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Face-name association task reveals memory networks in patients with left and right hippocampal sclerosis☆

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ABSTRACT

We aimed to identify reorganization processes of episodic memory networks in patients with left and right temporal lobe epilepsy (TLE) due to hippocampal sclerosis as well as their relations to neuropsychological memory performance.

We investigated 28 healthy subjects, 12 patients with left TLE (LTLE) and 9 patients with right TLE (RTLE) with hippocampal sclerosis by means of functional magnetic resonance imaging (fMRI) using a face-name association task, which combines verbal and non-verbal memory functions. Regions-of-interest (ROIs) were defined based on the group results of the healthy subjects. In each ROI, fMRI activations were compared across groups and correlated with verbal and non-verbal memory scores.

The face-name association task yielded activations in bilateral hippocampus (HC), left inferior frontal gyrus (IFG), left superior frontal gyrus (SFG), left superior temporal gyrus, bilateral angular gyrus (AG), bilateral medial prefrontal cortex and right anterior temporal lobe (ATL). LTLE patients demonstrated significantly less activation in the left HC and left SFG, whereas RTLE patients showed significantly less activation in the HC bilaterally, the left SFG and right AG. Verbal memory scores correlated with activations in the left and right HC, left SFG and right ATL and non-verbal memory scores with fMRI activations in the left and right HC and left SFG.

The face-name association task can be employed to examine functional alterations of hippocampal activation during encoding of both verbal and non-verbal material in one fMRI paradigm. Further, the left SFG seems to be a convergence region for encoding of verbal and non-verbal material.

1. Introduction

Hemispheric lateralization of memory within the mesial temporal lobe (mTL) has been the subject of functional MRI studies for many years. According to the classic material-specific model, the dominant (usually the left) mTL predominates in mediating verbal memory functions (Frisk and Milner, 1990) and the non-dominant (usually the right) mTL in non-verbal or visual memory functions (Kelley et al., 1998; Smith and Milner, 1981). However, this rather strict view had to be weakened as more and more studies emerged documenting postoperative verbal memory decline in patients after right temporal resection (Gleissner et al., 2002; Saling, 2009; Sidhu et al., 2016). For the non-verbal domain, there is even less evidence for a strict lateralization to the right mTL. Literature rather suggests an involvement of both mTL in visuo-spatial memory (Glikmann-Johnston et al., 2008; Saling, 2009; Sidhu et al., 2016). Instead of the classical material-specific model dynamic interactions between both mTL depending on specific task demands have been suggested (Saling, 2009).

The understanding of memory processes within the mTL is of particular importance with regards to memory outcome after anterior temporal lobe resections in patients with temporal lobe epilepsy (TLE) as it is known that surgery within the mTL bears the risk of relevant losses in episodic memory function. Patients with good memory abilities prior to surgery are especially more likely to decline in memory performance than patients with poor preoperative memory (Gleissner et al., 2004). Therefore, functional reorganization processes in patients with mTL damage and TLE have been the focus of many fMRI studies in recent years. It became apparent that TLE patients tend to reorganize their verbal and non-verbal memory functions to the contralesional mTL

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(Alessio et al., 2013; Banks et al., 2012; Cheung et al., 2009; Milian et al., 2015; Powell et al., 2007; Richardson et al., 2003; Sidhu et al., 2013).

Only few studies, however, have investigated reorganization processes within the whole brain. Alessio et al. (2013) found evidence of a more diffuse and bilateral cortical representation of verbal memory functions in left TLE (LTLE) patients, especially in the middle and ventro-lateral frontal regions, but also occipital, parietal and temporal areas, as compared to right TLE (RTLE) patients and healthy controls. Using a visual memory paradigm, they were able to demonstrate in RTLE patients more widespread and bilateral areas of activations than in LTLE patients and healthy controls during the encoding, but not the retrieval stage. Altered memory networks in TLE patients have also been reported by Sidhu et al. (2013), who were able to demonstrate that patients with LTLE recruited more contralateral regions, especially in the frontal and temporal lobe during word and face encoding, whereas RTLE patients engaged the middle frontal gyrus bilaterally during word encoding but showed activity increases only within the temporal lobes during face encoding as compared to healthy controls. Both studies used two material-specific paradigms for verbal and non-verbal memory functions, i.e. encoding of words to investigate left mTL memory functions and abstract drawings or faces for the assessment of right mTL memory functions. Using different paradigms to assess memory reorganization in left and right TLE patients is burdensome for the patients due to the necessity of longer scanning times and also renders direct comparison between both patient groups difficult.

In the current study, we investigated the networks underlying verbal and non-verbal memory functions in left and right TLE patients with hippocampal sclerosis (HS) compared to healthy subjects based on one paradigm that can address both right and left mTL memory functions within a unified framework. Therefore, we performed an fMRI study in patients with left and right TLE as well as healthy controls using a face-name association task. This task was designed to address both verbal and non-verbal memory functions relatively equally as face-name associations have been shown to rely on both mTLs and elicit bilateral hippocampal activations in healthy subjects (Kirwan and Stark, 2004; Klamer et al., 2013; Sperling et al., 2003).

The aims of our study were: (i) To test the hypothesis that LTLE and RTLE patients show less activation than healthy subjects within the respective hippocampus (HC) affected by sclerosis. (ii) To investigate whether responses in other brain areas involved in face-name encoding in healthy participants also exhibit altered activations in LTLE and RTLE patients. (iii) Finally, we addressed whether activation in these areas is behaviourally relevant and can predict memory performance as demonstrated by correlations between hemodynamic response amplitudes with verbal and non-verbal memory scores.

2. Materials and methods

2.1. Subjects

We examined 21 right-handed TLE patients with unilateral HS including 12 LTLE patients (7 females, mean age 36.6 years, SD = 12.42, range 18–57) and 9 RTLE patients (2 females, mean age 52.2 years, SD = 13.77, range 21–70), who underwent presurgical evaluation at the University Hospital Tübingen. All patients had clear signs of hippocampal sclerosis on 3T structural MRI, including unilateral hippocampal atrophy and increased T2 signal intensity, as determined by experienced neuroradiologists. Further details regarding patient characteristics can be found in Table 1.

Furthermore, we included 28 healthy participants (21 female, mean age 28 years, SD = 6.17, range 18–46). All patients and healthy controls were native speakers of German and strongly right-handed (mean handedness quotient >0.97 in the group of healthy subjects as well as both patient groups) as assessed by the Edinburgh Inventory (Oldfield, 1971).

The study was approved by the Ethics committee of the University of Tübingen and was in accordance with the guidelines of the Declaration of Helsinki. All participants gave written informed consent.

2.2. Neuropsychological memory tests

To assess verbal learning and memory, we used a wordlist learning and memory test which required to memorize a list of 15 words (Verbaler Lern- und Merkfähigkeitstest, VLMT, (Helmstaedter and Durwen, 1990; Helmstaedter et al., 2000)). We assessed the 'immediate recall' memory score, i.e. the sum of words correctly reproduced during the five learning trials (max. 75).

Non-verbal learning and memory were evaluated using a revised version of the DCS (Diagnostikum für Cerebralschädigung (Lamberti and Weidlich, 1999)) during which subjects had to learn 9 geometrical figures. We assessed again the 'immediate recall' score, i.e. the sum of correctly reproduced figures during the five learning trials (max. 45).

As memory performance levels decrease with age (Jenkins et al., 2000; Park et al., 2002), we employed the standardized memory performance as compared to an age-matched reference population in the form of percentile ranks instead of absolute values (i.e. raw scores).

Furthermore, we assessed the level of verbal crystallized intelligence in each participant using the German multiple choice vocabulary test (MWT-B, Mehrfachwahl-Wortschatz-Intelligenztest (Lehrl, 2005; Spreen and Strauss, 1998)), which has been shown to correlate with the Full Scale IQ of the HAWIE-R (Satzger et al., 2002).

2.3. Magnetic resonance data acquisition

MRI studies were performed on a Siemens Magnetom Sonata [Maestro Class] 1.5 T Scanner (Siemens AG, Erlangen, Germany). All data were acquired using an 8-channel array head coil for reception and the body coil for transmission. In order to obtain a high-resolution anatomical image of each subject's brain, a sagittal T1-weighted 3D–MPRAGE sequence was used (TR/TI/TE = 1300/660/3.19 ms, flip angle 15°, field of view = $256 * 256$ mm^2, matrix = $256 * 256$, 176 slices, voxel size = $1 * 1 * 1$ mm^3). Additionally, a field map was recorded for distortion correction of the functional images caused by magnetic field inhomogeneity. For the fMRI task, 175 gradient-echo planar T2*-weighted images covering the whole brain were acquired (TR = 4000 ms, TE = 64 ms, field of view = $192 * 192$ mm^2, matrix = $64 * 64$, voxel size = $3 * 3 * 3$ mm^3, gap = 0.3 mm, 38 interleaved slices). The first two images of each experimental run were discarded in order to reach equilibrium of magnetization.

2.4. Stimuli and fMRI task design

The stimuli were visually projected on a translucent screen positioned at the end of the scanner table using a video projector outside the magnet. Subjects saw the presentation via a mirror attached to the head coil. Outside the scanner room, a Windows Laptop using the software 'Presentation 0.6' (http://www.neurobehaviouralsystems.com) was connected to the video projector. Participants conveyed their responses via use of a two button box with their right thumb.

To investigate verbal and non-verbal memory functions, we used a face-name association paradigm, which comprised six encoding blocks. Each block consisted of four face-name pairs with simultaneous presentation of the face-name pair and a presentation duration of 7 s per each pair (plus 1 s black screen), and subjects were explicitly asked to memorize them (Fig. 1). This alternated with the control condition in which two scrambled versions of the previously shown faces were presented (Conway et al., 2008), and subjects had to indicate by button press whether the two pictures were identical or not (Fig. 1). This required response was implemented to ensure the participant's attention and cooperation.