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Sex differences in verbal and nonverbal learning before and after temporal lobe epilepsy surgery

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ABSTRACT

Women outperform men in a host of episodic memory tasks, yet the neuroanatomical basis for this effect is unclear. It has been suggested that the anterior temporal lobe might be especially relevant for sex differences in memory. In the current study, we investigated whether temporal lobe epilepsy (TLE) has an influence on sex effects in learning and memory and whether women and men with TLE differ in their risk for memory deficits after epilepsy surgery. 177 patients (53 women and 41 men with left TLE, 42 women and 41 men with right TLE) were neuropsychologically tested before and one year after temporal lobe resection. We found that women with TLE had better verbal, but not figural, memory than men with TLE. The female advantage in verbal memory was not affected by temporal lobe resection. The same pattern of results was found in a more homogeneous subsample of 84 patients with only hippocampal sclerosis who were seizure-free after surgery. Our findings challenge the concept that the anterior temporal lobe plays a central role in the verbal memory advantage for women.

1. Introduction

Women show better results than men in a range of learning and memory tasks [1], which may indicate a general female superiority in episodic memory [2]. This is especially true for verbal memory, where women are better at reproducing prose stories [3], learning and recall of word lists [4], and performing verbal fluency tasks [5]. A male advantage in nonverbal memory may be restricted to the mental representation of space [1]. Further, women outperform men in many nonverbal memory tasks, e.g. object location [6,7] or face recognition [8,9]. The neuroanatomical basis for sex differences in episodic memory is still to be determined. Several morphological, neurochemical and physiological differences between the sexes involved in the memory process have been found, which could potentially influence sex differences in memory capabilities [1]. For instance, women show a more pronounced fMRI-activation in the left hippocampus compared with men when learning pseudowords, while men demonstrate a higher activation than women in the right hippocampus while learning abstract designs [10]. Furthermore, a better immediate and delayed story recall in women was correlated with more cerebral blood flow to the left temporal pole, while men showed no such association between resting regional cerebral blood flow and verbal memory [11]. These results suggest that anterior temporal lobe structures play a crucial role in the episodic memory advantage for women.

Memory abilities are strongly linked to structures in the temporal lobe, including the hippocampus [12]. According to the material-specificity model, the two hemispheres of the brain are assumed to be asymmetrically organized with regard to memory abilities. While the left temporal lobe may be specifically responsible for verbal memory processes, nonverbal memory may be predominantly processed by the right temporal lobe [13]. Material-specific memory deficits have been linked to temporal lobe dysfunction, as found in patients with unilateral temporal lobe epilepsy (TLE). Patients with left temporal lobe epilepsy (L-TLE) show a significant impairment in word list learning and retention [14], and recall of a prose passage [15]. Similarly, a distinct deficit in the learning and retention of abstract designs can be found in patients with right temporal lobe epilepsy (R-TLE) [16,17].

Previous research has investigated the differential influence of TLE on memory performance in women and men. In some studies, a greater memory proficiency in women has been confirmed for patients with TLE as typically found in healthy participants [18,19]. However, other studies showed no difference in memory function between women and men with TLE [20,21]. It is thus unclear, so far, whether TLE may diminish sex differences in memory. In a similar vein, a small number of studies have investigated whether the memory function of women and men with TLE is differently affected by temporal lobe surgery. On the one hand, some studies found no difference preoperatively, but women had better verbal memory than men postoperatively [20–22].

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This may imply that active epilepsy suppresses the typical memory advantage of women over men, and that epilepsy surgery restores the sex difference in memory. On the other hand, another study found better verbal memory for women both pre- and postoperatively [23]. This rather suggests that sex differences in memory are unrelated to structures in the temporal lobe. Yet other studies could not demonstrate any sex effect on verbal memory, neither before nor after temporal lobe resection [24,25]. Most research in this area has focused on verbal memory measures, so far. Thus, research on sex differences in nonverbal memory following temporal lobe resection in right TLE is even more scarce, and results again point in different directions [24,25]. In conclusion, studies in patients with TLE so far could not univocally demonstrate sex differences in verbal or nonverbal memory neither in patients with TLE per se nor after temporal lobe surgery.

In the present study, we thus addressed the following questions. Does the anterior temporal lobe play an essential role for the memory advantage of women typically measured in healthy participants? Further, are women and men differentially affected in their memory function by temporal lobe resection for the relief of refractory TLE? And third, does verbal versus nonverbal material have a mediating effect on sex differences? To address these aims, we examined whether women and men with TLE show differences in their learning or delayed recollection of lists of words and abstract designs. Patients who have undergone thorough evaluation for epilepsy surgery were tested both before and one year after left or right temporal lobe resection. Based on the studies in healthy individuals, we expected that women with TLE would also show better learning and delayed memory performance than men with TLE. In variance to most previous research in patients with TLE, we investigated memory for both verbal and nonverbal material. Earlier research attributes female superiority in episodic memory to better encoding in women [9]. We therefore assumed that the memory advantage in women with TLE should accumulate over multiple learning trials. We further assumed that if structures in the left and right temporal lobes were relevant for sex differences in material-specific memory, then a sex effect for verbal memory should be reduced or absent in patients with L-TLE, while a sex effect for nonverbal memory should be reduced or absent in patients with R-TLE. We also hypothesized that sex differences in memory should be further diminished following unilateral temporal lobe surgery. However, this latter hypothesis is contrary to some studies in the field of TLE referred to above, in which men usually showed stronger postoperative decreases (or less increase) after temporal lobe resection than women, thus restoring the advantage for women over men as typically seen in healthy individuals [20,21]. These studies therefore rather suggest that epilepsy surgery releases the memory advantage of women over men, again. This alternative hypothesis would state that active epilepsy rather than the temporal focus has a diminishing influence on the memory sex effect, and that a difference between women and men with TLE should reappear postoperatively.

2. Methods

2.1. Patients

Data were retrospectively obtained from 257 patients with TLE (135 women, 122 men) who had undergone pre- and one year postoperative assessment at the Epilepsy-Center Berlin-Brandenburg, Germany, between 1998 and 2015. The following exclusion criteria were used: a) age < 16, b) vocabulary IQ-score < 75, c) MRI abnormalities outside the temporal lobe, d) seizures originating from both temporal lobes according to ictal EEG, e) prior brain surgery, f) malignant brain tumors (WHO grade III–IV), g) postoperative strokes, h) no sufficient proficiency in German language (translation necessary or limited understanding of test instructions as documented), i) one year follow-up neuropsychological assessment not carried out, j) severe psychiatric diagnoses (e.g. severe depression, psychosis, and dementia), k) atypical language dominance as determined by either WADA-test or fMRI. 180 patients were eligible after exclusion according to these criteria. Three patients had missing values in the nonverbal learning test and were thus also excluded from further analyses. Eventually, 177 patients were included in the study. 53 women and 41 men received left temporal lobe surgery, 42 women and 41 men underwent right temporal lobe surgery. Surgery was performed at the Department of Neurosurgery, Charité-Universitätsmedizin Berlin. In the vast majority of cases, anterior temporal lobe resection included amygdalohippocampectomy (163 patients), which is described in detail elsewhere [26]. Other surgical procedures were extended lesionectomy in the temporal lobe (6 patients), temporal lobe resection without amygdalohippocampectomy (6 patients), temporal lobe resection with amygdalectomy sparring the hippocampus (1 patient), and temporal lobe resection with hippocampectomy sparring the amygdala (1 patient). All patients were neuropsychologically tested before and one year after surgery as part of a routine pre- and postoperative assessment. The study was approved by the ethics committee of Charité-Universitätsmedizin Berlin.

2.2. Memory tests

Memory was tested before surgery ($M = 6.2$ months, $SD = 7.8$) and at a one-year follow-up assessment ($M = 12.3$ months, $SD = 2.0$).

2.2.1. Verbal memory

Verbal learning and recall were assessed with the German adaptation of the Rey Auditory Verbal Learning Test (VLMT, Verbaler Lern- und Merkfähigkeitstest [27]). The examiner read aloud a list of 15 words which patients were asked to repeat in any order. This procedure was repeated five times. Patients were then instructed to learn and recall a different list of 15 words in one trial for distraction. Subsequently, patients were asked to recall as many words as possible from the first word list. After approximately 30 min the first word list had to be recalled again. The total number of words recalled over all five learning trials and number of words recalled after 30 minute-delay were used for analyses.

2.2.2. Nonverbal memory

Nonverbal learning and delayed recognition were assessed with the NVLT (Nonverbaler Lerntest [28]). 120 nonsense figures on printed cards were presented consecutively for 3 s each. In a first list of 20 items, eight figures were included that recurred five times during the further test. The test then immediately proceeded with five consecutive recognition lists each including the eight target items randomly intertwined with 12 unknown distractor items. Patients were instructed to decide for each item presented whether they had seen it before. For analysis, we used total numbers of correctly recognized figures over all five recognition test trials corrected for false positives (difference values between true positives and false positives, possible range from −12 to 8 items) and number of correctly recognized figures after a 30 minute-delay (again corrected for false positives).

2.3. Statistical analysis

Differences in clinical, demographic or neuropsychological variables between patient groups were tested using univariate analyses of variance (ANOVAs), Kruskal-Wallis tests and χ^2 tests. We used repeated measures analyses of covariance (RANCOVAs) to investigate the difference between women and men with left or right temporal lobe resection on verbal and nonverbal learning, as well as delayed memory performance. To further explain significant interaction effects of the main analysis, we conducted additional hierarchical analyses of covariance (ANCOVAs) or RANCOVAs depending on the effects. p values <0.05 were regarded as statistically significant, p values between 0.05 and 0.10 were considered as statistical trends (two-sided test). In addition to F and p values, effect sizes are reported as partial eta squared (η^2).