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Abstract

Autobiographical memories are often seen as the building blocks of mental simulation and therefore recruit brain regions remarkably similar to the default mode network (DMN). Traditionally, the impact of emotional content on a personal memory is associated with the contribution of valence and emotional arousal. So far, very little attention has been paid to the role of structural differences within the DMN or a retrieval network for emotional personal memories. The objective of this study was to examine the possible structural characteristics and variabilities within regions of the DMN crucial for emotional autobiographical memory between healthy participants that is associated with intensity and valence. Regional differences in gray matter volume were examined with the General Linear Model using voxel based morphometry (VBM) and DARTEL registration. Positive valence demonstrated a significant correlation with greater gray matter volume in the right inferior frontal gyrus and the hippocampus/parahippocampal gyrus, regions crucial for recollection, memory access and memory construction processes. Negative valence showed gray matter enhancement in the left medial frontal gyrus. VBM regression analysis revealed that low intensity showed significant greater gray matter volume in the main hubs of the DMN, namely in the right posterior cingulate cortex, left inferior temporal gyrus and the medial frontal gyrus, with negative valence highlighting almost the same prefrontal region. Results from this study showed structural variability across a variety of regions being engaged in retrieval mechanisms of autobiographical memory associated with the MTL-subnetwork, dorsal medial PFC subsystem and the main hubs within the DMN.

Keywords: VBM, autobiographical memory, valence, intensity, default mode network

Zusammenfassung

Autobiographische Erinnerungen werden häufig als grundlegende Voraussetzung für die intrinsisch generierten Gedankengänge des neuronalen Default Mode Netzwerkes (DMN) angesehen. Der emotionale Gehalt einer persönlichen Erinnerung unterscheidet sich traditionell auf zwei Ebenen, der Valenz und der Intensität eines Ereignisses. Bisher wurde struktureller Variabilität auf neuronaler Ebene innerhalb des DMN in Bezug auf das Abrufen emotionaler persönlicher Erinnerungen wenig Aufmerksamkeit geschenkt. Das Ziel dieser Studie war es, die strukturelle Variabilität zwischen gesunden Probanden in Abhängigkeit der Variablen Valenz und Intensität zu untersuchen. Regionale Unterschiede im Volumen der grauen Hirnsubstanz wurden mittels voxel-basierter Morphometrie (VBM) und DARTEL untersucht. Positive Valenz korrelierte signifikant mit höherem Volumen grauer Hirnsubstanz im inferioren frontalen Gyrus und im Hippocampus sowie parahippocampalem Gyrus. Diese Regionen werden mit der Rückerinnerung als auch mnestischen Zugangs- und Konstruktionsprozessen assoziiert. Negative Valenz korrelierte mit größerem Volumen der grauen Hirnsubstanz im linken medialen frontalen Gyrus. Des weiterem konnte gezeigt werden, dass geringere Intensität mit signifikant höherem Volumen der grauen Hirnsubstanz in den Kernbereichen des DMN, dem posterioren cingulären Cortex, dem inferioren temporalen Gyrus und dem medialen frontalen Gyrus korrelierte. Insgesamt zeigen die Ergebnisse dieser Studie strukturelle Variabilität innerhalb vieler Regionen des DMN und seiner Subsysteme, die mit mnestischen Mechanismen des autobiographischen Erinnerns in Verbindung stehen.

Schlüsselwörter: autobiographisches Gedächtnis, Valenz, Intensität, Default Mode Netzwerk

Contents

Introduction

Memories of one's own life are "of fundamental significance for the self, for emotions and for the experience of personhood" (Conway & Pleydell-Pearce, 2000, p. 261). In the current literature, a precise definition of autobiographical memories remains elusive. Based on a classification of declarative memory by Tulving (1972), they are often seen as episodes, consisting of semantic and episodic elements (Spreng, Mar, & Kim, 2009; Williams, Conway, & Cohen, 2007). According to Tulving (1987), we process, encode, consolidate, and retrieve information in multiple memory systems. The semantic memory system refers to general knowledge about the world, storing facts about life in form of schemata or categories. In contrast, episodic memory is about recalling personally experienced events with an exact spatiotemporal reference, meaning the particular experience took place at a unique point in life, in an explicit place. Extending this theory on autobiographical recall, a few inconsistencies emerge. As stated by Williams et al. (2007) the distinction between semantic knowledge and individual features forming an episodic event become blurred when examining a full autobiographical experience. Semantic information is formed from a personal memory by abstraction or generalization; personal episodic details of a particular memory get integrated into the semantic general knowledge system by generating scripts and schemata (Williams et al., 2007). Showing the impact of the interactive relation of these systems on autobiographical remembering. However, Tulving (1985) later extended this classification, including the concepts of familiarity and recollection. Familiarity refers to the feeling of being intimately connected to the memory when retrieving personal semantic knowledge, which has been described as 'noetic awareness' (Tulving, 1985). The recollection of a variety of different types of information when recalling an episodic event is connected to the feeling of re-experiencing, which has been termed 'autonoetic conciousness'. Often referred to as 'mental time travel', (Conway & Jobson, 2008; Schacter et al., 2012; Spreng et al., 2009; Suddendorf & Corballis, 2007; Tulving, 1985, 2002) this concept implies that "the self being remembered is the same self engaged in recollection" (Spreng et al., 2009, p. 490). Thus, the unique feature of episodic events (or autobiographical memory in general) is the re-collective experience as pointed out in the self-memory system (SMS) proposed by Conway and Pleydell-Pearce (2000).

This conceptual framework about the (re)construction of autobiographical memories, consists of two major elements: the ’working self’ and an ’autobiographical knowledge base’. The working self is thought of as control/processing system (Conway & Jobson, 2008) and can be seen as dynamic part of the self, comprised of a set of currently active goals and images of the self. Therefore, it regulates the construction of memories by modulating the access to an autobiographical knowledge base (Williams et al., 2007). This is achieved by shifting and altering cues so that specific information can be evoked. The autobiographical knowledge base contains two different entities, highlighting different levels of specificity in the wide range of autobiographical retrieval. ’Autobiographical knowledge’ provides information of the past, present and future self, ranging from very abstract to event-specific frames of information (Conway & Jobson, 2008). It is arranged hierarchically, with lifetime periods (e.g., when I was in school) at the top, followed by general autobiographic events. These are more specific and include repeated events or a sequence of related events (Conway & Pleydell-Pearce, 2000). The second entity of the knowledge base incorporates episodic memories (as defined in Tulving’s original theory, 1985).

To successfully recollect a specific autobiographical memory, it is necessary for these entities to interact on their multilayered indexes (for example life-theme: school time; general events: breaks between classes) to form a cluster of activation that is connected to a unique episodic event (for instance, the time when Christian broke his leg during a break in elementary school; Conway & Pleydell-Pearce, 2000; Williams et al., 2007). This constructivist approach to autobiographic memory retrieval assumes that personally relevant memories are (re)constructed from knowledge stores differing in levels of specificity, rather than each being stored as a complete record of an event. In addition, the retrieval is seen as an iterative process (Cabeza & Jacques, 2007), relying on self-referential processing, as well as search and monitoring procedures (more on that in the neural basis section).

In line with Tulving’s theory (1985) of autonoetic consciousness, Spreng et al. (2009) state that scene construction and self-projection seem to be most relevant for experiencing an autobiographic recollection in full. Others note the important role of autobiographical memories in social interactions. As Cohen (1998) pointed out, they supply us with topics of conversation and help us to empathize with others. This view is supported by a review from Bluck (2003) highlighting the significant contribution of autobiographical memories to social bonding throughout life. Such memories for personal experiences come along with several phenomenological characteristics. They are associated with higher levels of vividness and emotion, accompanied by more sensory and perceptual details and different stages of specificity (Cabeza & Jacques, 2007; Conway & Jobson, 2008, 2012; for a review see Holland & Kensinger, 2010).

Neural Basis of Autobiographical Memory

Existing research strongly suggests that the medial temporal lobe, especially the hippocampus formation, plays an important role in encoding, consolidation, and retrieval of autobiographical memories. It is not surprising then, that the medial temporal lobe and the hippocampus are often seen as the hub of an autobiographical memory retrieval system (Holland & Kensinger, 2010; Moscovitch et al., 2005; Svoboda, McKinnon, & Levine, 2006). The main advantage of including paradigms of autobiographical experiences into memory research is that one can address questions regarding consolidation theories by looking at differences between recent and remote memories. The traditional consolidation theory states that hippocampal representations of long-term memories become independent of the hippocampus through the establishment of a neocortical representation of these memories over time (Moscovitch, Nadel, Winocur, Gilboa, & Rosenbaum, 2006). In opposition, Nadel and Moscovitch (1997) argue that the hippocampus is permanently involved in the retrieval of memories, regardless of their remoteness.

According to the multiple trace theory (Moscovitch et al., 2005) the hippocampus is viewed as a 'pointer' to cortical regions that stored the different details and features of an event. The hippocampus formation binds and indexes this information in an organized way, so that it later can be retrieved. Hence, hippocampal damage leads to anterograde and retrograde amnesia, by preventing the binding and indexing of new information and the destruction of existing pointers impairing the coordinated re-experiencing of an event (Moscovitch et al., 2005). The authors even propose that "recollection of autobiographical episodes . . . will always depend on the hippocampus. Recognition of ... aspects of emotions will be impaired, following amygdala lesions. In addition, in recollecting an autobiographical episode, damage to these structures should lead to loss of the information mediated by these extra-hippocampal structures." (Moscovitch et al., 2005, p. 43).

Converging evidence strongly supports the idea that memories are not stored in a particular region, but rather in an activation network over several cortical regions (Cabeza & Jacques, 2007; Svoboda et al., 2006). The neuronal pattern underlying the recall of a specific memory are strongly dependent on the types of information being retrieved, which can be shown by an overlap of activation during encoding and retrieval of an autobiographical event. This phenomenon has been defined as 'recapitulation of activity' (Buchanan, 2007; see also Holland & Kensinger, 2010) and has been shown to be evident for a variety of sensory-specific cortex regions (see Kahn, Davachi, & Wagner, 2004; Wheeler, 2005; Wheeler, Petersen, & Buckner, 2000). For example, Wheeler et al. (2000) showed activity of visual cortices for the recollection of visual information during retrieval. Buchanan (2007) argues that in the same manner emotional context for a specific episodic event could be related to retrieval based activation within structures crucial for emotional processing. However, extensive research shows that besides the specific activations of different types of information there is also a core set of brain regions being generally activated during autobiographic retrieval. Recent meta-analyses indicate that in addition to the hippocampus this standard autobiographic memory network consists of regions in the medial and lateral prefrontal cortex, in the medial and lateral temporal cortices, the temporoparietal junction, the posterior cingulate/retrosplenial cortex and in occipital and cuneus/precuneus regions (Cabeza & Jacques, 2007; P. L. Jacques, 2012; Spreng et al., 2009; Svoboda et al., 2006).

The core network shows a stronger left-lateralized activation (Cabeza & Jacques, 2007; Maguire, 2001) and additionally seems to be modulated by qualitative aspects of a memory (such as emotion, vividness, significance, amount of details). Lateral and ventromedial frontal lobe structures, which have been connected to memory search processes and post-retrieval monitoring, interact with medial frontal regions, which are associated with self-referential processing (Cabeza & Jacques, 2007; Holland & Kensinger, 2010; P. L. Jacques, 2012) in terms of autonoetic consciousness defined by Tulving (1985). Recollection seems to be mediated by the hippocampus, as mentioned above, and the retrospenial cortex. Occipital and parietal regions (namely sensory visual cortex, cuneus/precuneus) underlying visual imagery and orienting attention to internal representations and may cause the feeling of re-experience of an autobiographical event (Cabeza & Jacques, 2007; Holland & Kensinger, 2010).

Svoboda et al. (2006) further demonstrate an altered pattern of brain activity for emotional characteristics of autobiographical retrieval. For one this network is congruent with the standard network mentioned above but shows stronger bilateral and emotion-specific activations. These findings are in line with the assumption of preferential right hemispheric involvement in emotional processing and social cognitive processes. Moreover, a greater amount of deactivation in regions associated with cognitive processing has been found (Svoboda et al., 2006). Additionally, activation patterns are also including the amygdala, which is believed to modulate the encoding and retrieval of emotional information of a memory, the insular cortex, which is sensitive for emotional representations and the orbitofrontal cortex.

Autobiographical Memory System and Default Mode Network

Recently, researchers have shown an increased interest in resting-state functional connectivity analyses to study neural networks on a macro-architectural level. This is achieved by measuring interdependent temporal patterns of functional activity at 'rest', meaning participants are not occupied with a specific task (Damoiseaux et al., 2006; Fox & Raichle, 2007; Greicius, Krasnow, Reiss, & Menon, 2002). The last two decades have seen a growing trend towards patterns of connectivity, pointing towards a core set of brain regions engaged in stimulus-independent thought (Spreng & Grady, 2010), called the 'Default Mode Network' or 'DMN' (Damoiseaux et al., 2006; Raichle et al., 2001; for a review see Andrews-Hanna, 2011; Buckner, Andrews-Hanna, & Schacter, 2008). Among the first to describe this network was a meta-analysis conducted by Shulman et al. (1997), examining task induced deactivation. Their results showed a stable pattern of brain regions being generally active during the passive task condition 'rest' versus goal directed tasks (see also Buckner et al., 2008). Core regions of the DMN included the medial prefrontal cortex (mPFC), posterior cingulate cortex (PCC) and retosplenial cortex (Rsp), inferior parietal cortex (IPC) and medial and lateral temporal lobe structures (MTL/LTL) including the hippocampus (Shulman et al., 1997).

Several studies have documented that the DMN refers to a set of brain regions being negatively correlated with goal directed behavior and external perceptual actions (Damoiseaux et al., 2006; Raichle et al., 2001; for a review see Buckner et al., 2008). But as Andrews-Hanna (2011, p. 255) argues, when examining task induced deactivations the presence or absence of brain regions should “be interpreted in the context of the experimentally directed task and should not be used as the sole definition of the regions that comprise the default network", leaving the question in which processes the DMN does engage unanswered. Buckner et al. (2008) review that the DMN functions to process and control self-relevant mental simulations in order to prepare for as well as evaluate upcoming future events.

As research in the field extended, different approaches have been used to investigate the underlying behavioral and cognitive features of the DMN. Spreng et al. (2009) demonstrated in a quantitative meta-analysis of fMRI studies on autobiographical memory, theory of mind, navigation and the default mode, that conformity was found, consistent with the proposed DMN, within the medial-temporal lobe, precuneus, posterior cingulate, retrosplenial cortex, and the temporo-parietal junction as well as lateral prefrontal and occipital cortices. Autobiographical memory in particular was associated with left-lateralized involvement of the frontal lobe (especially MPFC, MFG, SFS and rACC), the parietal lobe (Precuneus, TPJ, and posterior cingulate cortex PCC) and the temporal lope (STS, ITS, hippocampus H, parahippocampal cortex PHC, amygdala AMG, middle temporal gyrus MTG). In the right hemisphere tasks involving autobiographic memory have been demonstrated to recruit the middle frontal gyrus MFG and temporal lobe with parahippocampal cortex PHC, hippocamus H, amygdala AMG, middle temporal gyrus MTG, superior temporal sulcus STS and temporo-parietal junction TPJ (Spreng et al., 2009).

To further evaluate these findings, Spreng and Grady (2010) examined the neural mechanisms underlying autobiographical memory, prospection, and theory of mind within the DMN in an fMRI study. Results showed an overlap of activity for autobiographical memory and prospection in frontal and parietal midline and medial temporal lobe structures in comparison to theory-of-mind. Additionally, the hippocampal formation showed essential importance for autobiographical memory and prospection. This finding is consistent with the greater re-collective features involved in these mental states (Hassabis, Kumaran, & Maguire, 2007; Spreng & Grady, 2010). Therefore, the DMN is postulated as crucial for reconstructing and re-experiencing a personal event (mental time travel see Conway & Jobson, 2012; Spreng et al., 2009; Tulving, 1985), envisioning the future, or imagining oneself into the minds of others (Buckner et al., 2008; Spreng & Grady, 2010). The extensive research findings of a more generally DMN engaged in self-referential thoughts led to the assumption that these regions are necessary for an autobiographical memory system but not specific to it, and rather support more general cognitive functions (see review by Schacter, Addis, & Buckner, 2007). The reconstructive properties of autobiographical memory can be seen as an important feature of the DMN, allowing past experiences to guide current behavior and plan for the future (Dudai & Carruthers, 2005; Holland & Kensinger, 2010). These findings are consistent with the results from the studies of Buckner et al. (2008) as well as Svoboda et al. (2006) and highlight a set of regions for autobiographical memory remarkably similar to the default network including MPFC, PCC/Rsp, MTL, including PHC and the HF. Among the first to describe this overlap was a PET-study investigating focused and random episodic memory (referring to free association used during analytic therapy) compared to a semantic memory control task (Andreasen et al., 1995).

According to Andrews-Hanna, Reidler, Sepulcre, Poulin, and Buckner (2010), the DMN consists of multiple components that are best understood as functionally and anatomically distinct “interacting subsystems” (Buckner et al., 2008, p. 1). A ’dorsal medial prefrontal network’ (Andrews-Hanna et al., 2010; Schacter et al., 2012), which is associated with self-referential processing and involves dorsal medial prefrontal cortex (dmPFC), lateral temporal cortex (LTC), temporal parietal junction (TPJ) and the temporal pole (TP). The other network comprises the hippocampus (H), parahippocampal cortex (PHC), Retosplenial cortex (Rsp), ventral medial prefrontal cortex (vMPFC), and ventral parietal regions, referred to as the ’medial temporal subsystem’ (Andrews-Hanna et al., 2010; Buckner et al., 2008) or ’parieto-temporal subsystem’ (Kim, 2012). The ’MTL network’ supports memory retrieval and manages the construction of mental scenarios from past events. These two systems converge on the most important ’hub’ regions of the DMN, namely posterior cingulate (PCC) and the anterior MPFC (Andrews-Hanna et al., 2010; Buckner et al., 2008; see also Schacter et al., 2012).

It seems likely that autobiographical memory can be seen as a basic function of the default mode network when looking at the tasks that have continuously activated the DMN. When participants are asked to remember a personal past event the recollective experience (as pointed out above in the term ’autonoetic awareness’ defined by Tulving (1985) (see also Cabeza & Jacques, 2007) and ’scene construction’ (Hassabis & Maguire, 2007; Schacter et al., 2012; Spreng et al., 2009) are thought of as key-features activating both the DMN and the retrieval network. These important processes probably reflect self-referential processing involved in such mental simulations, which can be linked to the ’hubs’ of the DMN, PCC and anterior MPFC, as well as to the ’dorsal medial PFC-subsystem’ (Andrews-Hanna et al., 2010; see also Schacter et al., 2012). Recent research findings revealed that the posterior cingulate and the anterior medial prefrontal cortex are functionally connected to all other brain regions - and subsystems - comprising the DMN (Andrews-Hanna et al., 2010; Buckner et al., 2008). They are involved in a great amount of self-referential behaviors, their activity being significantly correlated with personal significance, mentalizing about one self or experiencing affect (Andrews-Hanna et al., 2010). Their activity is greater for real memories in opposition to imagined ones (Hassabis et al., 2007; Summerfield, Hassabis, & Maguire, 2009), and the anterior mPFC is thought to mediate self-referential information in memory, raising its activation proportional to self-relevance incorporated by the stimulus shown (Macrae, Moran, Heatherton, Banfield, & Kelley, 2004). Another finding supporting this theory is the preferred activation of the anterior medial PFC for autobiographical memory versus laboratory- based episodic retrieval (Cabeza & Jacques, 2007). In addition, both structures have been related to affect processing, engaging in negative emotions and pain (see Andrews-Hanna, 2011) as well as reward processing, suggesting contribution to the “valuation of personally significant affective information” (Andrews-Hanna, 2011, p. 262).

The dorsal medial PFC system, however, seems to be more engaged in social information and is associated with “introspecting about mental states” (see Andrews-Hanna, 2011, p. 262). Specifically, this subsystem of the DMN is associated with the concept of ’theory of mind’ (Spreng & Grady, 2010) also defined as ’mentalizing’ (Andrews-Hanna, Smallwood, & Spreng, 2014; Schacter et al., 2012). As Spreng et al. (2009) state, mentalizing plays an important role in autobiographical remembering and recent research suggests involvement of the dorsal medial subsystem when evaluating on autobiographical episodes in a more general, meta-reflective manner (D’Argembeau et al., 2013). The authors further show influence of social relationships on autobiographical memory with a great amount of personal self-defining experiences including other people’s presence and mental states.

The ’MTL-Subsystem’ (Andrews-Hanna, 2011) along with the PCC has been shown to be involved in autobiographical memory retrieval (or memory retrieval in general) in a variety of studies (Cabeza & Jacques, 2007; Spreng et al., 2009; Svoboda et al., 2006). Other analyses show this network is associated with prospection/imagining the future and navigation (Spreng & Grady, 2010; Szpunar, Watson, & McDermott, 2007), additionally highlighting the common neural activations of these processes. Taking into account all the evidence this suggests the hypothesis that the MTL-subsystem functions as basis for mental simulation, therefore engaging in scene-construction, to prepare for future events in the present (Andrews-Hanna, 2011). Scene-construction incorporates the retrieval of semantic, episodic and contextual details as well as a subsequent integration of these details into a consistent temporal and spatial scope. Thus, the specific role in autobiographical memory retrieval seems to be 'memory-based construction', in the form of providing a spatio-temporal framework for episodic details (Andrews-Hanna et al., 2014).

Overall, there seems to be some evidence to indicate that the act of remembering one's own life incorporates all these subsystems working within the frame of a DMN. To further examine the functional specificity of the proposed subsystems and its role in 'autobiographical thought' Andrews-Hanna et al. (2014) conducted a multiple neuroimaging study, examining two aspects thought essential in autobiographic memory, episodic retrieval and mentalizing. Results across three different approaches (fMRI, resting state connectivity and meta-analyses of fMRI studies using neurosynth) demonstrated distinct clusters of activation involved in episodic retrieval and mentalizing, with the first activating the 'MTL network' and the PCC. Mentalizing was generally associated with the 'dorsal medial subsystem' as well as the PCC, ventral MPFC and anterior temporal cortex regions including the amygdala. The important finding was that autobiographical tasks showed an overlapping pattern of activity in both networks.

All of the studies reviewed here support the hypothesis that recalling past memories comprehends multiple (interacting) tasks mediated by the two subsystems and their hubs. Such as: retrieval of episodic and semantic details of autobiographical knowledge, bringing these specific details into a right spatial and temporal frame and evaluating on one's own as well as others emotions and significance contributing to the particular memory (Andrews-Hanna et al., 2014). In addition to its major role in self-generated thought, various dynamic interactions with other large scale brain networks have been reported for the DMN (Andrews-Hanna et al., 2014; Menon, 2015), namely the dorsal attention network (DAN), the frontoparietal control network (FPCN) and the salience network (SN). The dorsal attention network (DAN) encompasses the frontal eye fields, inferior precentral sulcus, superior occipital gyrus, superior parietal lobe and the middle temporal motion complex (Andrews-Hanna et al., 2014) and is associated with visuospatial processing. Anticorrelations between the DMN and DAN have been observed, meaning activity of the DAN results in deactivation of the DMN. This interactive relationship is thought of evidence for the dichotomy between internal forms of attention, such as autobiographical thought engaging the DMN and external forms of attention, such as processing environmental stimuli. A process called perceptual decoupling (Menon, 2015). The frontoparietal control network (FPCN) however, shows a different pattern of correlations and anticorrelations wih the DMN and DAN, depending on the kind of task involved. Main hubs of the FPCN include dorsolateral prefrontal cortex, inferior anterior parietal lobe and posterior parietal cortex regions. This central-executive network is involved in maintaining and mediating working memory and goal directed processes through cognitive and executive control of attention (Andrews-Hanna et al., 2014; Menon, 2015). Spreng, Sepulcre, Turner, Stevens, and Schacter (2013) could show the FPCN is involved in tasks such as autobiographical planning and visuospatial planning, while the former task additionally engaged the DMN (leaving the DAN anticorrelated with the FPCN) and the later the DAN (leaving the DMN anticorrelated with the FPCN). During autobiographical planning, coupling between DMN and FPCN was observed when reflecting on the necessary components to achieve a personal aim. This fits well into the current opinion that these large-scale networks act in cooperation to achieve certain operations. When involving the DMN this special operations “reflect temporally extended evaluation of self-generated thought” (Andrews-Hanna et al., 2014, p. 40) and this is where the salience network (SN) fulfills its purpose.

The salience network (SN) is a higher order core brain system that engages in behaviorally significant stimulus detection as well as focusing and reorienting attentional resources to salient information in order to perform on goal-directed tasks (Menon, 2015). Therefore, salient information detected by the SN encompasses “surprising stimuli and stimuli that are pleasurable and rewarding, self-relevant, or emotionally engaging” (Menon, 2015, p. 597). The SN includes the anterior insula (AI), the dorsal anterior cingulate cortex (dACC) as well as subcortical limbic structures such as the amygdala, ventral striatum, dorsomedial thalamus and hypothalamus, which show strong intrinsic connectivity (Menon, 2015). The AI subserves many different functions, but its key role lies in saliency detection. The subcortical structures seem to be responsible for the emotional and reward-related saliency of information and the dACC engages in conflict monitoring and response selection processes. But the salience network is also involved in reorienting attentional resources and therefore is a responsible candidate for the dynamic switching between external attention processing by the lateral frontoparietal control network (FPCN) and internal forms of attention maintained by the DMN (Menon, 2015). Bressler and Menon (2010) proposed that, during cognitive demanding tasks the SN recruits the FPCN, while suppressing DMN activity in order to keep attention focused. A remaining question for future research is whether the SN can enhance DMN activity for salient intrinsic information. Andrews-Hanna et al. (2014) argue that the ventral PCC could be involved in salient internal representations. J. P. Hamilton, Farmer, Fogelman, and Gotlib (2015) propose that the ventromedial prefrontal cortex (vmPFC) and the posterior cingulate cortex (PCC) attribute valence to internal representations and subsequently elaborates on them proportional to the intensity of the attributed valence in a self-centered manner. Thus, J. P. Hamilton et al. (2015) state, that the DMN and SN counterpart each other.

Emotional content of autobiographical memory

As was mentioned in the previous chapter, extensive research reported shared clusters of connectivity and activation in brain regions within distinct subsystems of the default mode network related to autobiographical tasks. An objective of this study was to examine the possible structural characteristics and variabilities within this network during the retrieval of autobiographical memories that are strongly emotional. Traditionally, the impact of emotional content on a personal memory is associated with the contribution of two main factors, namely the impact of valence (pleasantness: positive or negative) and emotional arousal (i.e., intensity felt during the experience).

Retrieval of emotional memories from one's own personal past comes along with many different features. Individuals report them with greater feelings of vividness and richness at recollection, reflecting the conceptual state of 'autonoetic awareness' (Tulving, 1985; see also Holland & Kensinger, 2010). In addition, emotional memories differ in levels of specificity and show less probability to be forgotten than neutral ones (Berntsen & Rubin, 2002). Recent studies in the field indicate that arousal during an emotional experience has a stronger influence on vividness and richness at retrieval than experienced valence (Berntsen & Rubin, 2002; Bohanek, Fivush, & Walker, 2005; Ford, Addis, & Giovanello, 2012; Talarico, LaBar, & Rubin, 2004).

Regardless of the research findings examining the role of arousal in autobiographical memory retrieval different findings have been reported concerning valence. For example, Talarico, Berntsen, and Rubin (2009) found that positive valence of a retrieved event was accompanied by more incidental or peripheral details of that event. In a study conducted by Kensinger and Schacter (2006) positive memories were accompanied by more sensory details and Talarico et al. (2004) found greater appraisals of vividness and recollective qualities for positive versus negative events. One possible explanation for this enhancement could be that positive memories serve as a basis for self-conceptual thought and social interactions (Rasmussen & Berntsen, 2009; see also Ford et al., 2012). This would be in line with the prior identified key features of autobiographical retrieval: self-referential processing and introspection about mental states of others (Andrews-Hanna, 2011) and possibly could be linked to their neural underpinnings.

However, the negative valence of personally experienced events shows different characteristics. Negative emotional memories are recalled with more crucial information of the to be remembered event (Talarico et al., 2009). Furthermore, Kensinger and Schacter (2006) found that when contrasting positive and negative narratives of an identical public experience (a baseball game), the negative experience led to more specific details and higher memory accuracy. One possible explanation for this could be that negative emotional content engages in a more analytic and detailed fashion of processing (Doerksen & Shimamura, 2001). Following these research findings, a study by D'Argembeau and der Linden (2008) accounts for these inconsistencies by linking the enhancement of contextual and sensory details following either a positive or negative memory with self-referential processing. When the information to be encoded is positive in nature and participants were asked to focus on positive self-referential processing, such as their hopes and dreams, higher activity in the posterior cingulate and parahippocamus was found (Touryan et al., 2007). Interestingly, the same effect was observed when the authors of this study asked participants to focus on negative self-referential processing, such as their duties: They showed the same enhancement in posterior cingulate and parahippocampal activity when processing negative items. These findings could suggest that the regions observed play an important role in self-referential processing, which is in line with DMN literature, highlighting the specific role of the posterior cingulate in the evaluation of personally significant information. (Andrews-Hanna, 2011).

Neural findings underlying the impact of valence and intensity (i.e. arousal) on memory retrieval

The qualitative gap between emotional autobiographical memories and neutral ones led to the early assumption that there might be a specialized processing system for such memories, driven by emotion (for example see Williams et al., 2007). This idea was soon contrasted by research proposing that emotional memories underlie the same neural processes as neutral memories and rather recruit special mnestic mechanisms for emotional involvement within a memory network (Christianson, 1989; Crombag, Wagenaar, & Van Koppen, 1996). Addressing this question, a study by Maratos, Dolan, Morris, Henson, and Rugg (2001) investigated the role of negative, neutral and positive context on emotional memory retrieval, showing that retrieval in a negative context resulted in amygdala activity. Interestingly, amygdala activity was equally present for negative and positive stimuli, suggesting its general role in emotional affect. In addition, their study demonstrated greater involvement of the medial PFC specific to positive stimuli possibly linked to its function in reward processing (O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001). Therefore, these findings strongly suggest that the retrieval for emotional and neutral memories underlies the same brain regions with supplemental involvement of regions crucial for emotional processing (Buchanan, 2007).

Brain activity during autobiographical memory retrieval is mediated not only by the intensity of an emotion (arousal) but also by its positive versus negative quality (valence). Several research findings investigating the contribution of these factors on neural circuits underlying memory retrieval highlight a role for the hippocampus and the amygdala (Daselaar et al., 2007; Dolcos, LaBar, & Cabeza, 2005; Greenberg et al., 2005; Markowitsch et al., 2000). An early study by Hamann, Ely, Grafton, and Kilts (1999) showed enhanced amygdala activity at encoding for successful memory retrieval of both positive and negative stimuli compared to neutral stimuli. Activation in the hippocampus correlated with amygdala activity, favoring the idea that the amygdala modulates activity in memory retrieval related brain regions for emotional memories (Hamann, 2001), a theory also called modulation hypothesis (McGaugh, 2002). This theory suggests that the enhancement for emotional memories compared to neutral ones is due to modulation of the amygdala on memory-based processes activating hippocampal and parahippocampal structures (McGaugh, 2002).

Further support for the modulatory effects of the amygdala on emotional memories comes from lesions studies examining the effects on medial temporal damage including or sparing the amygdala (Buchanan, 2005a). Patients were asked to recall personal emotional memories that occurred prior to brain damage. Results from this study demonstrated that patients with amygdala damage reported viewer unpleasant events and rated their recalled unpleasant memories as less intense than patients with medial temporal lobe damage sparing the amygdala. To address the question of laterality Buchanan (2005b) replicated their study in patients with unilateral temporal lobe damage. Results demonstrated a more differentiated pattern, where the observed positivity bias only occurred in right sided temporal lobectomy patients. Right-sided lesion patients recalled significantly fewer unpleasant memories, rated their unpleasant recollection as less intense and used fewer unpleasant words describing their remembered experiences compared to patients with left sided brain damage and healthy controls (Buchanan, 2005b). This evidence indicates that the right amygdala plays a key role in retrieving emotionally unpleasing highly intense memories.

Summarizing these results Buchanan (2007) argues that the right amygdala engages in the early stages of memory construction, helping to access highly intense memories in the search phase of memory retrieval, with damage to that particular region leading to less probability that an intense memory can be traced. These findings fit well with previous research from Markowitsch et al. (2000), showing that amygdala activity correlated with memory accuracy. However, the results from lesion studies also suggest that the amygdala could be involved in the re-experiencing of emotion felt during the initial memory, with amygdala damage leading to a reduction of the emotional (re)experience at retrieval (Buchanan, 2005a, 2005b, 2007).

Likewise, Dolcos, LaBar, and Cabeza (2004) found support for the modulation hypothesis in an event-related fMRI study using the subsequent memory paradigm. Amygdala and hippocampus activity were higher and showed a more powerful correlation for emotional arousing items than for neutral ones. Kensinger (2004) conducted an fMRI study examining how the differential neural processing systems underlying valence and arousal mediated memory enhancement. Their results demonstrated greater activity in the left amygdala and hippocampus for emotional arousing compared to neutral and non-arousing stimuli. In addition, activation of amygdala and hippocampus correlated significantly, also indicating modulation of the hippocampus through amygdala activity. The left inferior and dorsolateral prefrontal cortex and the left hippocampus showed greater activity for valenced and neutral non-arousing items. It follows that the hippocampus might always be engaged in memory retrieval, regardless of emotional valence and intensity. Kensinger (2004) therefore propose a two routes model of emotional memory, with highly intense memories being mediated by an amygdala-hippocampus network and valenced less or non-intense memories being processed by a prefrontal-hippocampal network. Many studies in autobiographical memory research demonstrated a significant correlation between hippocampus activity and successful recollection (Dolcos et al., 2005; Greenberg et al., 2005; Kensinger, 2004; LaBar, 2007; Piefke, Weiss, Zilles, Markowitsch, & Fink, 2003) and Daselaar et al. (2007) linked hippocampal activity to the initial search phase of memory retrieval, highlighting its role in accessing memory traces.

Similar to Kensinger and Corkin's proposal (2004) of two distinct networks contributing to the factors valence and intensity of autobiographical memory, other fMRI studies suggest an important role of prefrontal structures, particularly for both valence and low arousal. In an fMRI study Piefke et al. (2003) found that positive (relative to negative) memories activated medial prefrontal cortex (mPFC), whereas negative (relative to positive) activated a right temporal region. The medial PFC findings are consistent with results of functional neuroimaging evidence that links medial PFC with reward and appetitive processing (O'Doherty et al., 2001). However, medial PFC sometimes responds to negative emotions which suggests that it could be involved in arousal rather than positive valence (Phan, Wager, Taylor, & Liberzon, 2002). A possible solution of these inconsistencies could be that distinct subregions of the prefrontal cortex are differentially involved in positive versus negative valence and arousal (Dolcos et al., 2004). Mickley and Kensinger (2008) showed higher subsequent memory retrieval for positive and negative items correlating significantly with activity in the inferior frontal gyrus. Additionally, Dolcos et al.

(2005) showed preferential engagement of the right inferior frontal gyrus when successfully retrieving autobiographical memories and Daselaar et al. (2007) demonstrated right inferior frontal activity during the initial search phase of memory construction.

Objective and Hypotheses

So far, very little attention has been paid to the role of structural differences within the DMN or a retrieval network for emotional personal memories. Thus, according to the findings above, it is the aim of this study to investigate whether or not there is any structural variability within regions crucial for emotional autobiographical memory between healthy participants that is associated with intensity as well as valence of autobiographical memory. The regions of interest for the structural analysis are therefore the main hubs within the default mode network associated with (emotional) autobiographical memory. Namely, the prefrontal cortex (PFC), the Cingulate Gyrus (ACC, PCC), precuneus regions, and the temporal lope structures (TL) with focus on the hippocampus formation (HC), parahippocampal gyrus/ retrosplenial cortex (PHG/RSC) and the amygdala (AMY). To find structural differences within this network in healthy participants related to the intensity level and valence of emotional autobiographical memories could provide information about structural correlates underlying emotional processing in memory retrieval. Moreover, it shall be attempt to link these expected differences of autobiographical memory retrieval to the subsystems within the default mode network.

H1: There are structural differences between participants who recollect more unpleasant memories and participants who recollect more pleasant ones.

H2: There are structural differences between participants who rate their recollections as highly intense and participants who rate them as less intense.

H3. There are differences within regions of the autobiographical memory system (AMS): namely in Prefrontal Cortex, Cingulate Gyrus as well as in the temporal lobe (including HC Formation, AMG) bilaterally.

Material and Methods

Participants

The current study took place within the framework of an imaging genetics study (for further information see Bartova et al., 2015; Meyer et al., 2014; Rabl et al., 2014) at the

Division of Biological Psychiatry, Department of Psychiatry and Psychotherapy, Medical University of Vienna, Austria. It was partly funded by the Special Research Project SFB-35 (project number F3514-B11) and the Program Clinical Research (project number KLI148-B00) of the Austrian Science Fund (FWF), and the Oesterreichische Nationalbank, Anniversary Fund (project number 13903).

Participants were (recruited via word of mouth marketing, online advertisements and announcements on bulletin boards) invited to the outpatient clinic of the Department of Psychiatry and Psychotherapy, Medical University of Vienna (MUV), Vienna, Austria. All considered subjects underwent a clinical assessment composed of previous history, neurological and medical examinations involving electrocardiography, blood pressure measurement and routine laboratory testing. Detailed psychiatric examination included the diagnostic application of the German version of the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I) (Wittchen, Zaudig, & Frydrich, 1997). Evaluation of depressive symptoms were assessed by the 21-item version of the Hamilton Rating Scale for Depression (HAM-D) (M. Hamilton, 1960).

General exclusion criteria contained the presence of any concurrent or major lifetime major medical disorder, clinically significant abnormalities in routine laboratory screening or general physical examination, previous serious head injury or loss of consciousness, current or previous substance abuse (excepting nicotine and caffeine), concurrent use of psychotropic medication, age under 18 and over 45, left-handedness, origin of other than European ancestry, metallic implants or other contraindications to magnetic resonance imaging (MRI) as well as current pregnancy or breast feeding in case of female subjects. All adult subjects fulfilled the general exclusion criteria of the study protocol and were financially compensated for their expenditure of time.

Sixty-six participants were included into the pre-processing step, however one female subject had to be removed from further analysis, having calculated volumes with an overall covariance below two standard deviations from the studied population. The remaining sample consisted of sixty-five subjects (32 female) aged from 19 to 29 (age mean: 23.95). The descriptions of the study procedure and protocol were assumed from Bartova et al. (2015) and Meyer et al. (2014).

Procedure

MRI Data Acquisition

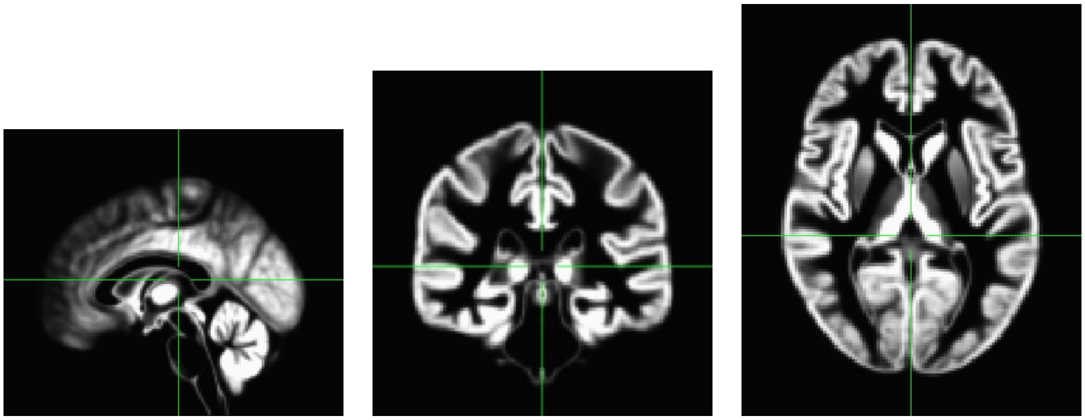
Imaging data were obtained on a 3 Tesla (3T) TIM Trio scanner equipped with a Siemens 12-channel head coil. Head movements were restricted using foam pads. Structural images were acquired using a 3D magnetization-prepared rapid acquisition with a gradient echo sequence (3D MPRAGE, repetition time (TR)/echo delay time (TE) = 2,300/4.21 ms, flip angle = 9°, inversion time = 900 ms, and voxel size = 1 x 1 x 1.1 mm) at the MR center of excellence, Medical University Vienna.

VBM-DARTEL Analysis

Voxel-based Morphometry (VBM) allows an automated and objective investigation of neuroanatomical differences in vivo on a whole brain level (Ashburner & Friston, 2000; Mechelli, Price, Friston, & Ashburner, 2005). The basic idea behind this technique is to localize volumetric differences in concentration of brain tissue using high-resolution structural MRI scans. To do so, a series of preprocessing steps are acquired that involves segmentation, registration, modulation and smoothing of the original brain images.

In this study, VBM was used to examine neuroanatomical correlates of emotional autobiographical memory ratings. Pre-processing was performed using DARTEL as implemented in SPM8 (2009). DARTEL is an algorithm for diffeomorphic image registration that aims to increase the accuracy of intersubject alignment and furthermore allows the registration of each subject to a reference, specific to the study sample (Ashburner, 2007).

The first preprocessing step involved segmenting the original T1-weighted images into rigidly aligned tissue types: Gray Matter (GM), White Matter (WM) and Cerebrospinal Fluid (CSF). This was done using the 'New Segment' approach (same algorithm as in 'Unified Segmentation' see Ashburner & Friston, 2005), which is the standard protocol provided in SPM8. Consecutively, DARTEL used the affine-segmented gray and white matter images in its nonlinear image registration procedure (Ashburner & Friston, 2009), to estimate the deformation flow fields that align them best together. In an iterative process, it alternates between creating a number of templates, specific to the sample population, produced by their own mean and warping each subject's tissue probability maps to the current template used (for an example see figure 1). The last step of the DARTEL approach involved normalizing from the template space to MNI (Montreal Neurological Institute) space and finally generates the Jacobian scaled warped gray matter images, in which regional volume of gray matter is preserved following spatial normalization. As normalizing to a stereotaxic space removes differences between scans, it is crucial to put this information back at some point during preprocessing. In order to correct for differences in brain volume, this means rescaling the intensities of gray matter volume at each voxel dependent on the amount of expansion/contraction used to normalize. Often referred to as modulation step (Ashburner & Friston, 2005; Good et al., 2001) in VBM analyses not using DARTEL registration, it usually takes place before smoothing the data with a Gaussian kernel.



(a) Sagital plane (b) Coronal plane (c) Horizontal plane

Figure 1. Example of the created sample-specific DARTEL template

DARTEL incorporates modulation and smoothing into the normalization step, aiming to preserve as much as possible from the original data (Ashburner & Friston, 2009). In the current analysis, images were smoothed with an 8-mm full width at half maximum Gaussian kernel. By checking for sample homogeneity after preprocessing, one outlier was detected and excluded from further analysis. On the smoothed, normalized and Jacobian warped gray matter images voxel by voxel statistics were finally applied.

Behavioural data

Recruitment process for the second part of the assessment, including the autobiographical memory test, was resumed a couple of months after the acquisition of MRI scans. Prospective participants fulfilling the same inclusion criteria as mentioned above were re-invited. In the follow-up session, participants underwent the same procedure ensuring clinical normal health and observing their psychological status via the Hamilton-Screening (HAM-D) (M. Hamilton, 1960).

Autobiographical memory was assessed with a German version of the ’top 5 emotional memory interview’ (Buchanan, 2005a, 2005b). Participants were asked to recollect five of their most emotional experiences in life. Subsequently, all participants were requested to date their narrated recollections as accurately as possible, providing at least month and year of the event. That followed the evaluation of each memory on a seven point rating scale, concerning pleasantness, intensity, significance, novelty, vividness and frequency of rehearsal. ’Pleasantness’ (most unpleasant memory to most pleasant memory), ’Intensity’ (not intense at all to most intense memory), Significance (made no difference in life to changed life as much as any event), Novelty (totally routine to equal to most unusual event), Vividness (no image to as clear an image as the original) and Frequency of rehearsal (never to as often as any event in life). These instructions and rating scales were adapted from Buchanan (2005a, 2005b).

As stated above, valence and intensity are seen as crucial variables indicating emotional involvement in the current autobiographical memory literature. Therefore, the subjective Pleasantness and Intensity ratings were used to examine these emotional characteristics of the recollected memories. The behavioral data raw scores of the pleasantness and intensity scales for each memory as well as demographic factors of the study sample (Age, Gender, etc.) were conducted using R (2015). Overall mean for the variables ’Valence’ and ’Intensity’ were calculated and included into further statistical analysis as covariates of interest.

Statistical Analysis

Regional differences in gray matter volume between healthy participants in regions related to emotional content of autobiographical memory were examined with the General Linear Model in SPM8 (2009) using MATLAB (2012). Two multiple regression analysis (with similar default settings) were performed, one including ’Valence’, the other ’Intensity’ as covariates of interest. Accounting for nuisance variables, age and gender were entered into the design matrix. As global normalization total gray matter volume (TGV) was used as a confound and included into the statistical design.

Due to the a priori hypothesis to expect variability of volume within regions of an autobiographical memory system (AMS) and the mentioned Default Mode Network a region of interest (ROI) approach was chosen. Reverse inference maps (corrected for multiple comparisons with $pFDR > .01$) of the terms 'autobiographical memory' and 'default mode network' were obtained from Neurosynth (http://neurosynth.org) , a database of fMRI data (Yarkoni, Poldrack, Nichols, Essen, & Wagner, 2011). Anatomical defined ROI's referring to the AMS were created using the PickAtlas toolbox (2010) in SPM8. Both masks were combined and utilized as explicit mask included into second-level analyses. An absolute masking threshold of 0.1 was applied. Gray matter volume differences among subjects were assessed statistically using one- tailed t-contrasts after correction for multiple comparisons utilizing false discovery rate (FDR) at a threshold of $p < .05$. A probability of less than 0.05 was considered significant. The extent threshold was set to k = 50. All coordinates are reported in Montreal Neurological Institute (MNI) space.

Results

Sample Characteristics

Table 1 illustrates socio-demographic characteristics of the study sample and descriptive statistics of behavioral ratings. Mean scores of the variables of interest were 4.32 ± 0.89 for 'Valence' and 5.74 ± 0.69 for 'Intensity'.

Table 1
Demographic characteristics and behavioral rating scores

Variable	Mean	S.D.	Range
Demographics			
Age	23.95	2.13	19 - 29
Behavoiral ratings			
Valance mean	4.32	0.89	2 - 6.2
Intensity mean	5.74	0.69	4 - 7

Participants showed no significant difference between age and gender (t = -0.18, p = .86). Furthermore, no significant relationship among overall mean scores of the behavioural variables 'Intensity' and 'Valence' was found (t = -0.66, p = .51). Age and the averaged rating score of the variable 'Intensity' (t = -1.3, p = .20) demonstrated no significant relation. Neither did age and the variable of interest 'Valence' (t = 0.31, p = .75).

Finally, there were no significant differences regarding men's and women's averaged 'Intensity' (t = 0.88, p = .38) and 'Valence' ratings (t = -1.25, p = .22). Distributions of the overall mean scores of the variables of interest ‘Valence’ and ‘Intensity’ are presented in figure 2.

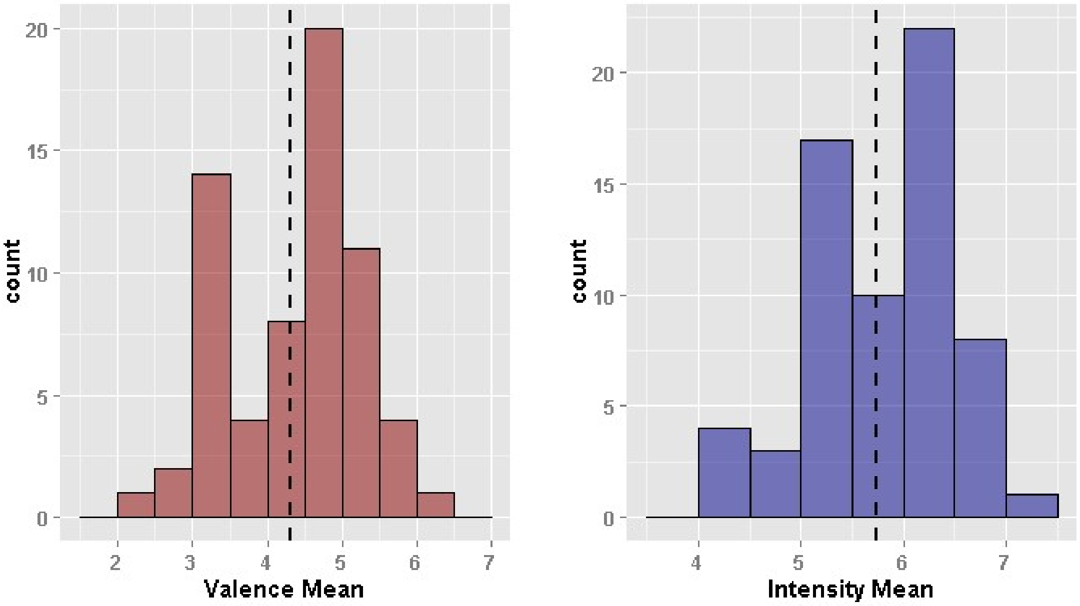


Figure 2. Distribution of variables of interest ’Valence Mean’ (4.32, SD = 0.89, range = 2-6.2 and ’Intensity Mean’ (5.74, SD = 0.69; range = 4-7).

VBM-DARTEL Analyses

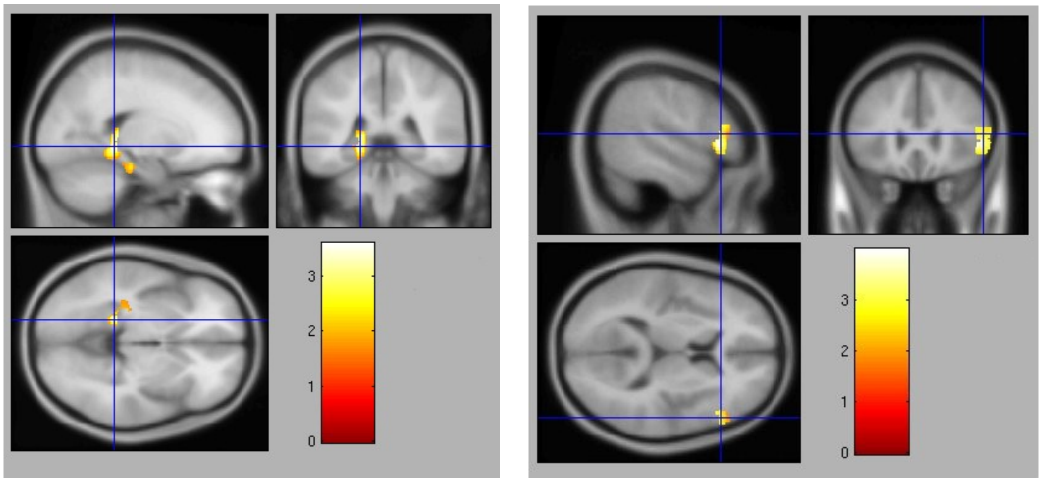
Results of the multiple regression analysis in predefined ROI-regions with Valence mean are presented in Table 2. The variable of interest, Valence, was positively correlated with regional grey matter volume in the triangular part of the right inferior frontal gyrus (IFG, *pFDR* = .014, MNI coordinates: 52 22 1) and the left hippocampus/parahippocampal gyrus (H, *pFDR* = .047, MNI coordinates: -20 -39 -5). The second cluster contained 765 voxels, with 254 voxels identified as left hippocamus by the Automated Anatomical Labeling (AAL) brain atlas (Tzourio-Mazoyer et al., 2002). Results concerning positive valence are illustrated in figure 3. Scatterplots illustrating the relationship between gray matter volume and positive emotional valence are presented in figure 4.

Table 2

Relative local grey matter volume associated with 'Valence mean'

Peak Region		*p(FDR)*	T	Coordinates			k
				x	y	z	
Positive emotional valence							
Inferior Frontal Gyrus	R	.014	3.96	52	22	1	675
Hippocampus/Parahipp. G.	L	.047	3.59	-20	-39	-5	765
Negative emotional valence							
Medial/Sup. Frontal G.	L	.045	3.61	-18	54	6	

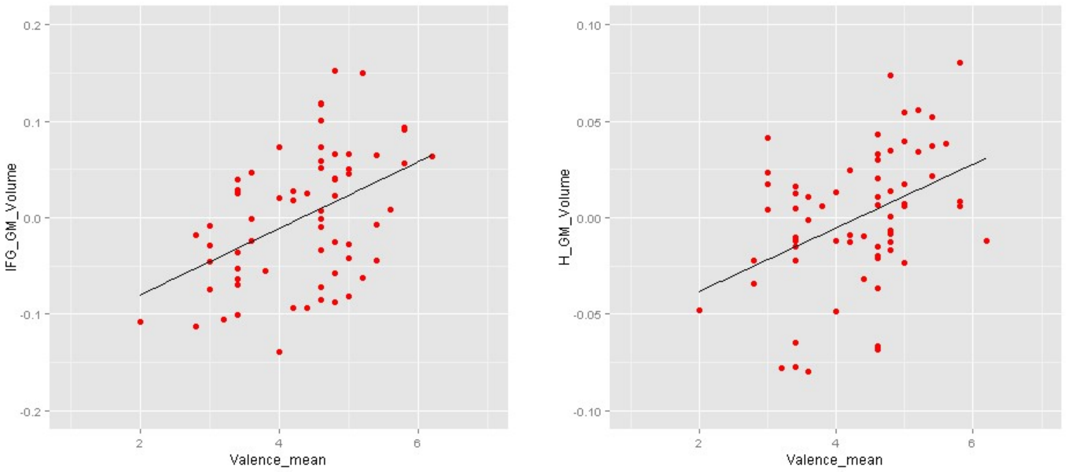
Note. Results reported for ROI regions (p = .05, FDR-corrected) with age, gender and total grey matter volume (TGV) as nuisance variables. Table illustrates contrasts of Valence (implicating positive and negative correlations), individual p-values showing the significance level for each particular region, R and L referring to right and left hemispheres, t-values, MNI-coordinates of the peak region in each cluster and cluster size (k).



(a) Inferior frontal gyrus

(b) Left Hippocampus

Figure 3. Significant correlation between gray matter volume and positive emotional valence i.e. high 'Valence mean'. Regions showing a significant correlation at $p < .05$ (FDR-corrected) in the inferior frontal gyrus IFG (a) and the left hippocampus H (b) are overlaid on sagittal (top left), coronal (top right) and axial (bottom left) sections of the T152_MNI template provide by SPM8. For visualization purposes, results are shown at a threshold of $p < .05$, FDR-corrected.



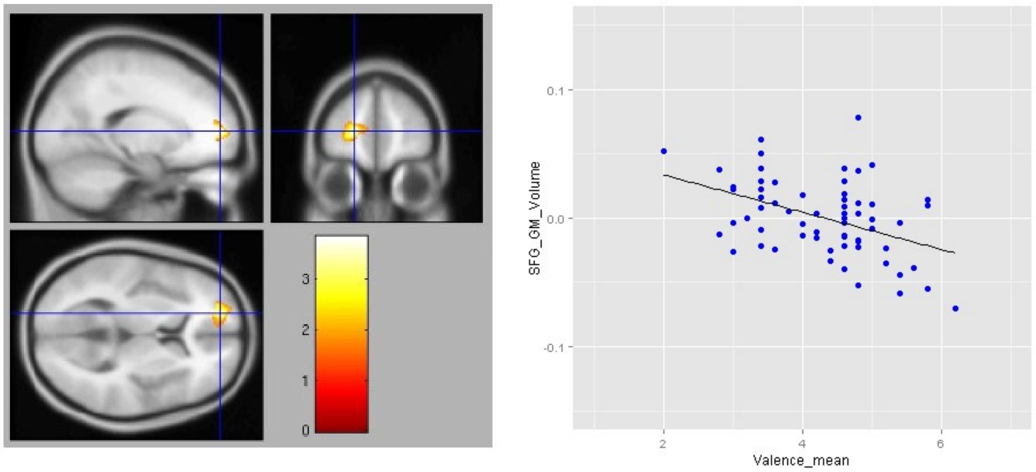
(a) Inferior frontal gyrus (b) Left Hippocampus

Figure 4. Scatterplots illustrating the relationship between gray matter volume and positive emotional valence corrected for multiple comparisons at $pFDR < .05$ (see figure 3). Significant correlations in right inferior frontal gyrus IFG ($pFDR = .014$; A) and the hippocampal cluster ($pFDR = .047$; B) with 'Valence mean '.

The negative contrast of 'Valence mean' resulted in a significant association with the left prefrontal cortex. The cluster found, persisted of 885 voxels, of which 424 voxels were assigned to the medial frontal gyrus (MFG) and 412 voxels to the superior frontal gyrus (SFG). Furthermore, 43 voxels of the discussed cluster were identified as belonging to the anterior Cingulate (ACC) defined again by the AAL brain atlas. However the cluster maxima (peak region) was located in the dorsolateral part of the left medial frontal gyrus (MFG, $pFDR = .045$, MNI coordinates: -18 54 6).

This finding demonstrates significant greater gray matter volume in the MFG being associated with negative emotional valence. Results concerning negative valence are presented in figure 5. Results of the VBM analysis in predefined ROI-regions with Intensity mean are presented in Table 3 and illustrated in figure 6. A positive significant relation between regional grey matter volume and 'Intensity Mean' was not observed.

Instead, three large clusters were negatively associated with gray matter volume as can be seen in figure 6. The first cluster observed, has its peak coordinate in the left inferior temporal gyrus (ITG, $pFDR = .014$, MNI coordinates: -38 -42 -14), with 1435 voxels referring to that region. Moreover, it extended into the left fusiform gyrus (identifying 1021 voxels), the left middle temporal gyrus (MTG, 346 voxels) and the left parahippocampal gyrus (with 118 voxels).



(a) (b)

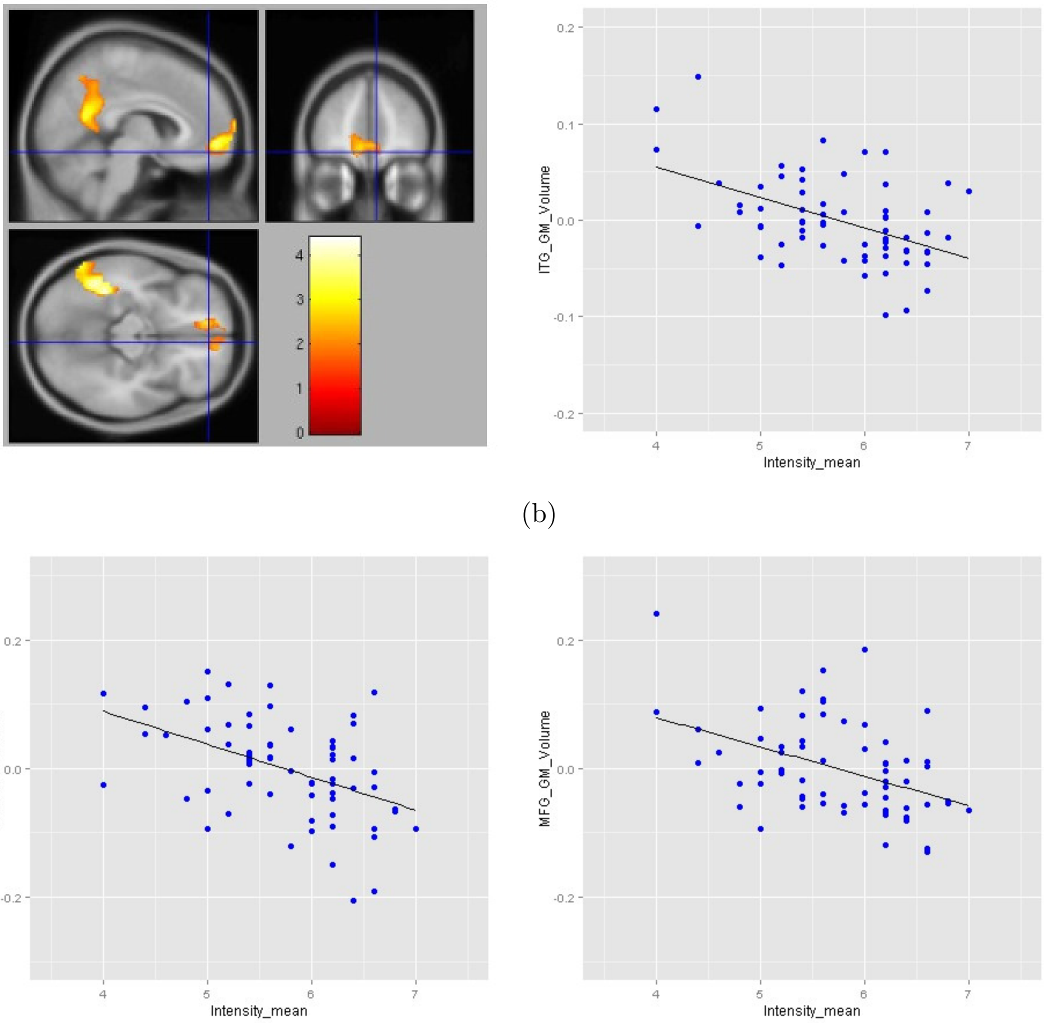
Figure 5. Significant correlation between gray matter volume and negative emotional valence i.e. low ’Valene mean’. The region showing a significant correlation at $p < .05$ (FDR-corrected) in the medial frontal gyrus MFG is overlaid on sagittal (top left), coronal (top right) and axial (bottom left) sections of the T152_MNI template provided by SPM8. (b) Gray matter volume at peak (x:-18 y:54 z:6) in the MFG cluster correlated negatively with ’Valence mean’ score ($pFDR = .045$).

Table 3

Relative local grey matter volume associated with ’Intensity mean’

Peak Region		*p(FDR)*	T	Coordinates			k
				x	y	z	
Low emotional Intensity (i.e. Arousal)							
ITG	L	.012	4.40	-38	-42	-14	3092
PCC	L/R	.014	4.07	2	-60	21	4651
MFG	L/R	.047	3.76	3	54	-6	2021

Note. Results reported for ROI regions ($p = .05$, FDR-corrected) with age, gender and total grey matter volume (TGV) as nuisance variables. Table illustrates contrasts of low Intensity (implicating negative correlations), individual p-values showing the significance level for each particular region, R and L referring to right and left hemispheres; L/R: bilateral, t-values, MNI-coordinates of the peak region in each cluster and cluster size (k). ITG: inferior temporal gyrus; PCC: posterior cingulate cortex; MFG: medial frontal gyrus.



(a) (b)

(c) (d)

Figure 6. Significant correlation between gray matter volume and low emotional intensity i.e. low 'Valence mean'. Regions showing a significant correlation at $p < .05$ (FDR-corrected) in the posterior cingulate PCC, inferior temporal gyrus ITG and the medial frontal gyrus MFG are overlaid on sagittal (top left), coronal (top right) and axial (bottom left) sections of the T152_MNI template provide by SPM8. For visualization purposes, results are shown at a threshold of $p < .05$, FDR-corrected. (a) Scatterplots illustrating the relationship between gray matter volume and emotional intensity in the ITG cluster (b), PCC cluster (c) and MFG cluster (d), corrected for multiple comparisons at $pFDR < .05$.

As biggest significant cluster associated with the negative contrast of the Intensity mean, parts of the limbic lobe (2572 voxels) and precuneus (1554 voxels) were identified bilaterally. Peak region was located in the right posterior cingulate cortex (PCC, $pFDR = .014$, MNI coordinates: 2 -60 21). The PCC, consisted of 1757 voxels (L/R) and the cluster extended further into the lingual gyrus (L: 125 voxels, R: 27 voxels).

The third cluster contained of the left and right medial frontal gyrus (MFG L/R) with 1263 voxels in this area. In addition the right superior medial frontal gyrus (SFG med. R; 285 voxels) and the left anterior cingulate (ACC L; 99 voxels) are part of the cluster. The local maxima (peak region) lies within the medial orbital part of the right superior frontal gyrus (SFG R; $pFDR < .05$, MNI coordinates:3 54 -6). Whole brain analyses with valence and intensity scores yielded no additional significant regions. Every voxel within each cluster of the VBM analyses has been allocated to its particular brain region by the Automated Anatomical Labeling (AAL) brain atlas (Tzourio-Mazoyer et al., 2002) using the WFU PickAtlas tool (Maldjian, Laurienti, Kraft, & Burdette, 2003).

Discussion

Emotional autobiographical memory retrieval is a very complex process involving many different factors contributing to distinct neural networks and sub-networks. Positive valence demonstrated a significant correlation with greater gray matter volume in the right inferior frontal gyrus and a second cluster comprised of the left hippocampus (peak region) and parts of parahippocampal, fusiform and lingual regions.

These results are consistent with many fMRI studies highlighting activity of the left hippocampus to successful memory retrieval and the feeling of recollection (Dolcos et al., 2005; Kensinger & Corkin, 2004; LaBar, 2007). In an fMRI study conducted by Daselaar et al. (2007) hippocampus activity was found early on, in the memory access/search phase of emotional memory retrieval, suggesting its key role in access to memory traces as is proposed by multiple trace theory (Moscovitch et al., 2005). Regarding the right inferior frontal finding, Dolcos et al. (2005, 2004) showed preferential engagement of memory retrieval in the right inferior frontal gyrus and engagement of the left inferior frontal gyrus being active during encoding. Likewise, Daselaar et al. (2007) showed preferential right inferior frontal activity during an initial search phase of memory retrieval, proposing its temporal role in strategic retrieval mechanisms.

Additionally, Mickley and Kensinger (2008) demonstrated higher subsequent memory retrieval for positive and negative events following activity in an inferior frontal region, almost similar to the one found in this analysis. In addition, activation of the hippocampus and parahippocampal gyrus was significant for all types of valence, including neutral items. Further examining their results Kensinger and Schacter (2008) showed preferential superior and inferior frontal activity for later remembered positive items versus negative ones.

Valence-based findings from this study fit well into the proposed MTL-sub-network of the DMN (Andrews-Hanna, 2011; Andrews-Hanna et al., 2014; Schacter et al., 2012). As positive memories tend to be remembered in a generative and heuristic way accompanied by more peripheral details (Mickley & Kensinger, 2008, 2009) it seems likely that participants reporting experiences that are positive show higher gray matter volume in structures related to the access and construction of such rich episodic/autobiographical recollections, referring to the left hippocampal/parahippocampal cluster. This is especially important when taking into account that the parahippocampal gyrus has been reported for being involved in visuospatial memory (Cabeza et al., 2004). Furthermore, elaboration processes related to a positive and more heuristic way of information processing and retrieval of conceptual associations are assumed to reflect higher gray matter volume in inferior frontal structures (Mickley & Kensinger, 2008, 2009).

Negative valence showed gray matter enhancement in a left prefrontal cluster containing parts of the medial and superior frontal gyrus and the anterior cingulate with its peak in the left medial frontal gyrus. Similarly, low intensity demonstrated an almost identical cluster, leading to the assumption that this particular frontal region engages in the processing of negative valenced low-arousing memory content. Furthermore, J. P. Hamilton et al. (2015) propose that the ventromedial prefrontal cortex (vmPFC) and the posterior cingulate cortex (PCC) attribute valence to internal representations and subsequently elaborates on them proportional to the intensity of the attributed valence in a self-centered manner. In their paper on depressive rumination in Major Depressive Disorder MDD and its role in the DMN, J. P. Hamilton et al. (2015) describe a model, which explains depressive rumination as a consequence of the increased functional connectivity between the DMN and the subgenual prefrontal cortex sgPFC. The functional integration of these structures leads to an altered processing of self-referential thought resulting in rumination. The sgPFC is involved in “affectively laden behavioral withdrawal” (J. P. Hamilton et al., 2015, p. 227) and is related with depressive states, sad mood inductions using sad autobiographical narratives, feelings of guilt and rejection. Thus, findings from this study support this functional integration model by highlighting the proposed regions with greater gray matter volume in association with negative valence and low emotional arousal.

The variable ’Intensity’ showed no significant positive correlation with gray matter volume in any brain region. However, VBM regression analysis revealed three large clusters being negatively correlated with the mean of the ’Intensity’ scale. This indicates that participants who rated their most emotional memories as less intense showed greater gray matter volume in a cluster that had its local maxima in the inferior temporal gyrus, which extended into the middle temporal gyrus and the fusiform gyrus. The second cluster where participants rated their most emotional memories as less intense and showed higher gray matter volume was located in the posterior cingulate and contained precuneus regions and a small amount of voxels extending into left parahippocampal and hippocampus regions. The third cluster, comprised of medial and superior frontal regions also including parts of the anterior cingulate cortex, had its peak in the medial frontal gyrus.

These rather contradictory results concerning the variable of interest ’Intensity Mean’ should be interpreted with caution. As functional and neuropsychological studies demonstrate, emotional arousal is associated with greater activity in the amygdala, hippocampus and medial prefrontal regions and one prediction could be that memories with high emotional arousal would reflect higher gray matter volume in these structures. As no positive correlation between ’Intensity Mean’ and gray matter volume was observed, this a priori hypothesis cannot be validated. Still the significant negative associations in this analysis provide some further information.

When looking at the paradigm used to elaborate on the influence of the factors ’Valence’ and ’Intensity’ on memory retrieval, interesting details are revealed. The instructions of the autobiographical memory interview (adapted from Buchanan, 2005b) clearly state to recollect five of their most emotional experiences in life. Hence, participants rating their most significant and most emotional memories as low in intensity might be particular informative. A negative correlation in this context means that gray matter volume was higher in participants with low intensity ratings.

Indeed, non-arousing, but still affective information seems to be independent from modulation trough the amygdala and therefore emotional processing and rather contributes to more general retrieval processes, such as elaboration (Kensinger, 2004). Further support for this interpretation comes from an fMRI study by (Kensinger & Corkin, 2004) examining successful memory retrieval for memories arousing and non-arousing in nature. They found distinct neural systems contributing to high and low arousal, with subsequent memory for non-arousing but valenced items associated with a prefrontal cortex –hippocampal network. Holland and Kensinger (2010) argue therefore, that non-arousing valenced stimuli are dependent on additional attentional, elaborative and monitoring processes as well as self-referential processing mediated by inferior, superior and medial prefrontal areas. In this vein, negative valence ratings and low intensity ratings both highlight medial and superior frontal regions as having greater gray matter volume. In addition, the PCC cluster showed greater gray matter volume in the left hippocampus.

Many different studies examining the phenomenological factors valence and intensity on memory retrieval have reported inconsistent findings regarding these two dimensions. Kensinger and Schacter (2006) found that negative emotional content is remembered more vividly with enhancement for visual details, as did Doerksen and Shimamura (2001). One possible explanation for this could be that negative emotional content engages in a more analytic and detailed fashion of processing. In opposition to that, D'Argembeau, Comblain, and der Linden (2003) linked positive emotional content to a richer, more detailed recollection at retrieval. However, D'Argembeau and der Linden (2008) argue that self-relevance is responsible for these contrary results, with positive memories more likely to be remembered as rich recollections if they are high in self-relevance and negative memories more likely to be remembered as rich recollections if they are low in self-relevance. Furthermore, D'Argembeau and der Linden (2008) showed that when examining the effect of valence on memories low in arousal (intensity) negative memories were remembered with more vivid and internal details by young participants, whereas older participants reported stronger recollection for positive low-arousing memories. These findings could reflect results from this study, in the way that positively and negatively valenced content in low arousing memories is possibly mediated by self-referential processing mechanisms in the PCC and mPFC.

In this vein, highly self-relevant low-arousing memories are associated with higher phenomenological details at recollection, reflecting greater gray matter volume in the third cluster observed, namely the inferior temporal gyrus, with parts of the middle temporal gyrus and the fusiform gyrus. These structures are associated with various contextual and sensory details that contribute to a reconstructed autobiographical memory.

Furthermore, participants who rated their most emotional memories as less intense could elaborate on their autobiographical narrative in a more meta-reflective and generic manner, reflecting the greater volumes in areas contributing to the PCC, medial PFC and the dorsal medial subsystem within the DMN (see Andrews-Hanna, 2011). These regions play an important role in self-referential processing, mentalizing, social narratives and social reasoning as well as conceptual processing and the PCC and amPFC specifically are associated with autobiographical thought and representation of value.

Taken together results from this study showed structural variability across a variety of regions being engaged in retrieval mechanisms of autobiographical memory associated with the MTL-subnetwork, dorsal medial PFC subsystem and the main hubs within the DMN. Ratings of positive memories showed significant positive associations in gray matter volume with regions crucial for recollection and memory access and memory construction processes.

Ratings of low intensity revealed significant greater gray matter volume in the main hubs of the DMN, the posterior cingulate and medial prefrontal cortex, with negative valence highlighting almost the same prefrontal region as having higher gray matter volume. The hubs of the DMN are related to the “valuation of personally significant information” (Andrews-Hanna, 2011, p. 262).

Another explanation for the results concerning ’Intensity’ comes from research reporting lower gray matter volume in association with higher efficacy of that region (Kanai & Rees, 2011). Kanai, Dong, Bahrami, and Rees (2011) showed that higher distractibility in daily life was associated with greater volume in the left superior parietal lobe. Moreover, a study by (Dumontheil, Hassan, Gilbert, & Blakemore, 2010) examined the development of self-generated thoughts in adolescence and found that an improvement in manipulating self-generated thought is associated with lower gray matter volume in the rostrolateral prefrontal cortex. Hence, Kanai and Rees (2011) argue that this discrepancy between efficacy and structure could be attributed to cortical pruning processes during the maturation of the human brain. Pruning removes weak and ineffective synapses and neurons and therefore reflects lower gray matter volume (Gogtay et al., 2004). In this vein, cortical pruning leads to an improvement in computational efficacy of the brain and is reflected by lower gray matter volume (Kanai & Rees, 2011).

However, this possible explanation must be interpreted with caution because it is quite difficult to address the question of the performance-structure relationship when using macroscopic MRI images. Future research will be needed to examine the proportions of different substructures of macroscopic gray matter volume and its relation to efficacy of the brain. Variability in gray matter volume could reflect synaptogenesis-related differences due to individual environmental challenges. Still, further insight into the microstructural organization of the brain will be needed to draw conclusions from VBM results.

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EDUCATIONAL BACKROUND

UNIVERSITY OF VIENNA: DIPLOMA STUDY PSYCHOLOGY (EQUIVALENT TO M.SC.),
OCTOBER 2008 – NOW (EXPECTED GRADUATION: NOVEMBER 2014)

Specializations: Neuropsychology/Clinical Psychology, Assessment & Diagnostics
Thesis title: “Structural alterations in relative grey matter volume related to autobiographical memory retrieval - a VBM –Study”

MEDICAL UNIVERSITY OF VIENNA: CO-REGISTERED STUDENT
MARCH 2011 – NOW

Subjects: curriculum in psychoanalysis; curriculum in fMRI applications and approaches; curriculum in pediatric psychiatry

HEBREW UNIVERSITY Of JERUSALEM: ROTHBERG INTERNATIONAL SCHOOL
JUNe 2014 – JULY 2014

Subjects: Trauma and Resilience: Theory and Practice from the Israeli Experience

PROFESSIONAL EXPERIENCE

SPEZICALISED ASSISTANT AT THE AUSTRIAN AUTISTIC FOUNDATION - ÖAH
FALL 2013 - NOW

Duties: integration counselor for autistic children in high school

RESEARCH INTERN AT THE MEDICAL UNIVERSITY OF VIENNA, IMAGING GENETICS LABOR
JANUARY 2013 - NOW

Supervisor: MD Prof. Lukas Pezawas; Bernhard Meyer, M.Sc.

Duties: recruitment, assessment and scanning of participants; applying second level statistics on fMRI images

NEUROPSYCHOLOGICAL ASSESSMENT COURSE

FALL 2013

Duties: conducting exploration interviews and assessing patients with neuropsychological deficits

INTERN AT GENERAL HOSPITAL OF VIENNA - PEDIATRIC NEURO-ONCOLOGY UNIT

JULY - SEPTEMBER 2013

Duties: Neuropsychological assessment and intervention with children and adolescents suffering from brain tumors

INTERN AT KOLPINGHAUS (NURSING HOME), GERIATRIC PSYCHOLOG UNIT

JULY – SEPTEMBER 2012

Duties: counseling, assessments (primarily MMSEs), (neuro) cognitive training with individuals and groups

INTERN AT THE AUSTRIAN AUTISTIC FOUNDATION - ÖAH
MARCH 2011 – JANUARY 2012

Duties: integration counselor for autistic children in high school

INTERN AT PRIVATE PRACTICE FROM MARTINA MARLISCH, M.SC.

SUMMER 2009

Duties: Assessment of cognitive skills and dyslexia in school children

CERTIFICATE

AID 2/3 Certificate at the University of Vienna - Qualification for administering the Adaptive Intelligence Diagnostic (AID)

COMPUTER SKILLS

MS Office
SPSS
R
SPM Toolbox implemented in Matlab
Currently learning: LaTex

LANGUAGE SKILLS

German (mother tongue)
English (level: C1)
French (level: A2)
Spanish (level: A2)