superior [1,2], medial [3,4], inferior [5,6]) and gender (female, male) on mean amplitude differences (hits minus correct rejections) in the 800-1500ms time window returned a significant affective content by location by hemisphere by site by gender interaction [$F(4.98,129)=4.41$, $p=.001$], which survived rescaling [$F(5.87,311)=4.31$, $p<.001$]. Separate repeat ANOVAs in men and women revealed a significant affective content by location by hemisphere by site interaction in men [$F(4.98,1290=4.41$, $p=.001$] and a significant affective content by location by site interaction in women [$F(3.45,93,2)=5.66$, $p=.026$].

Separate ANOVAs with factors of affective content (negative, neutral, positive) and retrieval success (hit, correct rejection) on mean amplitudes at electrode F4 showed a significant affective content by retrieval success interaction in women [$F(1.52,41.0)=5.26$, $p=.015$] but not in men [$p=.177$]. The old/new effect was significant for neutral pictures at electrode F4 in women [$t(27)=4.14$, $p<.001$] but not for negative [$p=.795$] or positive pictures [$p=.693$]. Men also showed a significant old/new effect for neutral pictures [$t(26)=3.32$, $p=.003$] but additionally showed a significant old/new difference for negative pictures [$t(26)=3.01$, $p=.006$], while the effect did not reach significance for positive pictures [$p=.129$]. However, the gender difference in old/new effects at electrode F4 was not significant for any affective content [negative: $p=.178$; neutral: $p=.281$; positive: $p=.301$].

7.2.5 Discussion

A number of predictions were made about the expected gender differences in the affective modulation of recognition memory and its electrophysiological correlates. Behaviourally, affective content was expected to increase response bias and remember rate more in women than in men. This hypothesis could not be confirmed as there was no significant interaction of affective content and gender on any of the behavioural measures. Instead, there was a main effect of gender, with men showing a higher, i.e. more liberal, response bias overall. Old/new discrimination did not differ between the genders and neither did the relative contribution of familiarity and recollection as assessed by the remember/know procedure. In this data, there is therefore no evidence of a behavioural difference in affective recognition memory between the genders.

Since the electrophysiological hypotheses of increased affective modulation of old/new effects in women were based on hypothesised behavioural differences which could not be shown, it is unsurprising that the electrophysiological data also showed unexpected patterns. In the early 300 to 500 millisecond time window, thought to index familiarity, there was no gender differences in the affective modulation of old/new effect sizes at electrode Fz. In fact, affective modulation of old/new effects can be demonstrated for neither women nor men. A marginal interaction hints at a difference between the genders in the affective modulation of old/new effect topographies, but again, no such modulation can be shown for either gender individually.

In the 500 to 800 millisecond time window, a putative correlate of recollection, there is a significant gender difference in the affective modulation of old/new effect topographies, with negative pictures eliciting a more parietal distribution in women than men. The size of the old/new effect between 500 and 800 milliseconds was not significantly modulated by affective content in women, but men showed a marginally significant affective modulation driven by larger effect sizes for negative than for neutral or positive pictures. In order to interpret the difference in topographies in the old-new effect found between men and women, a better understanding of the factors that drive old-new effect topographies in this time window is needed, as discussed in Chapter 6 above.

The overall picture that emerges is complex. Both men and women showed an affective modulation of behavioural measures of memory that did not differ by gender. Despite this statistically significant behavioural effect, there were no significant differences in old/new effect sizes at electrode Fz in the early 300 to 500 millisecond time window. Since the early frontal old/new effect is a proposed correlate of familiarity, this is consistent with the view that affective content modulates recognition memory by specifically increasing recollection. The 500 to 800 millisecond "recollection" effect again showed no significant modulation in women but a significant affective modulation, driven by larger effect sizes for negative than neutral or positive pictures, in men. The absence of any affective modulation of these memory effects in women is puzzling in light of a significant behavioural effect. It may be a result of a lower signal-to-

noise ratio due to fewer trials being included in the averages for females because of their lower hit rates (see Table 7.1).

Since the completion of data collection, another study of gender differences in the affective modulation of ERP old/new effects has been published. Glaser, Mendrek, Germain, Lakis and Lavoie (2012) did find a significant modulation of the old/new effect between 300 and 500 milliseconds in women, in form of a topographical difference between effects for negative and positive pictures. They found no such modulation for men but do not report any potential main effects of affective content which would indicate differences in old/new effect sizes. They found no gender difference in the affective modulation of the old/new effect between 500 and 1000 milliseconds. Behaviourally, they show a reduction in discrimination index for highly arousing (negative and positive) pictures in females only. The gender difference here likely arises from the inclusion of images of erotic content in the highly arousing positive group, since men have better memory for sexual content than women (McCall, Rellini, Seal, & Meston, 2007). The memory enhancement by erotic content in the positive condition is likely to have counteracted any lowering of the discrimination index for positive pictures in men only. The lower discrimination index for positive than for neutral pictures in women replicates the present findings, adding evidence to the conclusion that under certain circumstances, positive affective content does not carry a memory advantage.

In the 800 to 1500 millisecond time window, men and women differed significantly in the affective modulation of the distribution of old/new effects.

While affective content modulated old/new effect topography in the factors location, site and hemisphere, it did not influence the hemisphere factor in women. While there were topographical differences between old/new affects for pictures of different affective contents in both men and women, only women showed a significant affective modulation of old/new effects sizes at electrode F4, chosen as representative of the late right-frontal effect. In women, the late right-frontal effect was present only for neutral but not for negative or positive pictures. Chapter 6.2 suggests that the late right-frontal effect is an index of relevance to the present task and that affective stimuli are seen as inherently relevant, irrespective of whether they are targets in the task at hand, which suppresses the late right-frontal effect. This suppression was demonstrated for women but not men. In men, it is of interest to note that only negative and neutral but not positive pictures elicited significant late right-frontal effects. This suggests a valence specific differential processing of negative stimuli in men compared to women.

Taken together, results from the 500 to 800 and 800 to 1500 millisecond time windows suggest a negativity bias in the neural correlates of affective recognition memory in men that could not be demonstrated in women. This can be interpreted in light of a recent study of sex differences in effective connectivity during affective picture processing. Lungu, Potvin, Tikàsz and Mendrek (2015) found higher connectivity between amygdala and dorso-medial prefrontal cortex (dmPFC) in men than in women. Although this interaction only reached marginal significance (p=.006), an additional

significant positive correlation between connectivity (right amygdala to dmPFC) and testosterone level in the high arousal negative condition added further weight to the conclusion that men respond to negative stimuli with increased functional amygdala to dmPFC connectivity compared to women. Based on the dmPFC's involvement in social cognition and action selection, the authors conclude that men's processing of negative stimuli is more evaluative than women's, with an emphasis on selecting appropriate reactions. A modulation in functional connectivity between (right) amygdala and dmPFC for negative but not positive pictures in men would be consistent with the present finding of a significant late right-frontal effect for negative but not positive pictures in men. This could be interpreted as reflecting an increased need for evaluation and action selection for negative stimuli if they occur repeatedly. The differences in distributions of old-new effects shown in the present study add weight to the possibility of neurofunctional differences in the processing of affective stimuli between men and women. Affective memory studies using blocked designs at test would allow for a combination of ERP and fMRI measures to further explore such neurofunctional gender differences in affective processing.

It is important to note that despite differences found in the electrophysiological correlates of affective recognition memory between men and women, no differential effect of affective picture content on the behavioural measures collected could be shown between men and women. This mismatch could have several causes. As discussed above, overall gender differences in performance

could have led to differences in power to detect affective modulations between the genders. Given the relatively large trial numbers (48 old pictures per affective category) and sample size (n=28 per gender), this explanation, while possible, is unlikely. Secondly, gender differences in brain function may be too subtle to produce behavioural effects. A third explanation for the mismatch between gender modulation of electrophysiological correlates of memory and behaviour is that the modulations observed compensate for other differences between men and women, such as sex differences in brain structure, hormone level or related affective cognitive processes (see De Vries, 2004 for a similar argument), meaning that male and female brains differ in the way in which they achieve the same outcomes. Combining ERP and fMRI measures as suggested above could clarify the reason for the mismatch between the lack of gender difference in behavioural measures of affective memory and the differences in its electrophysiological correlates reported here.

If differences in the neurofunctional implementation of affective memory between women and men can be confirmed, this would have implications for the practical application of knowledge about the affective enhancement of memory. In a clinical context, such findings could lead to the development of gender specific behavioural interventions or medication protocols for conditions involving skewed affective memory. In education, a better understanding of how memory is enhanced by affective content differentially for males and females could lead to more person-centric teaching tools and strategies.

Chapter 8: Genetic Differences in Affective Cognition

8.1 Introduction

As discussed in Chapter 2, SNPs have increasingly been shown to have measurable effects at the behavioural and neurological level and are therefore of great interest in furthering understanding of individual differences in behaviour and brain function. One such SNP, the val66met polymorphism of the BDNF gene has been shown to have effects on cognitive processes, most notably memory, and affective processes. To date there has been very limited research on whether it also modulates affective memory and no investigation of how it affects the electrophysiological correlates of affective memory.

The BDNF gene is located on chromosome 11p in humans and encodes the BDNF protein, the most widely distributed neurotrophin in the brain which plays an important role in neuron survival and synaptic plasticity (Teixeira, Barbosa, Diniz, & Kummer, 2010). The val66met polymorphism of the BDNF gene is a change from guanine to adenine on the 196th nucleotide base which leads to a change in amino acids from valine to methionine at codon 66 (Sheikh, Hayden, Kryski, Smith, & Singh, 2010). This substitution affects the intracellular distribution and packaging of pro-BDNF, a BDNF precursor that in turn affects post-synaptic activity-dependent secretion of mature BDNF (Egan et al., 2003). Carrying at least one Met-allele has been shown to be associated with a reduction in volume of several brain regions relative to Val/Val homozygotes

in healthy participants, most notably the hippocampus (Bueller et al., 2006), parahippocampus and right amygdala (Montag, Weber, Fliessbach, Elger, & Reuter, 2009). Additionally, healthy Met-allele carriers but not Val/Val homozygotes show a negative correlation between age and amygdala volume (Sublette et al., 2008) and bilateral dorsolateral prefrontal cortex volume (Nemoto et al., 2006).

On a functional level, the Met-allele of the SNP has been shown to be associated with increased anticipatory cortisol stress response during a cold pressor test (Colzato, Van der Does, Kouwenhoven, Elzinga, & Hommel, 2011), as well as with higher rates of anxiety disorders (Tocchetto et al., 2011). However, the association between BDNF val66met allele and anxiety is not universally found. Lang et al. (2005), for example, showed that healthy Met-carriers had significantly lower, not higher, levels of trait anxiety.

As different levels of incidence of mood disorders are likely mediated by underlying differences in affective processing, Montag, Reuter, Newport, Elger and Weber (2008) assessed differences between BDNF val66met genotypes in affective response directly. They presented female participants with negative, neutral and positive IAPS pictures (Lang, Bradley, & Cuthbert, 2008) for six seconds during an auditory startle paradigm while fMRI was recorded. Startle probes elicited only auditory cortex activation. A region of interest including the bilateral amygdala revealed a stronger increase in activation in response to affective compared to neutral pictures for Met-carriers than for Val/Val homozygotes in the right amygdala. So while the Met-allele been shown to be

associated with reduced right amygdala size, right amygdala sensitivity to affective content seems to be increased in Met-carriers. Given evidence for a right-lateralisation of amygdala sensitivity to affective stimuli in men but not in women (see Chapter 7), BDNF val66met genotype is to be expected to have a stronger effect in men than women. Contrary to the hypothesis that the Met-allele would be associated with an increased negativity bias which favours negative mood, the effect was more pronounced for positive than for negative pictures. The authors note that this was the case despite a failure to match arousal ratings between positive and negative pictures, with positive pictures being associated with lower arousal. Using face stimuli that showed fearful, angry, happy and neutral expressions, Goldman et al. (2010) also found increases in activity of areas including the bilateral amygdala and bilateral anterior hippocampus that were stronger in Met-carriers than in Val/Val homozygotes. However, this relationship was only present in anxious and depressed participants and could not be shown in healthy controls. In summary, there is mounting evidence that the val66met polymorphism modulates both affective processing and risk for the development of mood disorders but the underlying mechanisms are likely complex and thus far not well understood.

A second area of influence of the val66met polymorphism is in cognitive functioning. Carrying one or two Met-alleles has been shown to be associated with significantly slowed processing speed, as well as significantly poorer performance on delayed recall and general intelligence tests in elderly

participants (Miyajima et al., 2008). Gajewski, Hengstler, Golka, Falkenstein and Beste (2011) recorded EEG while elderly participants completed a task-switching paradigm that included three changing tasks (a numerical decision, a parity decision and a font size decision). The task to be completed in each trial was either indicated by a cue or to be switched according to a memorised sequence. Behaviourally, Val/Val homozygotes showed longer overall reaction times than Met-carriers, a finding in direct contrast with Miyajima et al.'s (2008) results. BDNF genotype did not interact with either task cue type (on screen cue vs memory) or switch vs non-switch trial on reaction times. In the cued task condition, no effect of genotype was found. In the memory condition, Val/Val homozygotes showed significantly more increased error rates in switch trials than Met-carriers, suggesting a deficit that is mediated by memory performance. Importantly, Gajewski et al. (2011) showed that two ERP effects, the N2, which they interpret as an electrophysiological correlate of response control and selection, and the size of the P3, were correspondingly modulated by BDNF genotype. By contrast, in a large sample of 428 healthy participants, Schofield, Williams, Paul and Gatt (2009) found no difference in P3 effect size between Val/Val homozygotes, Val/Met heterozygotes and Met/Met homozygotes in an oddball paradigm. They did, however, report a significantly later latency of the P300 effect in Met/Met compared to Val/Val homozygotes at left and medial frontal and fronto-central as well as at right frontal sites. P300 was also delayed in Met/Met homozygotes compared to Val/Met heterozygotes at left and right frontal and fronto-central sites.

BDNF val66met has also been shown to modulate episodic memory. Egan et al. (2003) showed that healthy Met/Met homozygotes scored significantly lower on the revised version of the Wechsler Memory Scale, which tests verbal episodic memory, than Val/Val homozygotes or Val/Met heterozygotes. Hariri, Goldberg and Mattay (2003) also showed Val66Met differences in episodic memory for pictures using novel complex scenes. Val/Val homozygotes showed a significantly higher percentage of correct "old" and "new" responses than Met-carriers, consistent with Egan et al.'s (2003) findings. FMRI revealed decreased hippocampal activation during both encoding and retrieval in Met-carriers compared to Val/Val homozygotes.

Given the BDNF val66met polymorphism's association with modulations of both affective processes and memory, it is an interesting candidate SNP for the investigation of genetic differences in affective memory and its electrophysiological correlates. In an fMRI investigation of memory for neutral and mildly happy faces, van Wingen et al. (2010) showed an effect of BDNF val66met genotype on activity associated with both encoding (subsequently remembered vs subsequently forgotten) and retrieval effects (hits vs misses) in men but not in women. During encoding, male Met-carriers showed a larger increase in amygdala activation in subsequently remembered compared to subsequently forgotten faces than Val/Val homozygotes. During retrieval, male Met-carriers also showed a larger increase in left inferior frontal gyrus and posterior cingulate cortex activation in response to hits compared to missed than Val/Val homozygotes. There were no behavioural differences in memory

performance between BDNF genotypes or genders. Differences between memory for neutral and happy face stimuli and respective associated brain activation were not assessed.

Evidence for an effect of the BDNF val66met polymorphism on affective memory comes from a fine-mapping study of the genomic region that includes the BDNF gene and its neighbour BDNFOS. Cathomas, Vogler, Euler-Sigmund and Papassotiropoulos (2010) found the highest association of any of the 55 SNPs in the region between val66met and affective but not neutral word recall.

In sum, the Met-allele of the val66met polymorphism is associated with smaller right amygdala and hippocampus volumes and decreased memory performance but, in the absence of behavioural differences, with increased affect and memory related activation. BDNF val66met's effect on the right amygdala specifically makes it more likely to elicit differences in affective processing in men than women, as male affective processing is right-lateralised. Previous research is consistent with this prediction. An association between val66met and affective word recall has been demonstrated. A val66met modulation of affective processing and affective memory in the present data was hypothesised and expected to be more pronounced in men. ERP memory effects are hypothesised to be increased more by affective content for Met-carriers than for Val/Val homozygotes and this pattern should be observable even in the absence of behavioural differences.

8.2 Methods

Data from 55 participants with complete data sets from both the affective processing and affective recognition memory tasks as well as successful genotyping of the BDNF val66met SNP was available (for detailed genotyping methods see Chapter 4.6). The expected genotype frequencies for the BDNF val66met polymorphism in Caucasian populations are 63.7% for Val/Val homozygotes, 33.6% for Val/Met heterozygotes and 2.7% for Met/Met homozygotes (dbSNP ss11699008, www.ncbi.nlm.nih.gov/projects/SNP). As predicted by this expected distribution, there was only one Met/Met homozygote in the current sample. Val/Val homozygotes were therefore compared to all Met-carriers (Val/Met and Met/Met) in the analyses below. There were 36 Val/Val homozygotes and 19 Met-carriers in the current sample and the distribution was in Hardy-Weinberg equilibrium (χ^2=.073, p=.787), meaning allele frequencies in the sample were consistent with those expected in the wider population. Given the gender effects reported in Chapter 7, it was hypothesised that any genetic effects may differ between males and females and that combined analysis of data from both genders may miss effects that are present in only one gender or differ in direction between the genders. Despite the relatively small sample size, gender was therefore included as a factor in the analyses.

Behavioural data was analysed using ANOVA with factors of affective content (negative, neutral, positive), gender (female, male) and BDNF genotype (Val/Val, met-carrier). Any significant interaction involving both affective

content and BDNF genotype were followed up with paired-samples t-tests between affective content categories within each BDNF genotype group. For late-positive potential analysis, mean amplitudes between 400 and 1000 milliseconds post stimulus onset from the affective processing task was subjected to ANOVA with factors of affective content (negative, neutral, positive), location (frontal, centro-frontal, central, centro-parietal, parietal), site (left inferior[5], left medial[3], left superior[1], midline [z], right superior [2], right medial [4], right inferior [6]), gender (male, female) and BDNF group (Val/Val, met-carrier).

For analysis of the electrophysiological recognition memory data, mean amplitude differences for hits minus correct rejections from the affective recognition memory task was subjected to ANOVA with the factors affective content (negative, neutral, positive), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right), site (superior [1,2], medial [3,4], inferior [5,6]), gender (female, male) and BDNF genotype (Val/Val, Met-carrier) separately for three time windows: 300 to 500 milliseconds (thought to capture familiarity effects), 500 to 800 milliseconds (thought to capture recollection effects) and 800 to 1500 milliseconds (thought to capture post-retrieval evaluation and action selection). To verify whether significant topographical effects reflected qualitative differences between distributions, any results involving significant interactions with topographical factors were replicated in re-scaled data. Mean amplitudes at representative electrodes were then subjected to ANOVA with factors of affective content (negative, neutral,

positive) and retrieval success (hit, correct rejection) for each BDNF genotype group. T-tests compared old/new effect sizes for each affective category across BDNF genotypes.

8.3 Results

8.3.1 Anxiety and depression across BDNF genotypes

The self-exclusion criteria for this study included ongoing or history of clinical psychological issues, therefore only sub-clinical levels anxiety and depression are to be expected in this sample. Met-carriers did not differ significantly from Val/Val homozygotes in either BDI scores [p=.341], trait-STAI scores [p=.462] or state-STAI scores at study [p=.295] or test [p=641].

8.3.2 Affective processing

8.3.2.1 Stimulus ratings

Both BDNF groups converged with IAPS standard valence ratings, rating negative pictures as more negative and positive pictures are more positive than the two remaining affective picture sets respectively. Both Val/Val homozygotes and Met-carriers rated negative pictures as most arousing, followed by positive pictures and then neutral pictures. However, Met-carriers were more extreme in their arousal ratings of negative pictures than Val/Val

homozygotes, a pattern that was not observed in arousal ratings for positive pictures.

Valence and arousal ratings were subjected to ANOVA with factors of affective content (negative, neutral, positive), gender (female, male) and BDNF genotype (Val/Val, Met-carrier). There was no significant main effect of BDNF genotype or interaction of BDNF genotype and affective content on valence ratings. For arousal ratings, there was a significant affective content by BDNF group interaction [F(2,102)=4.48, p=.014].

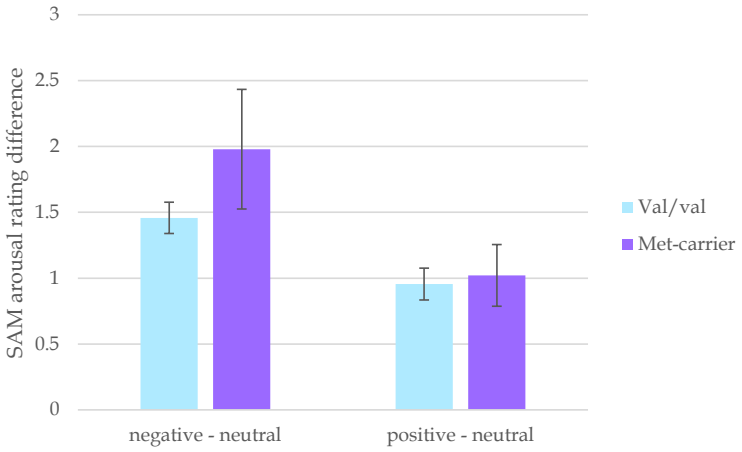


Figure 8.1 *Differences in SAM arousal ratings (1=low arousal to 5=high arousal) from neutral for negative and positive pictures split by BDNF group. Error bars indicate standard errors.*

Follow up independent samples t-tests on the difference in arousal ratings for negative and positive pictures from neutral pictures revealed a significantly larger arousal difference from neutral for negative pictures in Met-carriers than

in Val/Val homozygotes [t(53)=2.94, p=.005]. The increase relative to neutral for positive ratings did not differ significantly between BDNF groups.

8.3.2.2 Late-Positive Potential (LPP)

An affective content (negative, neutral, positive) by location (frontal, centro-frontal, central, centro-parietal, parietal) by site (left inferior[5], left medial[3], left superior[1], midline [z], right superior [2], right medial [4], right inferior [6]) by gender (male, female) by BDNF group (Val/Val, Met-carrier) ANOVA on mean amplitudes in the 400 to 1000 millisecond time window did not show a significant main effect of BDNF group or any interaction involving affective content and BDNF group.

8.3.3 Affective recognition memory

8.3.3.1 Discrimination index, response bias, remember rate

Table 8.1 below shows that both Val/Val homozygotes and Met-carriers achieved highest Pr scores for negative, followed by neutral and then positive pictures. For Val/Val homozygotes, this was driven highest hit rates for negative, followed by neutral and then positive pictures, combined with a lowest mean false alarm rate for neutral, followed by negative and then positive pictures. The same Pr pattern arose in Met-carriers as a function of highest hit rates for negative, followed by positive and neutral pictures and a

lower false alarm rate for neutral pictures than for negative and positive pictures. Response bias for both groups was most liberal for negative pictures, followed by positive and then negative pictures. Remember rates were higher for negative than for positive and higher for positive than for neutral pictures in Val/Val homozygotes. Remember rates in Met-carriers, while following the same pattern, barely differed between positive and neutral pictures.

		Picture valence		
		Negative	Neutral	Positive
Val/Val	Hit rate	0.729 (0.025)	0.637 (0.026)	0.608 (0.023)
	FA rate	0.085 (0.010)	0.076 (0.011)	0.116 (0.016)
	Pr	0.642 (0.024)	0.559 (0.022)	0.491 (0.021)
	Br	0.265 (0.033)	0.201 (0.029)	0.234 (0.029)
	Remember rate	0.567 (0.031)	0.464 (0.035)	0.488 (0.027)
Met carriers	Hit rate	0.714 (0.028)	0.644 (0.026)	0.648 (0.039)
	FA rate	0.125 (0.024)	0.072 (0.017)	0.127 (0.028)
	Pr	0.586 (0.023)	0.572 (0.023)	0.519 (0.027)
	Br	0.312 (0.051)	0.171 (0.036)	0.287 (0.055)
	Remember rate	0.606 (0.047)	0.507 (0.045)	0.508 (0.058)

Table 8.1 *Means and standard errors (in brackets) for hit rate, false alarm (FA) rate, discrimination index Pr, response bias Br and remember rate by picture valence and BDNF genotype group.*

ANOVA with factors of affective content (negative, neutral, positive), gender (female, male) and BDNF genotype (Val/Val, Met-carrier) was performed on discrimination index, response bias and remember rate. There was no significant between-subjects main effect of BDNF genotype or interaction of BDNF genotype and gender on any of the behavioural recognition memory

measures. There was no significant interaction involving both affective content and BDNF genotype on remember rates.

There was a significant affective content by BDNF genotype interaction on discrimination index Pr [$F(1.78,90.5)=4.78$, $p=.013$]. Figure 8.2 shows that while discrimination index Pr is higher for negative than for neutral pictures in Val/Val homozygotes, this difference is absent in Met-carriers.

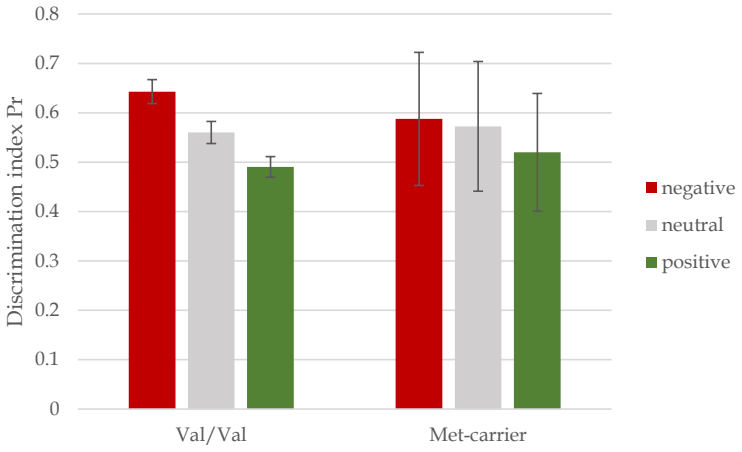


Figure 8.2 *Discrimination index Pr was highest for negative pictures and lowest for positive pictures in Val/Val homozygotes. In Met-carriers, Pr did not differ between negative and neutral pictures but is significantly reduced for positive pictures.*

Follow-up paired comparisons for each BDNF genotype confirmed significant differences between all affective categories in Val/Val homozygotes [negative vs neutral: $t(35)=4.67$, $p<.001$; positive vs neutral: $t(35)=5.40$, $p<.001$; negative vs positive: $t(35)=7.90$, $p<.001$]. Met-carriers, despite comparatively large standard

errors for all affective categories, showed significant differences in discrimination index between positive and neutral pictures [t(18)=2.77, p=.013] and between positive and negative pictures [t(18)=2.78, p=.012] but showed no significant difference in discrimination index between negative and neutral pictures.

8.3.3.2 Electrophysiological correlates of affective recognition memory

Figure 8.3 shows the differences in distributions of old/new effects between Val/Val homozygotes and Met-carriers in the 300 to 500ms time window. Visual inspection suggests stronger old/new effects for negative and neutral pictures in Val/Val homozygotes, which were frontally distributed and stronger towards the midline, while the old/new effect appears to be absent from the positive condition. Met-carriers, by contrast, showed the strongest and most widely distributed old/new effect in the positive condition, where it was apparent from frontal to parietal locations and from midline to inferior sites, with somewhat more pronounced weakening from the midline towards inferior sites in the right compared to the left hemisphere. For negative pictures, Met-carriers showed a somewhat weaker frontally distributed old/new effect comparable to those seen for negative and neutral pictures in Val/Val homozygotes, while the old/new effect in response to neutral pictures showed left-frontal distribution. Visual inspection of the waveforms and scalp maps of

the old/new effects in the 500 to 800ms and the 800 to 1500ms time windows did not suggest any apparent differences between the two BDNF groups.

Mean amplitude differences between hits and correct rejections in three time windows (300 to 500 milliseconds, 500 to 800 milliseconds and 800 to 1500 milliseconds) were subjected to ANOVA with the factors affective content (negative, neutral, positive), location (frontal, centro-frontal, central, centro-parietal, parietal), hemisphere (left, right), site (superior [1,2], medial [3,4], inferior [5,6]), gender (female, male) and BDNF genotype (Val/Val, Met-carrier). There were no significant interactions involving affective content and BDNF genotype in the two later time windows (500 to 800 milliseconds and 800 to 1500 milliseconds). In the 300 to 500 millisecond time window, a significant affective content by site by BDNF genotype interaction emerged [$F(2.09,107)=3.44$, $p=.034$]. The interaction survived rescaling [$F(2.04,115)=3.71$, $p=.027$] indicating the presence of a qualitative difference in topographies between old/new effects for different combinations of affective content and BDNF genotype. Figure 8.3 shows the distribution of old/new effects. The interaction of BDNF genotype and affective content on old/new effect sizes was strongest at superior sites.

ANOVA with factors of affective content (negative, neutral, positive) and retrieval success (hit, correct rejection) on mean amplitudes at electrode Fz did not produce a significant affective content by retrieval success interaction in either Val/Val homozygotes [$p=.163$] or Met-carriers [$p=.227$]. Paired-sample t-tests comparing mean amplitudes for hits and correct rejections at electrode Fz

for each affective content category (negative, neutral, positive) were performed separately for each BDNF genotype group. In Val/Val homozygotes, the old/new effect was significant at electrode Fz for negative [t(35)=2.66, p=.012] and neutral [t(35)=3.17, p=.003], but not for positive pictures [p=.644]. In Met-carriers, the old/new effect was significant at electrode Fz for negative [t(18)=2.50, p=.023] and positive pictures [t(18)=4.11, p=.001] but narrowly failed to reach significance for neutral pictures [p=.086]. Within the genotype groups, positive pictures elicited the smallest, and only non-significant, old/new effects in Val/Val homozygotes but the largest old/new effects in Met-carriers (see Figure 8.4).

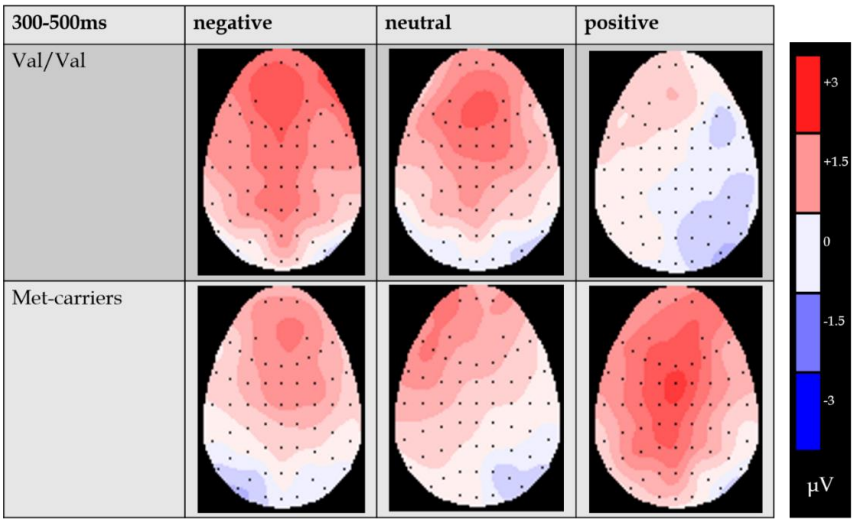


Figure 8.3 *The difference in distributions of old/new effects between Val/Val homozygotes and Met-carriers was modulated by affective picture content.*

Between-subject comparisons revealed that old/new effect sizes at electrode Fz did not differ significantly between Val/Val homozygotes and Met-carriers for negative or neutral pictures. For positive pictures, Met-carriers showed significantly larger old/new effects at electrode Fz than Val/Val homozygotes [t(53.91=2.09, p=.041].

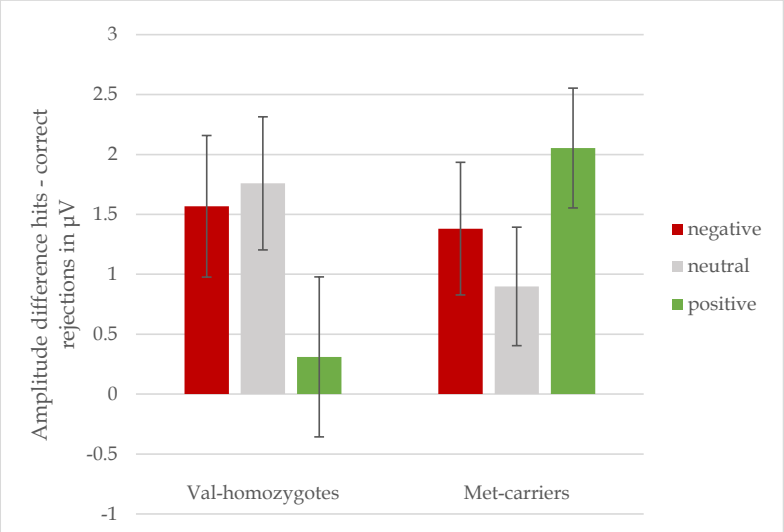


Figure 8.4 *Mean amplitude differences between hits and correct rejections at electrode Fz were significant for negative and neutral pictures in Val/Val homozygotes but for negative and positive pictures in Met-carriers.*

8.4 Discussion

It was hypothesised that the val66met modulation of affective processing and affective memory would be more pronounced in men than in women. Specifically, ERP memory effects were hypothesised to be increased more by affective content for Met-carriers than for Val/Val homozygotes, even in the absence of behavioural differences. Contrary to the first hypothesis, gender did not significantly interact with val66met genotype on any of the electrophysiological effects observed or on any behavioural measure. All participants showed differences in the affective modulation of discrimination index Pr by val66met genotype. There was no genotype influence on the difference between Pr for neutral and positive pictures, with Pr being higher for neutral than for positive pictures across genotypes. Pr for negative pictures was higher than for neutral pictures in Val/Val homozygotes only, while this difference was not significant for Met-carriers. Note that Figure 8.2 indicates much higher variability in Pr for all affective categories in Met-carriers than in Val/Val homozygotes. This is likely to be in part a reflection of the smaller sample size of 19 Met-carriers compared to 36 Val/Val homozygotes but may also indicate a genuine larger variability of memory performance in Met-carriers. Overall, val66met genotype affected Pr across genders for negative relative to neutral pictures. This is consistent with the observation that reported arousal increase for negative relative to neutral pictures is higher in Met-carriers than in Val/Val homozygotes, while reported arousal increase for positive relative to neutral pictures did not differ. The affective modulation of

Pr by positive affective content was also unaffected by BDNF val66met genotype. Genotype differences in electrophysiological correlates of memory on the other hand were observed for the affective modulation by positive content only. There was no evidence of a genotype modulation of the old/new effects between 500 and 800 milliseconds (thought to reflect recollection) or between 800 and 1500 milliseconds (thought to reflect post-retrieval evaluation). The early frontal old/new effect between 300 and 500 milliseconds was significant at electrode Fz for negative pictures across genotypes. The old/new effect for neutral pictures was significant in this time window in Val/Val homozygotes but not in Met-carriers, while the old/new effect for positive pictures was significant for Met-carriers but not Val/Val homozygotes. The stronger increase of old/new effects for positive pictures in Met-carriers than in Val/Val homozygotes is consistent with the hypothesis of a stronger affective modulation in Met-carriers. However, the selective lack of evidence for an old/new effect for positive pictures in Val/Val homozygotes, in light of a presence of the effect for neutral and negative pictures, is a novel finding and warrants further investigation.

One problem for the present study was the difference in sample sizes between Met-carriers and Val/Val homozygotes. For practical reasons, genetic information was not available before EEG recording for this study. Future studies could improve on this limitation by genotyping a bigger sample and then testing equal numbers of randomly selected participants for each genotype. This would of course raise ethical challenges pertaining to the

keeping and safekeeping of information linking participant details to their genetic information and the destruction of such linked information after the study concludes. However, despite equal sample sizes being preferable, the current study mitigated many of the limitations arising from unequal sample sizes by comparing effects for two affective categories relative to neutral within BDNF groups. While the absence of effects for all comparisons in the smaller sample would indeed make interpretation difficult, opposing patterns of selective absence of effects for one highly arousing affective category but not the other suggests a real difference between the groups. The overall sample size of the present study is another limitation, because it limits statistical power to reveal effects. Especially the size of the BDNF Met-carrier group of just 19 participants makes it likely that patterns of affective modulation of old/new effects could have been missed. Again, pre-selecting participants according to genotype could have avoided the problem of small group sizes, allowing the recording of ERP data of twice the number of participants in the Met-carrier group with unchanged cost or time expenditure.

There has been increasing evidence of an association of the Met-allele of the BDNF val66met polymorphism with changes in affective processing and vulnerability to mood disorders on the one hand and with a reduction in memory function and its brain correlates on the other. None of these associations have been universally found but in the cognitive field, a recent meta-analysis gave further weight to the notion that BDNF val66met affects memory. Modest but significant effects on BDNF val66met genotype were

found on memory performance, hippocampal volume and hippocampal activation during memory tasks in large combined samples of 5922, 2985 and 362 participants respectively (Kambeitz et al., 2012). However, Dodds, Henson, Miller and Nathan (2013) note that even these moderate effect sizes may be overestimated when it comes to fMRI evidence, due to the influence of voxel selection bias. They suggest that the problem can be avoided by selecting voxels of interest and identifying effects in independent samples. The present study presents a novel finding of a BDNF val66met influence on the affective modulation of an established electrophysiological correlate of recognition memory that differs by stimulus valence. As discussed in Chapter 1, affective memory likely plays an important part in the development and maintenance of mood disorders such as anxiety and depression. Understanding genetic influences on affective memory processes is therefore vital in better understanding individual differences in susceptibility to mood disorders. The study of ERP phenotypes in this area promises to complement and extend knowledge gained through fMRI studies by providing a tool for discerning different components of recognition memory. The present study found no evidence of a difference between genotype groups in the affective modulation of proposed electrophysiological correlates of recollection or post-retrieval processes but a differential modulation of the proposed neural correlate of familiarity by positive effect between BDNF val66met genotypes. Interestingly the affective modulation of memory by positive content differed between genotypes in ERP data, while all genetic effects obtained in behavioural data

acted on the modulation by negative affective content. This suggests a compensatory function of the neural difference between genotypes, such that larger old/new differences are necessary for positive stimuli in Met-carriers to achieve comparable behavioural output to Val/Val homozygotes.

If future research corroborates underlying anatomical or physiological differences between Met-carriers and Val/Val homozygotes necessitating compensatory neurofunctional strategies to match behaviour in healthy participants, this would have important implications for the treatment of conditions involving maladaptive affective memory. BDNF genotype could then be used as one factor informing the development of patient-specific treatment approaches, increasing the likelihood of treatment success.

Chapter 9: General Discussion

9.1 Summary of results and their theoretical implications

The research presented in this thesis aimed to answer a number of questions regarding the circumstances under which affective content modulates affective processing and memory and their electrophysiological correlates:

- Does processing of and memory for affective material differ by stimulus valence or arousal or a combination of both?
- Is the LPP an electrophysiological correlate of attention capture by affective stimuli?
- How do the effects of affective content on recognition memory change with increasing retention intervals?
- Is enhanced affective memory associated with increased attention to affective stimuli?
- Are there gender differences in affective modulation of cognitive processes and their electrophysiological correlates?
- Is there evidence for a genetic influence on affective cognition and its electrophysiological correlates?

The present chapter will summarise the findings pertaining to these research aims, discuss them in relation to the wider literature and identify theoretical implications and open questions for future research.

9.1.1 Does processing of and memory for affective material differ by stimulus valence or arousal or a combination of both?

Affective stimulus content has been shown to modulate a range of cognitive processes but often the question whether these effects are driven by stimulus valence or arousal is not addressed. In order to allow for conclusions about whether the different cognitive processes investigated are affected by all affective stimuli equally, irrespective of valence, or whether there are negativity or positivity biases in processing, the stimuli used in the experiments presented here were carefully selected based on both their valence and arousal IAPS standard values. In valence, stimuli from the three affective categories negative, neutral and positive did not overlap. Table 9.1 shows the mean IAPS standard valence ratings for negative, neutral and positive stimulus sets used in these experiments. Crucially, present participants' own ratings for each picture set were also collected within each experiment. For valence ratings, pairwise comparisons of participants' ratings confirmed a significant difference between the stimulus groups in the direction expected.

	Negative	Neutral	Positive
Set A	3.20 (0.10)	5.06 (0.03)	6.84 (0.07)
Set B	2.57 (0.04)	5.03 (0.03)	7.16 (0.04)

Table 9.1 *IAPS standard ratings for valence [Mean (SE)] for negative, neutral and positive pictures in the two stimulus sets used in the present experiments*

For arousal, the negative and positive stimuli were carefully matched and significantly higher in arousal than the neutral category (see Figure 9.1a). Here, participant ratings consistently showed a differing pattern (see Figure 9.1b). Present participants' mean arousal ratings for positive pictures were consistently significantly lower than those for negative pictures. This finding constitutes a novel demonstration of a systematic difference between participant samples' rating of the IAPS and their reported standard ratings with important implications for future research using the IAPS. It shows that standard ratings can no longer be assumed to approximate an individual sample's perception of IAPS pictures and it is crucial to collect participant ratings to confirm any stimulus categorisations on which conclusions are to be drawn. Moreover, the present finding demonstrates the need for a new, up-to-date IAPS standardisation, if the stimulus set is to continue being one of the most widely used sets in the literature. Studies using IAPS that are already published should be reviewed with a focus on whether they draw conclusions grounded in IAPS standard ratings, as such conclusions may be invalid in the absence of corroborating participants' ratings.

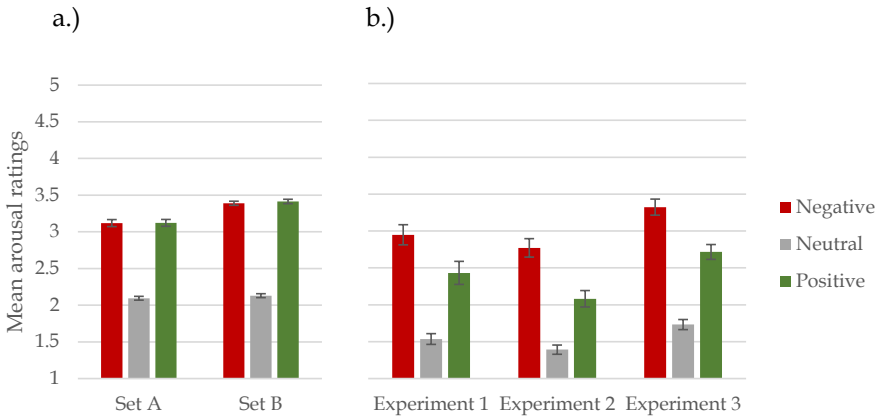


Figure 9.1 *a.) IAPS standard arousal ratings [Mean (SE)] for the two stimulus sets used, rescaled to the 5-point SAM scale used in the present experiments and b.) participants' own arousal ratings [Mean (SE)]. 1 = minimally arousing, 5 = maximally arousing. Despite matched IAPS standard arousal ratings, positive pictures were rated as significantly less arousing than negative pictures.*

In the case of the present study, the failed matching of arousal ratings lead to limitations in the ability to interpret differences in modulations of cognitive processes by negative versus positive picture content in some circumstances. Had the manipulation succeeded, a larger modulation by one affective content over the other would have shown a clear valence effect, while an equal modulation by both affective content types would have supported the view that arousal is the crucial stimulus feature. As negative pictures elicited stronger arousal than positive pictures in the present participant samples, a larger modulation by negative than by positive content is ambiguous and could have arisen from either the valence or the arousal difference between the

stimulus categories. A modulation that is larger for positive than for negative pictures can still unambiguously be interpreted as evidence of a valence effect. Equal modulations for both negative and positive picture content could suggest an all-or-nothing effect of affective content that is present for both valences but not modulated in strength by arousal. However, while less likely, it cannot be excluded that equal effect modulations for negative and positive pictures could have been caused by the interplay of a valence effect that favours positive pictures and a coexisting arousal effect.

In the case of the LPP, the answer to the question whether valence or arousal effects are the source of its affective modulation is complex. The LPP effect, the increase of the LPP in response to affective stimulus content, was consistently significant in all data presented here. However, Experiment 1 found a larger LPP effect for negative than for positive pictures, although the difference narrowly failed to reach significance. Experiment 3 found a significantly larger LPP effect for positive than for negative pictures. Although this difference in patterns is puzzling at first inspection, it provides strong evidence against a general valence effect on the LPP. Clearly the extend of the modulation of the LPP depends on factors beyond whether affective stimuli are positive or negative. It has previously been reported that the LPP increases with increasing arousal (e.g., see Schupp et al., 2000). However, the results from Experiment 3, where medium arousing positive pictures elicited significantly larger LPPs than highly arousing negative pictures (see Figure 9.1b) instead suggest an inverted U-shaped relationship. Modulation of the LPP increases from low to medium

arousal levels but when arousal gets too high, the modulation of the LPP becomes smaller again. This interpretation can also nicely account for the marginally larger LPP modulation by negative over positive pictures in Experiment 1, as reported arousal rates here were lower overall. A topographical difference between LPP effects for positive and negative pictures was also found, suggesting the involvement of different neural generators. More support for this conclusion comes from a recent combined fMRI and ERP study, which mapped variations in LPP amplitude to differences in the BOLD signal and found that different networks of brain areas correlate with LPP amplitude for positive and negative pictures (Liu, Huang, McGinnis-Deweese, Keil, & Ding, 2012). LPP amplitude for negative pictures was selectively correlated with BOLD activity in ventrolateral prefrontal cortex, insula and posterior cingulate cortex, while BOLD activity in occipitotemporal junction, medial prefrontal cortex, amygdala and precuneus selectively correlated with LPP amplitudes in response to positive pictures. Interestingly, bilateral amygdala activation was correlated with LPP amplitudes in response to positive pictures but showed an all-or-nothing response for negative pictures. If different neural networks and mechanisms are involved in the processing of negative and positive affective information, then it is possible that arousal modulates affective processing, such as that reflected in the LPP effect, differentially for the two valences. It is possible, for example, that there is a linear relationship between arousal and LPP amplitudes for positive pictures but an inverse U-shaped relationship between arousal and LPP amplitudes for

negative pictures. To test these hypotheses, future studies would need to employ much larger stimulus sets in order to be able to split each valence category into a number of arousal levels. Given a larger variety in arousal levels elicited, single trial analysis could prove useful in revealing the relationship between arousal, valence and LPP amplitudes.

Response bias Br was equally increased for both negative and positive picture content, indicating a modulatory effect of affective arousal irrespective of valence. The difference between the increase in Br for negative and positive pictures was not significant, suggesting an all-or-nothing effect of arousal. This more liberal response bias for affective compared to neutral pictures, combined with a selectively increased hit rates for negative pictures, resulted in a significantly increased discrimination index Pr for negative compared to neutral pictures. For positive pictures, the more liberal response bias for affective compared to neutral pictures resulted in a significant decrease in Pr compared to the neutral category. Consequently, the Pr modulation seems driven by a combination of a valence specific effect on hit rates and an all-or-nothing arousal effect on response bias.

The comparison of all three affective picture categories gives some confidence that a lack of difference between two categories, in light of a significant difference between two other categories, is not simply due to a lack of power. However, since arousal could not be matched, the possibility that underlying differences in arousal mediate differences in effect sizes that influence power cannot be discounted. To avoid this confound, future research requires the

inclusion of categories with distinct arousal levels that are matched closely between valences (i.e. low arousing neutral, medium arousing negative, medium arousing positive, high arousing negative, high arousing positive). Careful standardisation of stimuli for the specific study population before final stimulus selection would avoid confounds of population differences between the IAPS standardisation sample and study participants. While the commonly used IAPS stimulus set is fairly large, the selection of sufficiently large stimulus sets including several distinct groups of arousal levels can be difficult, especially when excluding stimuli containing potential confounds such as close-ups of human faces or sexual content. Ideally, future studies should instead create and use a new stimulus set composed of pictures specifically produced to vary in valence while controlling as many other aspects of the stimulus as possible (i.e. luminosity, complexity, presence of humans etc.). The IAPS set contains several stimulus pairs that vary in valence through the changing of one small detail, such as a gun being pointed at a person being replaced by a hairdryer. A new stimulus set comprised solely of stimulus triads varying small details to produce a negative, neutral and positive version of each stimulus would greatly reduce variation due to factors other than differences in affective content.

Overall, the results from affective processing, attentional disengagement and recognition memory tasks presented here show that affective valence does matter and cognitive processes are not just modulated by differences in affective arousal alone. Given the diversity of emotions even within affective

valences, negative encompassing emotions as distinct as fear, anger and sadness and positive encompassing emotions from joy to sexual arousal, a much more controlled approach may be necessary to fully understand what aspects of emotion affect cognition and by which processes. The key to this is the development of large stimulus sets that control as many confounds as possible, from basic perceptual differences like luminosity or complexity to social factors like the presence of people, and provide detailed categorisation information for any remaining potential confounds, such as for example the specific emotion elicited.

9.1.2 Is the LPP an electrophysiological correlate of attention capture by affective stimuli?

The LPP is widely accepted and used as a correlate of sustained attention to affective stimuli (e.g., see Hajcak & Olvet, 2008; Hajcak, MacNamara, Foti, Ferri, & Keil, 2013; Schupp, Flaisch, Stockburger, & Junghoefer, 2006; Weinberg & Hajcak, 2011). This interpretation is based on its similarities in time of onset and distribution to the P3 component, which has repeatedly been shown to be sensitive to differences in attention (e.g., see Patel & Azzam, 2005), and the assumption that affective stimuli differ from neutral stimuli in their intrinsic ability to capture attention, based on their increased survival value.

To test whether affective picture stimuli lead to increased LPP mean amplitudes by eliciting increased sustained attention, the present study

included not only an affective processing task during which LPPs were recorded but additionally an attentional disengagement task. Sustained attention to picture stimuli was measured by the time it took participants to disengage from the stimulus and respond to a probe presented beyond the edge of the picture. Participants also reported the level of arousal each picture elicited. If the LPP is a correlate of sustained attention which is increased in response to more arousing affective stimuli, then higher levels of arousal should coincide with longer reaction times in the attentional disengagement task and larger mean amplitudes in the LPP. Figure 9.2 below shows reported arousal levels for Experiment 3, during which both attentional disengagement and LPP data was collected. Consistent with the hypothesis that a picture's ability to hold attention varies with its arousal value, negative pictures elicited higher arousal responses than both other picture categories and were also associated with the longest reaction times for attentional disengagement. While positive pictures also elicited significantly higher arousal ratings than neutral pictures, the difference in response times for these two categories failed to reach significance, although the direction of the mean difference follows that seen in arousal ratings. If the Late-Positive Potential is a neural correlate of sustained attention then largest LPP mean amplitudes should occur in response to negative pictures, which were shown to hold attention significantly longer than either other picture category. Since the lack of statistical evidence of a difference in reaction times between neutral and positive pictures may reflect either a true underlying lack of difference of attention capturing ability or may be a result of

lack of power due to large variance in reaction times, one of two possibilities is to be expected: Either LPPs for positive pictures should not differ from those for neutral pictures (i.e. there is no LPP effect for positive affect) or mean LPP amplitude should be increased compared to neutral pictures but be significantly smaller than for negative pictures.

These hypotheses could not be supported. Instead, the increase in mean amplitude in response to affective compared to neutral pictures in the 400 to 1000 millisecond Late-Positive Potential time window was larger for positive than for negative pictures. This is a novel demonstration of evidence against the assumption that the Late-Positive Potential is an electrophysiological correlate of sustained attention in an affective context.

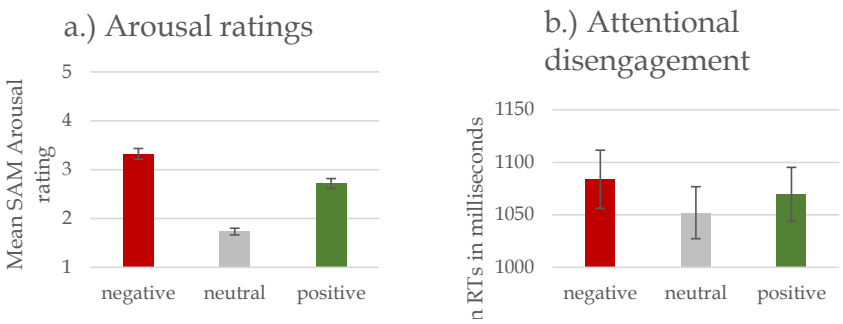


Figure 9.2 a.) Arousal ratings on the modified SAM arousal measure (1=minimally arousing, 5=maximally arousing) and b.) attentional disengagement mean reaction times in milliseconds. Arousal was significantly larger for negative pictures than positive and neutral pictures and significantly larger for positive than neutral pictures. Reaction times were significantly longer for negative compared to positive and neutral pictures but the difference between positive and neutral pictures failed to reach significance.

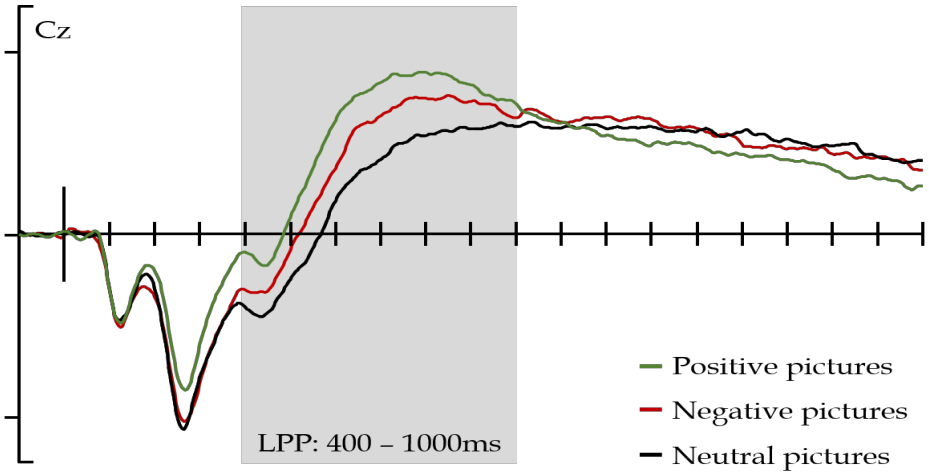


Figure 9.3 *The Late-Positive Potential for positive, negative and neutral pictures at electrode Cz. Positive pictures elicited more positive-going LPPs than negative pictures and LPPs in response to both negative and positive pictures were more positive-going than LPPs in response to neutral pictures.*

While at least negative pictures could be shown to be intrinsically more attention capturing and this is associated with higher arousal levels for negative than either positive or neutral pictures, mean LPP was significantly more increased for positive pictures, which held attention for a significantly shorter time than negative pictures. So the LPP is clearly modulated by affective content but these results provide evidence against the idea that the LPP merely tracks differences in sustained attention to affective compared to neutral pictures. This has implications both for further investigations into the nature of the LPP and for its use in affective research. Differences in LPP effects are commonly interpreted as differences in sustained attention to stimuli, an association that clearly cannot be assumed without supporting evidence in the form of other measures of attention. Moreover, even where sustained attention,

as assessed by an independent behavioural or functional imaging measure, and LPP effects correlate, a causal relationship cannot be concluded based on the present findings that the two, under certain circumstances, can be dissociated. While sustained attention and the LPP effect may share common antecedents, the LPP is clearly more than a direct electrophysiological correlate of sustained attention.

The fact that the assumption that the LPP is an ERP marker of sustained attention has been disproven here is not only of theoretical significance and therefore has consequences for research practice, it also informs, and crucially limits, practical applications of the LPP as an objective alternative to self-report in fields such as clinical psychology, marketing or teaching, at least in the context of sustained attention. While a more complete understanding of the relationship between stimulus valence and arousal and the LPP effect will likely eventually allow reverse mapping, so that conclusions about a participant's appraisal of a stimulus can be drawn from the size of their LPP effect compared to a neutral baseline, the LPP cannot be used to assess attention. Proposed applications of the LPP as an objective tool in assessing relative sustained attention to different stimulus categories, as is of use in clinical diagnosis and monitoring of therapeutic progress or in the assessment and comparison of different strategies in marketing or teaching, are therefore not possible. While differences in LPP effects likely capture information about processes partly driven by or associated with attention, the link is clearly not a direct one. Nevertheless, should future research confirm a consistent link

between stimulus arousal and the size of the LPP effect, a link which will likely differ between stimulus valences, then the LPP effect can provide a tool for assessing stimulus appraisals objectively. This is of great value especially in settings where self-reported stimulus appraisals may be skewed by social desirability or difficulty in accessing or verbalising said appraisals. While the novel demonstration of a mismatch between sustained attention and the LPP effect reported here limits its practical and research applications, it simultaneously increases the value of the LPP effect as an objective assessment tool by contributing to a more precise functional interpretation.

9.1.3 How do the effects of affective content on recognition memory change with increasing retention intervals?

Chapter 6.1 discusses the development of the affective modulation of recognition memory over time. Discrimination index Pr showed a sparing effect for affective compared to neutral pictures over time. Both positive and negative pictures were associated with a slower decline in Pr than neutral pictures. Interestingly, discrimination index Pr for positive pictures was lower than Pr for neutral pictures after 5 minutes and after one day delay but was insignificantly higher after one week, due to differences in response bias. Response bias became increasingly conservative over time for all picture categories but was more liberal for negative and positive than for neutral pictures at any test delay.

Together, these results represent evidence that rather than being a consequence of preferential encoding, affective memory effects arise as a result of slower forgetting of affective stimuli. The pattern of slower decline of affective recognition memory is consistent with two theoretical accounts. Modulatory emotional consolidation accounts (McGaugh, 2004; Sharot, Verfaellie, & Yonelinas, 2007) which propose that increased amygdala activation in response to affective stimuli modulates the consolidation of affective episodic memories in the medial temporal lobe, where they are retained. The amygdala's role ends with the completion of consolidation. This account predicts an initially slower rate of decline in recognition memory for affective compared to neutral stimuli while encoding is in progress, followed by an equal rate of decline in memory for affective and neutral material. The emotional binding account (Yonelinas & Ritchey, 2015), by contrast, proposes that the amygdala is involved in the storage of emotion-memory bindings that are formed when encoding affective stimuli. In the amygdala, emotion-memory bindings are more robust to forgetting because the rate of cell turnover is lower in the amygdala than in other memory-related brain areas. Figure 9.4 illustrates the respective predictions for the development of affective memory over time made by modulatory emotional binding accounts and emotional binding.

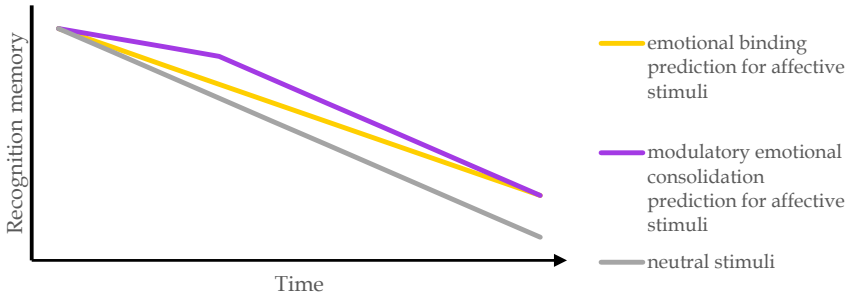


Figure 9.4 *Development of affective recognition memory over time predicted by modulatory emotional consolidation and emotional binding accounts. Yonelinas and Ritchey's (2015) emotional binding account of affective recognition memory predicts a steady rate of decline of memory for affective stimuli that is less steep than the rate of neutral memory decline. Modulatory emotional consolidation accounts predict an initially slower decline for affective compared to neutral stimuli followed by equal rates of decline once consolidation is completed.*

The number of different study-test intervals used in the present experiment is not sufficient to confidently decide between the two models. To test the predictions of modulatory emotional consolidation against those of emotional binding, a paradigm with a finer temporal resolution would be needed. A consistent increase of affective enhancement of memory performance over time would provide evidence in favour of emotional binding, while a change in the rate of increase of enhancement would support modulatory emotional consolidation accounts.

The present experiment does provide clear evidence for differences in the development of affective memory enhancement between positive and negative stimuli. For discrimination index Pr, the interaction between affective category (negative vs positive) and study-test delay on affective enhancement missed

significance but enhancement increased at the same rate for both affective categories and negative pictures were associated with higher enhancement. Given that negative pictures were rated as significantly more arousing than positive pictures, this finding is consistent with an arousal driven sparing of affective recognition memory. However, a valence-specific effect cannot be excluded based on the present data and future research including positive and negative stimulus groups with matched levels of arousal would be needed to decide whether valence plays a role in affective recognition memory enhancement. A future study to overcome these limitations would require a large affective picture set which would allow for the selection of a large set of stimuli based on arousal ratings from a sample of participants drawn from the same study population as the actual study sample. After selection, stimulus categorisation should be confirmed through ratings collected from another independent participant sample. If stimulus appraisal is consistent within the study population, a third group of participants should then complete a study phase like the one employed by the present research, followed by a higher number of recognition tests of sub-sets of stimuli at consistent intervals, such as seven recognition tests one day apart, depending on the number of matched stimuli available. Results of this experiment would allow for the increasing or decreasing of the temporal resolution of recognition tests as appropriate in order to decide between the patterns of memory sparing predicted by emotional binding and modulatory emotional consolidation accounts respectively.

9.1.4 Is enhanced affective memory associated with increased attention to affective stimuli?

As noted above, affective stimuli are commonly assumed to be attended to preferentially and previous research supports this assumption (e.g., see Gotlib & McCann, 1984; MacLeod, Mathews, & Tata, 1986). This is often cited as the reason for memory enhancements for affective stimuli, as increased attention leads to deeper processing and hence better memory. This view of affective enhancement of recognition memory posits a role of affective content during encoding only.

The present study assessed the ease of attentional disengagement from the same stimuli that were also used to assess affective modulation of memory. Comparing negative to neutral pictures, positive going effects were found in attentional disengagement, discrimination index, remember rate and old/new effects between 500-800 milliseconds. All these measures were consistently increased for negative compared to neutral pictures, suggesting an association between increased attention to affective material and increased recognition memory as assessed by behavioural and electrophysiological measures. However, the picture that emerges when considering the difference between positive and neutral stimuli is a more complicated one. Positive pictures elicited higher mean reaction times in the attentional disengagement task than neutral pictures, but the difference did not reach significance. However, recognition memory performance as measured by discrimination index Pr was significantly lower for positive than for neutral pictures, an effect in the

opposite direction of the non-significant trend seen in attentional disengagement. The proportion of remembered items, however, followed the pattern seen in attention scores, with negative pictures being recollected significantly more than neutral pictures and no significant difference between positive and neutral pictures, although the direction of mean difference matches for attention scores and remember rates. The ability of affective stimuli to preferentially capture attention is therefore associated with an increased role of recollection in recognition memory but not with memory performance, as measured by discrimination index, itself. Consistent with the negativity bias seen in attention capture and recollection, there is also a negativity bias in the old/new effects in the 500 to 800 millisecond time window, the proposed neural correlate of recollection. Taken together, the results of the present study show that increased attention to affective stimuli is not causally linked to recognition memory performance but rather to a modulation of memory quality, i.e. a higher rate of recollection. Conversely, this leads to the conclusion that increased memory performance for affective stimuli is driven by factors other than increased attention and future research must address the question of the nature of these factors.

The relationship between affective stimulus content, attention and the relative contribution of recollection to memory but not overall memory performance which was demonstrated here, has implications for the use of affect as a means to improve memory, such as in teaching. While increasing the affective salience

of material may not aide overall memory performance, it could be a useful tool for increasing recollection.

9.1.5 Are there gender differences in affective modulation of cognitive processes and their electrophysiological correlates?

Despite big advances towards equality of the genders over the last century, the stereotype of the emotional woman, compared to the logical, cerebral man, is still pervasive in today's society. Consistently with this stereotype, women are indeed significantly more vulnerable to mood disorder (Kessler, 1993; Maier et al., 1999; Weissman, 1977; Weissman, 1996) and emotion research shows that women are more emotionally reactive and expressive than men (Bradley, Codispoti, Sabatinelli, & Lang, 2001; Kring & Gordon, 1998). It is important to note, however, that both mood disorder rates and behavioural measures of emotional reactivity and expressiveness are likely to be modulated by learned, social factors. A social requirement for being "strong" will likely prevent more men than women from accessing mental health services and thus lead to an underestimation of the prevalence of mood disorders in the male population. The same social norm will likely lead to lower reported emotional reactivity where self-report measures are used. Socialisation will likely play a part in women's increased emotional expressivity. But do men and women differ in the way their brains process affective information and the way they utilise it in cognitive processing? Chapter 7 discusses this question with regard to the

measures of affective processing, attentional disengagement and picture recognition memory employed by the current study. Women reported overall higher arousal levels in response to all picture categories and were more extreme than men in their valence ratings, rating negative pictures as more negative and positive pictures as more positive than men. This may reflect a real underlying gender difference in affective experience or may be the result of a social norm for men to attenuate their self-reported affective reactivity. There was no gender difference in the slowed attentional disengagement for affective stimuli and therefore no evidence that either gender shows more increased attention to affective over neutral stimuli than the other. The LPP, which is modulated by affective stimulus content, showed topographical differences between men and women, indicating the contribution of different neural generators. Size differences in the LPP effect were also found, with women showing significantly larger LPP effects for positive than for negative pictures and no significant difference between the positive and negative condition in men. This result is a reversal of Syrjänen and Wiens' (2013) recent finding of larger LPP effects for positive over negative findings in males but not females. The apparent contradiction likely arises from their inclusion of pictures of sexual content in the positive stimulus set, which are known to be processed differentially by men and women (Bradley, Codispoti, Sabatinelli & Lang, 2001). For non-sexual pictures, women show a positivity bias in LPP effects that is absent in men.

One of the important questions relating to gender differences in affect is whether any such difference affects cognitive processes and if so, in what manner. In terms of behavioural performance, no evidence of a gender difference was found in the present study. Women and men did not differ significantly in recognition memory in terms of their discrimination indices or the relative contribution of recollection to recognition. There was evidence of a strategic difference however, with men showing overall significantly increased, i.e. a more liberal response bias than women. The gender difference on these measures was unaffected by affective picture content, however, showing a general difference in recognition memory response strategy rather than a gender difference in affective recognition memory.

In the absence of gender differences in the affective modulation of behavioural recognition memory performance, any electrophysiological differences found point to compensatory differences that ensure similar levels of functioning despite underlying physiological or anatomical differences between the sexes (De Vries, 2004). Such electrophysiological gender differences could indeed be shown for the ERP correlates of recognition memory. In females, despite increased behavioural memory performance for affective over neutral pictures, no affective modulation of the old/new effects in the 300 to 500 or the 500 to 800 millisecond time windows could be shown. Males did not show an affective modulation of the early frontal old/new effect either but showed increased old/new effects in the 500 to 800 millisecond time window compared to neutral or positive pictures. The pattern found for men is consistent with a larger

contribution of recollection to the recognition of affective compared to neutral stimuli, which was also found in remember/know judgements. However, given the lack of a gender difference in remember/know judgement patterns, the absence of these affective modulations in women is puzzling. In the 800 to 1500 millisecond time window, there was evidence of a late right-frontal effect for neutral pictures only in women and for both neutral and negative but not positive pictures in men. Men but not women showed a negativity bias in old/new effects in the recollection time window, while the electrophysiological correlates of post-retrieval processes were modulated by positive affect selectively in men, compared to the affective modulation for both negative and positive pictures in women. In other words, there is no clear negativity or positivity bias in either gender as is often postulated but rather differential effects of affective content of different valence on the ERP correlates of different memory processes.

The gender differences in electrophysiological response demonstrated here emphasise the crucial importance of accounting for gender in gaining a full understanding of the neurofunctional implementation of cognitive and affective processes. While many brain imaging studies routinely ensure a 50-50 gender split in participant samples, results are likely to be skewed by subsequent averaging. Certainly in the case of the neural correlates of affective memory investigated here, averaging across the genders produces results that are representative of neither gender. To gain useful insights into the neural correlates of affective cognition, gender should always be considered as a

factor. Only where a gender difference has been explicitly ruled out should whole sample averages be reported. This important conclusion leads to a great number of possible future directions in research. One very interesting question, for example, would be whether gender differences in the neural implementation of affective memory generalise to memory for non-affective material. Repeating now classic demonstrations of the electrophysiological correlates of familiarity and recollection with a between subjects gender factor for example could establish whether these are universal across genders or whether the correlates typically reported represent an average of two temporally or topographically different correlates from the two genders.

9.1.6 Is there evidence for a genetic influence on affective cognition and its electrophysiological correlates?

In recent years, there has been increasing evidence that small genetic differences such as SNPs play a role in individual differences in vulnerability to psychiatric disease. These differences are likely based on underlying differences in brain function and behaviour according to genotype. As Chapter 2.2 discusses, a number of SNPs have been shown to modulate affective processes and memory performance and their neural correlates in healthy populations. One such genetic difference in particular, the val66met polymorphism in the BDNF gene, has been shown to be closely linked to both differences in affective processing and cognition. Since these two domains are modulated by BDNF

genotype individually, it was hypothesised that affective cognition, meaning the modulation of cognitive processes by affective content, would also differ by BDNF genotype.

The present experiments showed no significant differences between Val/Val homozygotes and Met-carriers in depression or trait or state anxiety. Met-carriers gave significantly more increased arousal ratings in response to negative compared to neutral pictures than Val/Val homozygotes but showed no difference in attentional disengagement or LPP effect amplitudes. Discrimination index Pr was increased for negative over neutral pictures in Val/Val homozygotes but not Met-carriers. The only BDNF val66met modulation of the electrophysiological correlates of recognition memory occurred in the 300 to 500 millisecond familiarity time window. Here, the early mid-frontal familiarity effect was selectively absent for positive pictures in Val/Val homozygotes, while it was stronger and more parietally distributed than the effects for negative and neutral pictures in Met-carriers (see Figure 9.5).

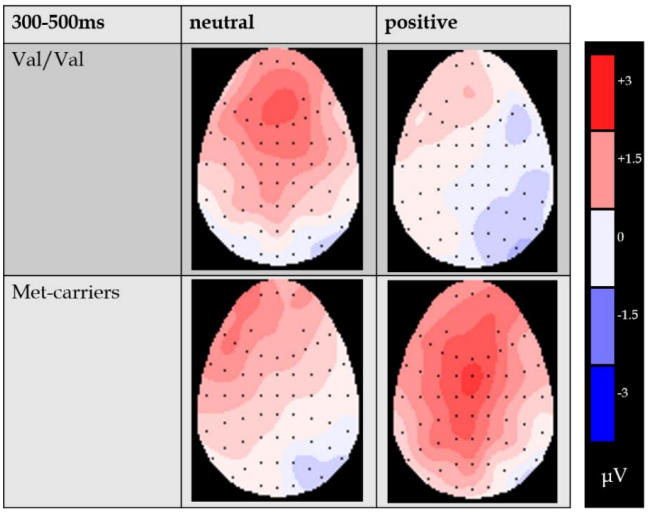


Figure 9.5 *The early mid-frontal old/new effect was selectively absent for positive pictures in Val/Val homozygotes.*

In sum, the only effects of genotype on behavioural measures acted on the difference between negative and neutral pictures: Met-carriers gave higher arousal ratings only for negative pictures than Val/Val homozygotes and showed no difference in discrimination index for negative and neutral pictures, while Val/Val homozygotes performed significantly better for negative than neutral pictures. Both genotype groups had higher discrimination index scores for neutral than for positive pictures. The difference in old/new effects for positive pictures in the 300 to 500 millisecond window did therefore not produce a difference in recognition memory.

The higher levels of arousal Met-carriers reported in response to negative pictures add to previous findings that Met-carriers suffer from anxiety disorders more frequently than Val/Val homozygotes. Participants in the

current study all had anxiety levels well below the threshold for clinical diagnosis and yet a higher reactivity to negative pictures was shown for Met-carriers. This higher reactivity is likely to contribute to a higher vulnerability to anxiety disorders, as it means that, given matched environments, Met-carriers with experience more stress than Val/Val homozygotes. Interestingly, Met-carriers' higher reactivity to negative stimuli was not coupled with a more pronounced increase in memory performance for negative compared to neutral pictures. Instead, no benefit of negative over neutral pictures could be shown in memory performance in this group, while Val/Val homozygotes showed such a benefit, as expected. Given the amygdala's well documented involvement in affective memory modulation, this finding is consistent with the reported smaller amygdala volume (Montag, Weber, Fliessbach, Elger, & Reuter, 2009) and higher age-related amygdala decline (Sublette et al., 2008) in Met-carriers. Future research comparing different age groups of Met-carriers and Val/Val homozygotes is needed to confirm whether affective reactivity and affective memory changes across the lifespan differ by BDNF genotype.

The demonstration of a difference in the electrophysiological correlates of recognition memory according to a genotype difference in a single SNP is remarkable. In demonstrates the value of the ERP method in the study of individual differences in genotype and their consequences for brain function and behaviour. Ultimately, this approach will advance the field of cognitive neuroscience by allowing a move away from noisy averages and towards more precise, personalised models which will uncover relationships between neural

function and behaviour normally masked by the averaging of sub-groups of participants whose responses may differ systematically.

9.2 Conclusion

The overall aim of the present research project and thesis was twofold: To increase understanding of affective modulation of cognitive processes and their electrophysiological correlates on the one hand and to explore the role of gender and genetic differences in this affective modulation on the other. It was shown that both sustained attention, as measured by the time required for attentional disengagement, and the LPP are modulated by affective content. But different patterns of effect strength for negative and positive pictures show clearly that the LPP is not, as widely assumed, an electrophysiological correlate of sustained attention. Affective picture content was shown to modulate recollection but not familiarity. Instead of the left-parietal electrophysiological correlate of recollection typically reported for words, the present study showed a fronto-central recollection effect for pictures. Consistent differences between reported IAPS standard ratings and the valence and arousal ratings obtained from participants in the present experiments highlight the need for participant self-report as part of any experiment using IAPS stimuli, as well as the more general need for a new, more controlled affective picture stimulus set.

Also reported here are two novel demonstrations of individual differences in affective modulation of recognition memory. The affective modulation of the

late right-frontal ERP effect differs by gender but is not associated with a behavioural gender difference. Comparisons of BDNF Val/Val homozygotes with Met-carriers found behavioural memory differences for negative pictures but a genotype difference in the modulation of the familiarity effect for positive pictures. Despite being limited by practical constraints on sample sizes, the present study demonstrates the utility of event-related potentials in exploring individual differences in affective and cognitive processing, as well as the need for a better understanding of individual differences in affect and cognition.

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"I'm sciencing as fast as I can"

Professor Hubert J. Farnsworth,

Bender's Big Score, 2007