DIPLOMARBEIT

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„Resting state functional connectivity reflects autobiographical memory valuation“

verfasst von

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Abstract

Recent research on the default mode network dealt with its engagement in the autobiographical memory network and linkage to specific personal characteristics. The valuation of autobiographical memories is linked to temporal and limbic brain regions. According to a positive rating preference and a connection to the left temporal lobe, it has been proposed that spontaneous rating tendencies might be represented in resting state activation differences. The diploma thesis at hand addresses the hypothesis that individual differences in valuating spontaneously retrieved autobiographical memories relate to participants´ intrinsic functional connectivity within regions of the autobiographical memory network.

Using functional magnetic resonance imaging, resting state images of 46 healthy, healthy participants were collected. To extend prior studies to the domain of valuation tendencies, participants were spontaneously asked for their top five emotional autobiographical memories from any time of their lives and requested for rating them on a pleasantness scale.

On the basis of anterior medial prefrontal cortex`s (amPFC) functions in the autobiographical memory system and the default mode network, this brain area was chosen as seed region. Resting state functional connectivity analysis described significant temporal correlations of the amPFC with default mode regions. A significant influence of the factor mean of valuation and the variables gender and age on resting state functional connectivity between amPFC and posterior cingulate cortex was observed ($p < 0.01$). Interestingly, the findings demonstrate a linkage between positive ratings of autobiographical memories and a stronger functional connectivity in the default mode network. The results of this study describe the association between recollection and future simulation processes and furthermore support the idea of the “constructive - episodic simulation hypothesis”.

Keywords: *autobiographical memory network, resting state functional connectivity, default mode network, medial prefrontal cortex*

Zusammenfassung

Die Erforschung des autobiographischen Gedächtnisses beschäftigt sich heutzutage mit der Identifikation zugrundeliegender neuronaler Netzwerke sowie dem Zusammenhang von Aktivierungsunterschieden im Gehirn mit persönlichen Eigenschaften.

Die vorliegende Diplomarbeit beschäftigt sich mit der statistischen Beziehung zwischen spontan wiedergegebenen autobiographischen Erinnerungen und der funktionellen Gehirnaktivität im Ruhezustand.

Zur Darstellung der funktionellen Gehirnaktivität wurden Magnetresonanztomografiebilder von 46 Personen gesammelt. Um die Studienlage rund um die Bewertung von autobiographischen Erinnerungen zu erweitern, wurden die StudienteilnehmerInnen unvorbereitet nach ihren fünf emotionalsten persönlichen Ereignissen gefragt. Zudem wurden sie dazu angehalten, die wiedergegebenen Erlebnisse auf einer siebenstufigen Positivität- bzw. Negativitätsskala zu bewerten.

Aufgrund seiner Funktionen im Autobiographischen Gedächtnisses und im Default Mode Netzwerks, wurde der mediale Präfrontalcortex im anterioren Bereich (amPFC) als “Seed” Region ausgewählt. Die Ergebnisse der funktionellen Konnektivitätsanalyse demonstrieren einen signifikanten Zusammenhang zwischen dem medialen Präfrontalcortex und Regionen des Default Mode Netzwerkes. In Anbetracht des Bewertungsmittelwertes und unter Berücksichtigung der Variablen Geschlecht und Alter, deuten die Ergebnisse der „statistical parametric mapping‟ Funktion auf einen signifikanten Zusammenhang zwischen dem medialen präfrontalen Cortex im anterioren Gehirnbereich mit dem posterioren Cingulum hin ($p < 0.01$). Interessanterweise deuten die Ergebnisse auf einen Zusammenhang zwischen positiven Bewertungen und einer stärkeren Funktionalität im Bereich des Default Mode Netzwerkes hin. Die Studienergebnisse beschreiben einen Zusammenhang zwischen Erinnerungsprozessen und der Vorstellung zukünftiger Ereignisse und unterstützen die “constructive – episodic simulation” Hypothese.

Table of Content

Theoretical Background

The term autobiographical memory (AM) refers to a cognitive event characterised by the recollection of personally experienced past events and its relevance for several human aspects. In the literature, the term autobiographical memory is normally used for encompassing self-related processes, for world-orientation issues and in this connection the ability for effective problem solving matters (Williams et al., 2007).

A rich set of personal information constitutes AMs as a result of the interplay of the higher-level mental functions (Andrews-Hanna, Saxe, & Yarkoni, 2014; Yang, Bossmann, Schiffhauer, Jordan, & Immordino-Yang, 2012) and of self-relevant processes (Conway & Pleydell-Pearce, 2000).

A key aspect of AMs is that they are transporters of individual relevant information. Recent progresses in this field have highlighted the need for conceptualizing the provided information to different parameters like for example the amount of generalisation [specific vs general AMs] (Addis, Moscovitch, Crawley, & McAndrews, 2004) or the age of memories [remote vs recent AMs] (Soderlund, Moscovitch, Kumar, Mandic, & Levine, 2012). Taking all this into account, one may suppose that the content of the reminisced experiences can be dated more or less exactly, can contain an individual amount of details or can be differently valuated for emotional content.

Since the empirical findings of Williams and Broadbent in the year 1986, which demonstrated that suicide attempters show a typical behaviour in giving self-related answers, the way AMs are recalled is connected with differences on the psychological dimension (Williams & Broadbent, 1986). This preliminary study was indicative for the assumption that given AMs could be related to personality traits. In fact, there is a large volume of published studies describing the relation between characteristics of AM and certain personal aspects, for example coping styles (Geraerts, Dritschel, Kreplin, Miyagawa, & Waddington, 2012), tendency for drug abuse (Gandolphe, Nandrino, Hancart, & Vosgien, 2013) and psychiatric illness (Raes, Williams, & Hermans, 2009).

Several studies investigating the relation between AM characteristics and personality, tested on people with specific psychiatric illness. For example, Sumner, Griffith, and Mineka (2010) analysed the data of 15 depression studies and concluded that the specificity of AM retrieval is associated with the amount of depressive symptoms and furthermore sensible to the prediction accuracy of the progression of the disease. In the same vein, Raes et al. (2009) proposed the positive impact of training AM retrieval strategies on depressive symptoms. Together, these studies provide important insights into the cognitive contact of individual memories with clinical relevance.

Given the connection between memory appraisal and several personal aspects, a link between autobiographical qualities and variations in neural activation patterns of consistently recruited brain regions during AM retrieval has been p roposed. Numerous studies have attempted to explain the neural correlates of AM systems (Fossati, 2013; P. L. St Jacques, Botzung, Miles, & Rubin, 2011). There is an unambiguous relationship between AM retrieval and the involvement of a large-scale interconnected brain network, encompassing several sub-networks, medial temporal network, prefrontal and limbic networks (Fossati, 2013). Svoboda´s meta-analysis of 24 fMRI studies (Svoboda, McKinnon, & Levine, 2006) assumes a core neuronal model consisting of preliminary left-sided activation nodes, incorporating the medial and ventrolateral prefrontal, medial and lateral temporal and retrosplenial/posterior cingulate cortex (PCC), the temporoparietal junction and the cerebellum.

To better understand mechanisms of AM qualities and their effect on the aforementioned brain regions, authors such as Moscovitch et al. (2005) were interested in the influence of the hippocampus recruitment on AM qualities. Others have highlighted the relevance of hippocampal activity for the amount of retrieved memory qualities (Addis et al., 2004; Piolino et al., 2004; Soderlund et al., 2012). Soderlund et al. (2012) attempted to draw fine distinctions in hippocampal engagement and the age of AMs, whereas the revealed activation has been argued with underlying effects of recency and remoteness. The authors pointed to the different ways of engaging the hippocampus in the AM network and concluded showing for a higher hippocampal integration for younger than older valuated memories. Some authors have mainly been interested in questions concerning hippocampal activation in qualitative criteria (Cabeza & St Jacques, 2007). Together, these studies outline that the hippocampus plays a prominent role in the autobiographical retrieval process and is undoubtedly a factor dependent on the contained information.

Furthermore, it has been suggested that aspects of the retrieved experience are associated with separable brain activation. The neural correlates of autobiographical contributing processes formed the central focus of a study by Cabeza and St Jacques (2007), in which the authors found that emotional and vivid recollection qualities are associated with the amygdala. A broader perspective was adopted by Svoboda et al. (2006) who argued that emotional qualitative factors, personal significance, level of detail and vividness were appropriate for an activation shift, meaning a deactivation of regions linked with mental processes.

In connection to the focus on brain parts related to their emotional functions in the AM process, there is considerable evidence that the amygdala plays a significant role in fear conditioning paradigms (Marek, Strobel, Bredy, & Sah, 2013), in the storage (Fernando, Murray, & Milton, 2013), in retrieval and encoding of emotional memories (Denkova, Dolcos, & Dolcos, 2013). The way in which the amygdala is linked to the AM process was intensively studied by Denkova et al. (2013). According to the authors the retrieval focus (i.e. whether the emotional content should be explicitly examined or not) and furthermore the valence of the reproduced individual events are associated with amygdala activation.

A large and growing body of literature has investigated the function of the medial prefrontal cortex (mPFC) in the network of retrieving personal memories. Recent evidence suggests that the mPFC is not directly responsible for the retrieved content of AMs. However, it can be said that the mPFC adds an individual touch to AMs, which is reflected in self-referential processes (Muscatell, Addis, & Kensinger, 2010), in the conscious re-experiencing of personal events (Oddo et al., 2010) and in assigning those events to specific times (Tranel & Jones, 2006). In line with this assumption it is suggested that the mPFC could play into this field by establishing an observatory based on the reconstruction of personal experiences (Svoboda et al., 2006) and acting as a control body in the memory system (Kensinger & Corkin, 2004). Nevertheless, Cabeza and St Jacques (2007) identified various constructive processes as memory search and controlled retrieval processes with left lateral prefrontal cortex involvement and monitoring processes, which are subscribed to the ventral medial prefrontal cortex (vmPFC). Together, these studies provide important insights into the participation of the mPFC in terms of self-referential processes to personal memory elements.

What we know about the neuronal networks engaged in the whole AM processes is, on the one hand, largely based upon empirical studies that investigated how single brain regions contribute to manifestation of reminisced memories. On the other hand, numerous studies attempted to explain the manner of how the comprehensive spatially distinct nodes of the AM are functionally connected, meaning similar activation patterns of different neuronal nodes under the same circumstances (Svoboda et al., 2006). In a PET-study measuring changes in relative regional cerebral blood flow of affect-laden AMs in healthy participants, Fink et al. (1996) reported the decisive importance of limbic regions for emotional mnestic processing.

In recent functional magnetic resonance imaging (fMRI) studies it has been shown that the grade of self-involvement in experienced events (Muscatell et al., 2010), the accessibility of personal memories (P. L. St Jacques et al., 2011), and the rehearsal of negative non-arousing events (Kensinger & Corkin, 2004) influence the intrinsically organisation of the AM network. Almost every paper that was written on the underlying neuronal networks of AMs focused on the interplay of emotional, self-relevant regions and brain parts responsible for memory aspects. Particularly in analysing relevant AM contributing networks an enhanced interaction between medial temporal lobe (mTL) network and mPFC network during elaboration of recollected memories was demonstrated (P. L. St Jacques et al., 2011).

Given that mPFC and mTL both support the detailed description of AMs, it might be possible that the valuation tendency for an individual experienced event influence the connectivity between these and other regions within the AM network. Several empirical investigations linked the amygdala to the AM network. One potential reason for that linkage was the emotional content of the retrieved personal events (Muscatell et al., 2010).

Indeed, several studies from the empirical literature dealing with valuation tendencies are characterised by a comparison with respect to specific groups of people (P. L. St Jacques et al., 2011) that is e.g. suffering from specific mental health problems and furthermore, they are making use of different approaches (e.g. lesion studies vs. fMRI studies).

The valence of AMs has been studied in just a few empirical investigations (Denkova et al., 2013). Nevertheless in the history of the investigation of personal memories lesion studies (Buchanan, Tranel, & Adolphs, 2006), event-related fMRI/activation studies (Denkova et al., 2013), and functional connectivity studies (St. Jacques et al., 2011) dealt with the valuation of reminisced personal events. The evidence from these studies is based almost exclusively on the rating of personal memories elicited during an interview.

Apart from different approaches dealing with rating behaviour a positivity-negativity effect (i.e. a systematically tendency for valuating memories) can be explained by the interaction of several factors. In focussing on empirical studies dealing with the phenomenon of valuation tendencies, it has been made clear that this effect is influenced by emotional conditions (Williams et al., 2007). In a study focused on determining rating tendencies, Teasdale and Fogarty (1979) manipulated mood states, happy or depressed, and asked for the spontaneous retrieval of positive or negative valued memories. Interested in the effect of mood on the reachability of emotional experiences, the results of this study revealed longer retrieval times for pleasant memories in the depression condition.

Moreover, the aim of autobiographical research is to clarify and subsequently develop concepts regarding neuronal foundations of the valuation of reminisced personal experiences. In adopting this idea, studies concentrated on the impact of damaged brain regions as the mTL (Buchanan et al., 2006) and from these observations the function of lesions on the rating of AMs were deduced. In the before cited study an emotion-memory interaction in comparing right temporal lobectomy participants with left temporal lobectomy participants in their ability collecting and valuating real-life events has been investigated. Interestingly, in this case the findings suggested a shift to the left temporal lobe leading to a positive bias in autobiographical recall. In a similar fMRI study P. L. St Jacques et al. (2011) compared PTSD patients with healthy controls. Decreased activity in typical temporal autobiographical brain regions and the mPFC during the retrieving process were expected. The results of this event-related fMRI study revealed a higher sensitivity of temporal regions, hippocampus and amygdala for negative events. This study described valuation sensitivity in medial prefrontal parts, whereas in the clinical group higher recruitment patterns of the vmPFC for negative reminisced experiences were detected.

In order to clarify these specified activation patterns further results of studies focusing on the intrinsically organization of the brain are taken into consideration. In this context, simultaneous activation of medial parts of the temporal and the prefrontal lobe connection in valuation stimuli conditions have been detected in a few studies (Sakaki, Nga, & Mather, 2013; P. St Jacques, Dolcos, & Cabeza, 2010): for example, the experience of negatively valenced pictures as less negative, which was reflected in the higher level of functional connectivity between the right amygdala and the ventral anterior cingulate cortex (P. St Jacques et al., 2010). A similar study with the intention of investigating the positivity effect in memory revealed increased functional coupling between amygdala and medial prefrontal cortex in resting state condition (Sakaki et al., 2013). Generally speaking, this means that the functionally measured connection between prefrontal regions and emotional parts of the mTL (amygdala) is sensitive to memory valuation tendencies.

Given that regions of the temporal cortex and prefrontal cortex are involved in the valuation tendencies (positive/negative) of AMs, it is possible that the valence influences the functional connectivity between those and other brain regions during resting state scanning. A comparison of the brain regions recruited specifically in valuating AMs reveals that particularly the left amygdala is more sensitive to positive and negative emotional personal details. In retrieving the literature concerning the valuation of different stimuli it can be said that several brain regions demonstrate more sensitivity to carry out subjective evaluations.

Functional imaging method is one of the main non-invasive method for determining the functional architecture of the brain under different conditions. Interestingly, the functional architecture of the resting, inactive human brain was the point of interest of many studies. There is consensus among brain imaging scientists that a homogenous, spatially distributed system of brain regions is engaged in the activation of the so-called resting state network (Fox et al., 2005; Greicius, Krasnow, Reiss, & Menon, 2003; Raichle et al., 2001). Recent evidence suggests that the activation network of brain regions in the rest condition is linked to the network of AMs (Andrews-Hanna et al., 2014; Buckner, Andrews-Hanna, & Schacter, 2008; Yang et al., 2012). Andrews-Hanna et al. (2014) analysed subsystems of the resting state network involved in distinct aspects of the AM process, including the retrieval of relevant information.

Since the AM network is viewed as interacting with the default mode network (DMN), the resting human brain has been found to have a robust and replicable association with internal cognitive phenomena (Buckner et al., 2008). The functional connectivity findings from this study make several contributions to the current resting state functional connectivity literature. Furthermore, the default mode of the human brain is linked to focussing on the non-external environment, and it is a proposed factor supporting aspects of AMs.

In focussing on the clinical relevance of this diploma thesis, the data at hand adds to previous psychiatric evidence for specific neuronal pattern identified in healthy participants. Previous studies dealing with the connections of AMs, DMN and psychiatric patterns provided for example consistent assumptions that rumination as a typical indicator for deviations of the resting state network (Nejad, Fossati, & Lemogne, 2013) and a discussed symptom for depression (Marchetti, Koster, Sonuga-Barke, & De Raedt, 2012) is correlated with an “over-general style” retrieving personal events (Raes et al., 2009; Sumner et al., 2010). It is suggested that the associations of these factors are investigated in future studies, since further research regarding the role of characteristics of the AM network would be of interest. The issue of the interaction of both described networks is an intriguing one, which can be briefly illustrated by studies using resting state scans and their correlation with autobiographical process characteristics. The previous studies dealing with the connection of the neurobiological patterns and autobiographical characteristics revealed functional dissociations between anterior and posterior in first-episode major depression. Those alterations correlated with rumination and over-general AM (Zhu et al., 2012). The functional connectivity data of this study extend the previous findings with respect to two main aspects in which an over-general form expressing personal memories was mirrored in a decreased functional connection of the resting posterior medial brain regions. Over-general memory is usually seen as a factor strongly related to major depression. A recent study interested in the role of reduced specificity of AM in depression vulnerability proposed a potential program dealing with the reduction of an over-general memory style as future depression therapy (Raes et al., 2009).

By drawing on the previously described interaction between the resting state functional connectivity and the AM network, the question arises concerning related individual differences in valuation of spontaneously retrieved AMs to participant´s intrinsic functional connectivity within regions of the AM network.

Up to now various methods have been developed and introduced in order to measure AMs. Traditionally, AMs have been assessed by confronting people with the association method (Williams et al., 2007; Williams & Broadbent, 1986), whereas valenced cue words should spark connotations of an individual event. In recent functional neuroimaging studies AMs have been measured in four different ways: generic cue method, pre-scan interview, independent source and prospective method (Cabeza & St Jacques, 2007).

Semi-structured interviews were deemed the most suitable and appropriate method for this study. The “Top 5 emotional memory interview” approach, designed by Buchanan et al. (2006), has a number of attractive features: the retrieval process is not altered by training effects, the authenticity and the episodic character of the retrieval process is guaranteed and the objectivity of rating the retrieved personal events is considered.

Although extensive research has been carried out on the rating of AMs, high uncertainty still exists concerning its neuronal backgrounds. The mechanisms by which the valuation of personal experiences is linked to the inactive brain, have not been clearly established. This diploma thesis thus seeks to remedy these voids by investigating the resting state functional connectivity of the anterior medial prefrontal cortex (amPFC) in dependence of the rating for pleasantness of AMs. Furthermore, it is proposed that a higher functional connection between the amygdala and mPFC is an indication for a positive valuation tendency.

Materials and Methods

Subjects

During recruitment 46 participants were contacted via online advertisement, announcements on bulletin boards and word of mouth for the resting state scanning. The following inclusion criteria were applied: volunteers, aged 18 – 45, right - handed, German-speaking and European family background. The absence of any past or present psychiatric diagnoses except nicotine dependence was requested and tested via psychiatric exploration, using the Structural Clinical Interview for DSM-IV Axis I disorders (SCID-I). Participants scoring above seven in the 21 - item version of the Hamilton Depression Scale (HAM-D) were also excluded. Clinical normal health was guaranteed through an assessment of standard physical examinations, electrocardiography (ECG), blood pressure measurement and routine laboratory screening. The entire procedure of the study was orally explained to the participants and all of them gave written consent.

Procedure

First, resting fMRI blood-oxygen-level-dependent (BOLD) data was acquired (the data for this study was acquired as a part of a larger functional and structural study on depression). The duration of the resting fMRI scan was 6 minutes. Participants were instructed to lie down with eyes closed and think of nothing in particular. Furthermore, it was important not to fall asleep.

The recruitment process for the second part of the assessment, including the AM test, was resumed a couple of months later. The same set of participants was contacted via telephone and invited for a second assessment including an additional psychiatric screening. At the beginning of the follow-up session participants were confronted with the “Top 5 emotional memory interview“ (Buchanan et al., 2006) prior to any other procedure. After that, the psychological status was observed with the Hamilton-Screening (HAM-D). Furthermore, as mentioned above, the same procedure for ensuring clinical normal health was fulfilled. In the AM task participants were asked for five spontaneously retrieved personal events. To protect the AM from any influencing effects of the assessment the interview has always been conducted before any other questionnaires as a part of a longitudinal study.

Magnetic resonance imaging

MRI hardware and technical parameters

Imaging data were acquired on a 3T Siemens TIM trio scanner with a Siemens 12–channel head coil. Head movements were limited by the use of foam pillows and registered during functional image acquisition. Structural data were received by the application of a 3D MPRAGE sequence, characterized by TR/TE = 2300/4.21 ms, flip angle = 9 degrees, inversion time = 900 ms and a voxel size of 1 x 1 x 1.1 mm. Functional data were obtained via a phase-corrected blipped gradient echo (GE) and a single shot EPI sequence (TR/TE = 42/2,000 ms, 96 x 96 matrix, 210 mm square FOV, 20 axial slices, slice thickness = 4 mm, slice gap = 1 mm). Furthermore functional imaging data were acquired by the use of an interleaved slice acquisition scheme. Conventionally, functional imaging data were obtained during the same session as the structural data acquisition.

Preprocessing

Resting state functional connectivity analyses were performed on AFNI (http://afni.nimh.nih.gov/afni), which is installed in a system based on the R software setting (http://cran-r-project.or/). To prepare the imaging data for statistical analysis several preprocessing steps were completed. Those procedures included reconstruction, slice–time correction, rigid–body motion correction and the alignment. In utilizing a 12–point affine transformation, the alignment to the individual anatomical brain was guaranteed. In order to ensure magnetization equilibrium the first five volumes were deleted. Furthermore, to reach identical trial length (175 TRs) the last seven volumes have been eliminated. To observe possible noise signals and localized transient hardware mistakes ANATICOR artifact regression analysis was consulted to resting state time series (see http://afni.nimh.nih.gov/sscc/hjj/anaticor/) (Chen et al., 2012). To inspect nuisance, supplementary characteristic values have been assessed from eroded white matter (WM) and cerebrospinal fluid (CSF) masks created by Freesurfer anatomical segmentation processed using FreeSurfer software version 5.1.0 (http://surfer.nmr.mgh.harvard.edu/) on a Linux system (Red Hat Enterprise Linux 5, x86_64 architecture). For quality improvement of fMRI data and temporal filtering purpose a broad frequency band (0.008–0.15 Hz) was used. For spatial filtering a spatial Gaussian blur (full width at a half maximum (FWHM = 6 mm)) was applied. Finally imaging data were turned to Talairach–Tournoux stereotactic space.

Creation of tables and figures

The statistical volumetric results were constituted with AFNI on an averaged anatomical brain, which included all participants of the whole SFB study (Meyer et al., 2014). The preparation of statistical plots were created with R. 3.1.1. and gimp 2.8.14 (git://git.gnome.org/gimp) was used for artwork.

Statistical analysis

Functional connectivity

For data quality control purpose functional datasets were restored and visually examined for essential artefacts before and after the preprocessing procedure. AFNI was applied for the computation of functional connectivity and statistical parametric maps. Demographic statistical analysis and plots were induced with the LINUX version of R. Functional datasets were basis of calculation for functional connectivity maps. Principally, functional connectivity is declared as "…the temporal correlation of a neurophysiological index in different brain areas" (Friston, Frith, Liddle, & Frackowiak, 1993). A-priori defined seed regions were correlated with time series of all other voxels of the brain. On the basis of anterior medial prefrontal cortex`s (amPFC) functions in the autobiographical memory system and the default mode network, this brain area was chosen as seed region (Andrews-Hanna et al., 2014; Schacter, Addis, & Buckner, 2008; Yang et al., 2012). For that reason time series were taken from a 4mm spherical seed at the amPFC and averaged. Coordinates of the right and the left amPFC for the seed-based functional connectivity were inherited from a recent scientific writing (Fair et al., 2008). The obtained coordinates were modified from Montreal Neurological Institute (MNI) (x = 1, y = 54, z = 21) to Talairach-Tournoux space (TLRC) (x = 0, y = 51, z = 18). Furthermore, statistical parametric mapping (SPM) was executed to test the predetermined hypothesis for every separate voxel. This statistic was computed from single subject Fisher z-transformed connectivity maps and tested for a presumptive influence of the factor mean of valuation and the variables gender and age as covariates of no interest within a general linear model (GLM) using AFNI (3dttest ++). The idea of SPM was to tackle several statistical problems which come along with functional magnetic resonance imaging. The basic principle of voxel-by-voxel testing requires the permission for multiple testing of the same hypothesis, defined as multiple comparisons (Forman et al., 1995). An alternative method for testing each single voxel separately is to cluster coincident activated voxels in the same region. The cluster correction method has various appealing properties. The second benefit of using this method is a higher signal to noise ratio within the tested area (Heller, Stanley, Yekutieli, Rubin, & Benjamini, 2006). To remedy this problems, cluster-wise correction for multiple comparison was used. This was applied in the execution of the Monte Carlo Simulations (3dClustSim, 10,000 iterations, smoothness, estimations with 3dFWHMx, dimensions: 74 x 87 x 69 grid, 2.19 x 2.19 x 2.19 mm^3, a minimum cluster size of 20 voxels supplied a corrected *p* value of 0.05). Statistical significance for all corrected cluster was accepted at p values < 0.05.

Top 5 emotional memory interview

The variety of information and qualities expressed by AMs requires different types of measurement. Furthermore, the documentation of past personal experiences can be directly integrated in the procedure of a study otherwise or participants are introduced in documenting experienced individual events during a specific time frame on their own. According to fMRI studies, personal memories are requested during or before the scanning procedure. Critically viewed, this training effects results in dealing with autobiographical details over a long time and before the real investigation might have influence on the results. Piolino et al. (2004) noted that this effect is responsible for changes in memory traces and influences the reproduction process of AMs.

Because of the attempt to focus on the valuation of personal events, other parameters like the amount of generalisation (Addis et al., 2004) or the modulating effect of the age of AM (Piefke, Weiss, Zilles, Markowitsch, & Fink, 2003) have not been taken into consideration. Several studies propose an influence of these variables on the recall of AMs. Other than that, consequences on the valuation of memories have not been considered yet.

AM was assessed with a German version of the “Top 5 emotional memory interview” (Buchanan et al., 2006). Participants were briefly asked for their spontaneously retrieved top-five most emotional memories. Furthermore, participants were reminded that accuracy and validation of the memories were not essential. First, all considered experiences were written down. Additionally, participants were asked to date their reported personal experiences as accurately as possible. Furthermore, evaluation of the narrated memories on a 7-

point scale was demanded, including pleasantness, intensity, significance, novelty, vividness and frequency of rehearsal.

Results

Behavioral Results

For every retrieved personal experience raw scores of the pleasantness scale of the “Top 5 emotional memory interview” were constructed. Means and standard deviation for n = 46 subjects are presented in Table 1.

Table 1

Ratings of the Pleasantness Scale

Memory	Mean	Standard Deviation
rating 1	3.85	2.60
rating 2	4.17	2.54
rating 3	4.49	2.66
rating 4	4.17	2.6
rating 5	4.76	2.54
ratings (1-5)	4.29	1.09

Imaging Results

Functional Connectivity: Main effect

Resting state functional connectivity analysis with a-priori defined seed region amPFC is in line with previous reports, which means significant temporal correlations were mainly registered in DMN regions (Andrews-Hanna et al., 2014; Buckner et al., 2008). Statistical significant clusters ($p < 0.01$) involves the right postcentral gyrus (-40, 26, 41), left thalamus (14, 37, 17), left anterior cingulate (19, -31, 8), right anterior cingulate (-21, -31, 10) and posterior cingulate (-12, 35, 19) (Fig. 1).

Functional connectivity: Group effect

Statistical parametric maps for the amPFC were calculated. The revealed *t*–values for every voxel are displayed in coloured figures on the right side of Figure 1. For the seed region a $p < 0.01$ was chosen manually. The variables age and gender were entered in the model as covariate of no interest. Significant difference effects between the mean of the pleasantness scale on resting state functional connectivity between amPFC and right medial frontal gyrus, right cingulate gyrus, left thalamus and left uvula were noticed after correcting for multiple comparisons (Table 2). In accordance with hypothesized link between the AMN and DMN, the results demonstrate significant differences in the valence of autobiographical memories in default mode regions (Fig. 1).

Furthermore the influence of the functional connectivity on the valence of autobiographical memories was calculated (Fig. 2). According to the regression model the residuals of the functional connectivity explain 9.9% of the valuation effect ($F (1,38) = 4.2$, $p < 0.05$).

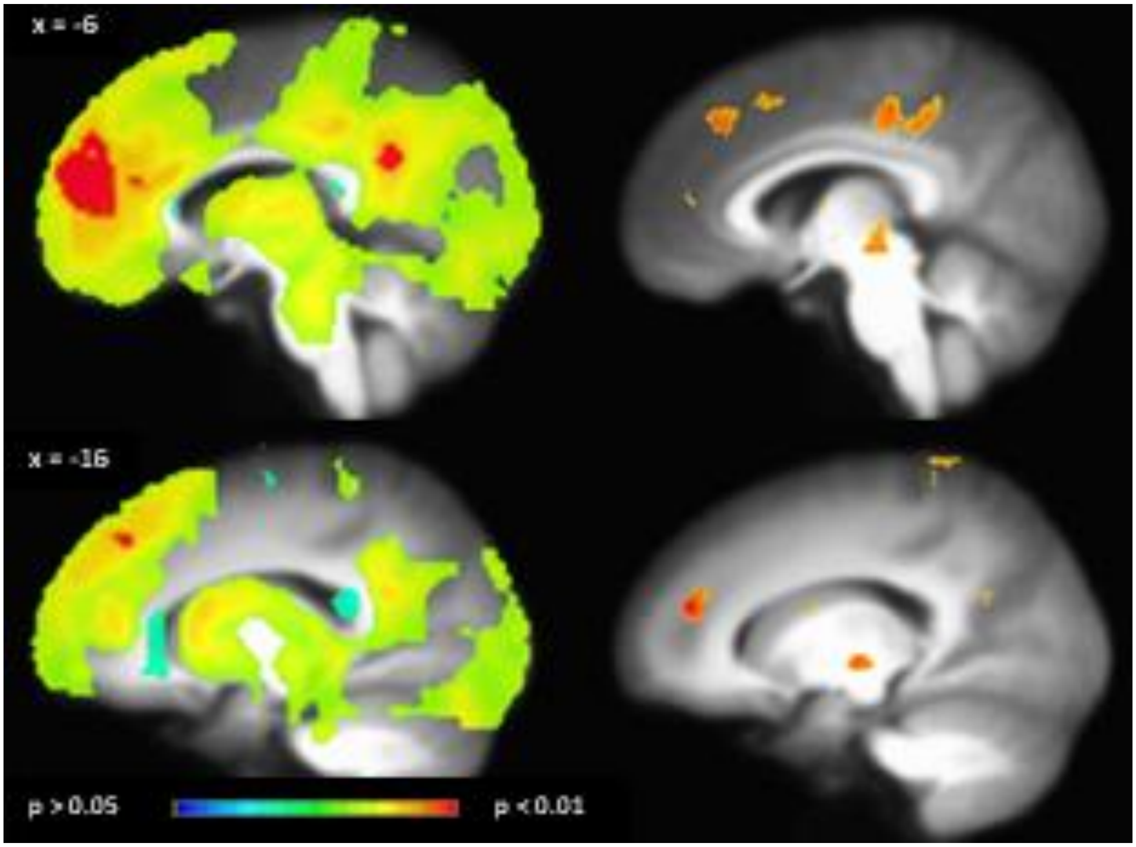

Figure 1 *Comparison between the functional connectivity main effect and functional connectivity group effect.* Functional connectivity regions significantly correlated with the anterior medial prefrontal cortex and the peak regions right medial frontal gyrus and right cingulate gyrus are shown on the left side of the picture (threshold $p < 0.01$, cluster corrected with max. 13 voxels). Results shown on the right part illustrate significant clusters right medial frontal gyrus and right cingulate gyrus in dependence of the valuation of personal memories (threshold $p < 0.01$, cluster corrected with max. 4.5 voxels). Results were displayed on an averaged anatomical template and corrected for multiple comparisons.

Table 2

Significant clusters of the functional connectivity group analysis

Region	*x*	*y*	*z*	Number of Voxels	*p* corrected
Right medial frontal gyrus	-16	-42	19	368	<<0.01
Right cingulate gyrus	-6	35	38	286	<<0.01
Left thalamus/red nucleus	3	22	-1	198	<<0.01
Left uvula/declive	21	70	-23	183	<<0.01

x, *y*, *z* coordinates in Talairach space, *p corrected* cluster corrected *p* values

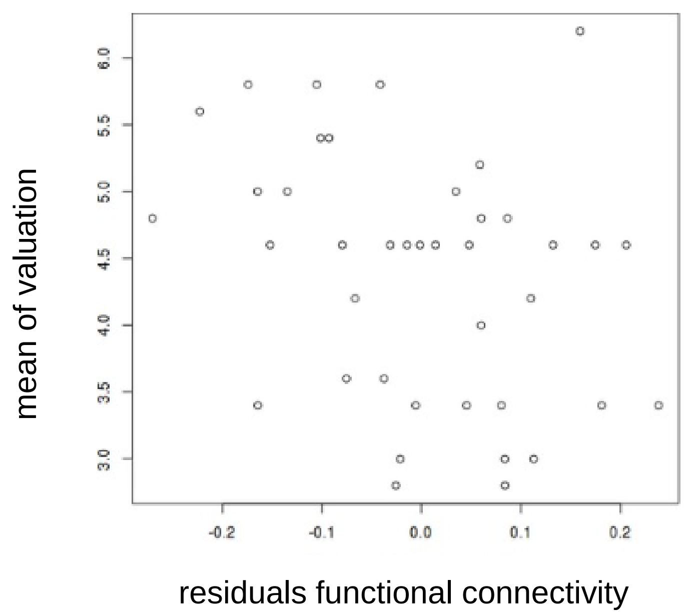

Figure 2 *Regression analysis model predicts the valuation of autobiographical memory.* Those subjects who have the strongest functional connectivity rated their personal memories more positive, according to the valence scale of the “Top 5 autobiographical memory interview”.

Discussion

The diploma thesis at hand had the aim of determining the relation between resting state functional connectivity and the valuation tendency for AMs. The initial goal of this study was to appoint the functional connection between the amPFC and brain regions associated with AM and DMN. Furthermore, this study tended to assess the hypothesis that for healthy participants the relation between the medial prefrontal cortex and limbic structures are stronger for positive valuated experiences than for negative ones.

The choice of the amPFC as seed region for executed functional connectivity analysis was because of amPFCs function as a meaningful node of two operating systems, the DMN and AMN (Andrews-Hanna et al., 2014; Schacter et al., 2008; Yang et al., 2012). The functions of the named brain regions (Figure 1) are the participation in several cognitive brain networks, encompassing episodic memory and associative learning, attention areas and furthermore emotion and social behaviour (Leech, Braga, & Sharp, 2012; Maddock, Garrett, & Buonocore, 2003; Vogt, Vogt, & Laureys, 2006). Overall, the finding of resting state functional relationships among mPFC and PCC is in conformity with the findings of previous work in the field of resting state network (Buckner et al., 2008; Fransson & Marrelec, 2008; Greicius, Supekar, Menon, & Dougherty, 2009). The graphical representations are in accordance with so far suggested functional and structural roles in term of the DMN that claimed the PCC as a virtually interacting turntable in the resting brain network (Fransson & Marrelec, 2008; Greicius et al., 2009).

Overall, the finding of autobiographical valuation effects in healthy adolescents and adults is in line with previous studies demonstrated prefrontal and limbic interactions sensitive for memory evaluation (Sakaki et al., 2013). The graphical representations (Figure 1) of memory valuation effects in healthy adolescents and adults ascertained within this study are on the one hand conform with previous results, on the other hand there are some discrepancies to discuss.

In contrast to previous research demonstrating the involvement of the amygdala (Buchanan et al., 2006; Denkova et al., 2013; Fink et al., 1996; P. L. St Jacques et al., 2011) and the hippocampus (Addis et al., 2004; Moscovitch et al., 2005; Piolino et al., 2004; Soderlund et al., 2012) in AM processes, this study has been unable to find a connection of those regions to the valuation of personal memories. This discrepancy may be related to differences in defining the term AM and measuring qualities of retrieved emotional events (Maguire, 2001). Focussing in this connection on the application of fMRI, the interference may be related to the use of event-related (Addis et al., 2004; Soderlund et al., 2012) or resting state studies. Apart from the possibility whether AMs are investigated during the scanning session (event-related fMRI) or not (resting state fMRI), another minded factor is the collection method of AMs (Maguire, 2001).

With regard to the link between autobiographical memory qualities and default mode properties the existing results can be prior evidence in valuation tendencies (Addis, Wong, & Schacter, 2007; Andrews-Hanna et al., 2014; Hassabis, Kumaran, Vann, & Maguire, 2007; Schacter et al., 2008). These studies are in complete agreement with the idea that imaging future situations or simulating past events depends on identical neuronal circuits. But in contrast to the present results those authors mainly claimed for the implication of prefrontal and medial temporal regions (Hassabis, Kumaran, Vann, et al., 2007; Schacter et al., 2008).

Apart from the debate dealing with retrieval and imagination functions of typical brain regions (Schacter et al., 2008), a limited number of fMRI studies have investigated the link between valence behaviour and activation patterns in emotional circuits (Buchanan et al., 2006; Denkova et al., 2013; Kensinger &

Corkin, 2004; Maddock et al., 2003; P. L. St Jacques et al., 2011). While the available literature is ambiguous, it should tentatively be pronounced that the “constructive–episodic simulation hypothesis” hold the same idea as we do (Schacter & Addis, 2007). This thesis describes the constructive nature of episodic memory, which claims for existing similarities concerning past recollection processes and envisioning future situations. In the same manner D'Argembeau and Van der Linden (2004) investigated the influence of valence of events on the subjective evaluation of past episodes and the individual pre-experience of future episodes. Interestingly in comparison with negative events, positive situations were linked with gorgeous impressions of re–experiencing past events and pre–experiencing future episodes. With the theoretical basis of the episodic simulation hypothesis it would be interesting to assess valuation tendencies with the “Top 5 emotional memory interview” in an event-related fMRI setting.

While positive valuation tendencies are related to amygdala activation (Buchanan et al., 2006) and amygdala–mPFC functional coupling (Sakaki et al., 2013), it is noteworthy that the present findings are not in line with these assumptions. Interestingly, the statistical analysis of this study emphasize the putative importance of the PCC as a crucial node for observed valence – dependent AM effects (Figure 1).

A number of fMRI studies investigated the functioning of the PCC in the AM context (Leech et al., 2012; Maddock et al., 2003; Martinelli, Sperduti, & Piolino, 2013). Notably, this functional connectivity analysis emphasizes the presumable importance of the PCC in the AM valuation process. In accordance with the present results a handful of studies report on the connection between PCC activation and valence decision tasks (Maddock et al., 2003). Interestingly, it has been suggested that this brain region is responsible for processing of emotional criteria and the regulation of information in the episodic process (Maddock et al., 2003; Martinelli et al., 2013).

However, it has been proposed that abnormalities in behavioural aspects of AM processes and differential hemodynamic activity medial prefrontal and anterior cingulate regions are correlated with symptoms and progression of major depressive disorder (Roy et al., 2010; Williams et al., 2007; Young, Bellgowan, Bodurka, & Drevets, 2013). A preliminary review on major depression emphasizes deviations in self-referential and brooding cognitions, which are also linked to abnormal interactions between default mode regions and cortical midline structures (Nejad et al., 2013).

While the response of limbic regions as the amygdala is linked to the valence of emotional episodic stimuli (Markowitsch & Staniloiu, 2011; P. St Jacques et al., 2010), it should be noted that the PCC is described as an integral node of the emotional autobiographical memory network (AMN) (Maddock, Garrett, & Buonocore, 2001) and constitutes a relevant input region for medial prefrontal regions (Greicius et al., 2009), which encourages the plausibility of the present study results and is possibly connected with prior work focussing on the cognitive control aspects of the mPFC in emotional episodic processes (Kensinger & Corkin, 2004; Kohn et al., 2014).

While the present diploma thesis presents novel insights into the connection between AM valuation and neuronal resting state patterns, this study is not without limitations. Firstly, the previously mentioned alterations should not be overstated, as positivity biases are linked to older participants (Sakaki et al., 2013; P. St Jacques et al., 2010). Furthermore, it should be noted that although the results reveal a strong functional connectivity between the cingulate cortex and the medial prefrontal cortex, the findings do not permit any causal statement (Friston, 2011). In this connection, statistical dependencies of two different brain regions are represented in correlation coefficients and do not guarantee statements of their common influence. To tackle with the mediating influence of the amPFC on the PCC effective connectivity studies in this context might be inevitable (Fransson & Marrelec, 2008; Muscatell et al., 2010; Zhang et al., 2013). Finally it should be mentioned, that the scope of this study was limited to terms of focussing just on the valuation tendency of AMs, furthermore more research is required to determine the efficacy of the used “Top 5 emotional memory interview”.

Conclusion

For now it can be summarized that the question concerning the function of the PCC in default brain network and AMNs has already been unpacked and answered in a multitude of ways and from many perspectives. Hence, it could conceivably be hypothesized that there might be a connection between the ways how AMs are valuated and the resting state interaction of brain regions. Despite both separate networks involve a broad research field, which occupies the scientific community with an amount of outstanding and contradictory issues, however, it is worth mentioning that there exist some expectations of overlapping effects.

This study enhances our understanding of a linkage between the AM network and the resting human brain network. This idea is strongly integrated with previous findings and ideas (Buckner et al., 2008; Hassabis, Kumaran, & Maguire, 2007; Schacter et al., 2008). The simulation and prediction of future events on the one hand is a promising area for research, but on the other hand the understanding of valuation tendencies of past situations possibly advances the scientific knowledge in the field of the imagination of prospective situations.

It would be interesting to assess the connection of individual autobiographical retrieval and valuation habits with their underlying neuronal patterns more accurately. Additionally, a pivotal status of the valuation tendency for personal retrieved experiences is also justified from a clinical perspective in that previous AM studies have shown a connection to mental disorders as depression (Dalgleish & Werner-Seidler, 2014; Nejad et al., 2013; Sumner et al., 2010; Zhu et al., 2012).

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List of Tables

List of Figures

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