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Female verbal memory advantage in temporal, but not frontal lobe epilepsy

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ABSTRACT

Women show better performance than men on a range of episodic memory tasks. Evidence regarding a neuroanatomical localization of this effect remains ambiguous. It has been suggested that anterior temporal lobe structures are responsible for sex differences in verbal memory, yet temporal lobe epilepsy (TLE) and TLE surgery do not affect women's verbal memory advantage. Instead, frontal lobe regions may be relevant for female verbal memory superiority, i.e. by enabling more efficient encoding and retrieval strategies in women. The aim of the present study was to investigate whether women's verbal memory advantage can be found in patients with frontal lobe epilepsy (FLE), and how patients with FLE and those with TLE differ with regard to sex differences in verbal memory. Fifty patients with unilateral FLE (26 women, 24 men) were compared with 183 patients with unilateral TLE (90 women, 93 men) on both verbal learning and delayed memory. We found that women showed better verbal memory than men in the TLE group, but not in the FLE group. In addition, we found that patients with TLE showed worse verbal learning than those with FLE. Our findings support the idea that women's advantage in verbal memory may be related to frontal lobe function.

1. Introduction

Women have better episodic memory than men (Andreano and Cahill, 2009; Herlitz and Rehnman, 2008). This might be due to sex-specific strategy use during encoding and retrieval of information (Andreano and Cahill, 2009; Pletzer, 2014). For example, women's better verbal memory has been related to increased use of organizational strategies, such as semantic or phonological clustering (Berenbaum et al., 1997; Kramer et al., 1988; Weiss et al., 2006; Sunderaraman et al., 2013). Furthermore, women prefer verbal strategies to solve spatial memory tasks, while men prefer nonverbal strategies (Frings et al., 2006). In general, women seem to perform better than men on memory tasks especially when verbalization of material is possible (Andreano and Cahill, 2009). In the present study, we studied neuroanatomical correlates of women's better verbal memory in patients with focal epilepsy.

The temporal lobe and the hippocampus are crucial for episodic memory (Squire and Zola-Morgan, 1997). In addition, frontal lobe structures may support memory encoding and retrieval through organizational and controlling processes (Fletcher and Henson, 2001; Ojemann and Kelley, 2002). For instance, semantic clustering during word list recall is related to frontal lobe functioning (Long et al., 2010; Manning et al., 2012; Savage et al., 2001). Accordingly, patients with frontal lobe lesions show reduced semantic clustering (Baldo et al., 2002; Gershberg and Shimamura, 1995). In the present study, we hypothesized that the greater tendency of women to use verbal strategies may have a basis in the frontal lobe.

Sex-specific brain activations during episodic memory tasks have been demonstrated both within temporal and frontal regions (Piefke et al., 2005; Young et al., 2013). For example, functional neuroimaging studies have related higher activation of anterior temporal lobe structures with better verbal memory performance in women than men (Banks et al., 2012; Ragland et al., 2000). What is more, functional neuroimaging studies also showed greater activation in frontal regions in women than men during verbal memory retrieval (Young et al., 2013; Nyberg et al., 2000). Similarly, women show increased activation of frontal regions compared with men during working memory tasks (Goldstein et al., 2005; Hill et al., 2014). Taken together, evidence from functional neuroimaging studies suggests that both frontal and temporal lobe regions may be relevant for women's verbal memory advantage. Still, functional imaging studies alone cannot determine whether the activated temporal and frontal structures are necessary for memory differences between women and men. Imaging research needs to be validated by studies using various models of temporal and frontal pathology.

Previous research has shown that women with temporal lobe epilepsy (TLE) have better verbal memory than men with TLE (Berenbaum et al., 1997; Berger et al., 2017; Helmstaedter et al., 1999).

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Furthermore, women's verbal memory advantage remains unaltered even after TLE surgery (Berenbaum et al., 1997; Berger et al., 2017). These findings suggest that temporal lobe structures may not be necessary for women's memory advantage, as suggested by functional neuroimaging studies (see above). So far, no previous study has investigated sex differences in memory in patients with frontal lobe epilepsy (FLE). Based on the literature outlined so far, we hypothesized that FLE but not TLE attenuates women's advantage in verbal memory.

Compared with the extensive literature on memory deficits in patients with TLE, research on memory functioning in patients with FLE is scarce. Impaired verbal memory in patients with FLE compared with healthy participants has been previously reported (Giovagnoli et al., 2005; Centeno et al., 2012; Exner et al., 2002; Rayner et al., 2015; Patrikelis et al., 2016). While some studies suggest that verbal memory deficits in FLE are less pronounced than in TLE, other studies found similar verbal memory impairment in patients with FLE and TLE (for a review, see Centeno et al., 2010; Patrikelis et al., 2009). The present study wants to add to the existing research on verbal memory differences between patients with FLE and TLE. We hypothesized that patients with TLE show worse verbal memory than patients with FLE.

In order to test our hypotheses, the present study compared women and men with unilateral refractory FLE or TLE in verbal learning and delayed memory. To this aim, we employed a widely recognized verbal memory test, the German Version of the Rey Auditory Verbal Learning Test (Helmstaedter et al., 2001), which is sensitive to detecting sex differences in healthy participants (see e.g. Bleecker et al., 1988; Van der Elst et al., 2005; Gale et al., 2007; Sundermann et al., 2016).

2. Material and methods

2.1. Patients

We retrospectively selected patients with intractable focal epilepsy who had undergone preoperative assessment for epilepsy surgery at the Epilepsy-Center Berlin-Brandenburg for further analysis. A proportion of patients included in this study overlapped with the patient sample reported in a previous investigation (Berger et al., 2017). Seizure focus localization was determined using extensive ictal and interictal electroencephalogram (EEG) recordings in conjunction with seizure semiology and detection of structural lesions according to magnetic resonance imaging (MRI). Patients were included that had definite unilateral FLE or TLE, were older than 16 years, and for whom a neuropsychological report was available (n = 422). Exclusion criteria were used in the following order: verbal IQ score below 75 (n = 20); previous brain surgery (n = 37); significant MRI determined structural abnormalities outside the affected frontal or temporal lobe, respectively (n = 115); insufficient comprehension of the German language (as documented by the examiner, n = 17). Thus, 233 patients (26 women and 24 men with FLE, 90 women and 93 men with TLE) entered the study. Epilepsy surgery for relief of refractory FLE or TLE was conducted in 125 patients after pre-surgical evaluation (see Table 1). The study was approved by the Institutional Review Board of Charité − Universitätsmedizin Berlin (EA2/174/16).

For patients with FLE, MRI findings included suspicion of cortical dysplasia (n = 8), cavernoma (n = 4), polymicrogyria (n = 3), astrocytoma (n = 2), DNET (n = 2), heterotopia (n = 2), tumor of unknown origin (n = 2), ganglioglioma (n = 1), epidermoid cyst (n = 1), nonspecific pathology (n = 4), or no evidence for pathology (n = 21). For patients with TLE, MRI findings included suspicion of hippocampal sclerosis (n = 90), cortical dysplasia (n = 10), tumor of unknown origin (n = 10), cavernoma (n = 7), DNET (n = 7), ganglioglioma (n = 3), hamartoma (n = 3), heterotopia (n = 2), arachnoid cyst (n = 2), astrocytoma (n = 2), choroid plexus papilloma (n = 1), arteriovenous malformation (n = 1), nonspecific pathology (n = 7), or no evidence for pathology (n = 38).

2.2. Memory test

Verbal memory was assessed with the VLMT, a German adaptation of the Rey Auditory Verbal Learning Test (Verbaler Lern- und Merkfähigkeitstest; Helmstaedter et al., 2001). A list of 15 words was read aloud by the examiner consecutively over five trials. Patients were asked to recall as many words as possible immediately after each trial. 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 (trial 6). After approximately 30 min the first word list had to be recalled again (trial 7). Finally, the words of the first word list had to be identified from a list of 50 words. The total number of words recalled over all five learning trials and the number of words recalled after the 30 min-delay were used for analyses.

2.3. Other neuropsychological tests

Further neuropsychological tests were used to investigate the influence of possible covariates on memory and to rule out possible alternative explanations of our results. For instance, it may be that women show better verbal learning and memory retrieval due to better general verbal abilities (Hyde and Linn, 1988) or increased verbal working memory capacity (Speck et al., 2000). Also, it is known that depression can influence memory performance (Paradiso et al., 2001). Verbal IQ was estimated using a vocabulary test (Wortschatztest; Schmidt and Metzler, 1992). Verbal fluency was assessed with the alternating phonemic verbal fluency subtest of the RWT (Regensburger Worftlüssigkeitstest; Aschenbrenner et al., 2000). Verbal working memory was assessed with the Digit Span subtest of the Wechsler Memory Scale-III (Wechsler, 1997). Symptoms of depression were assessed with the BDI (Beck Depression Inventory; Beck et al., 1961). BDI scores were available for 194 patients, as the BDI was not used during the first 2 years of data collection (see Table 1).

Due to the retrospective design of the study, anxiety scores were not continuously assessed in our sample, and were only available for a small subgroup of patients. Thus, we do not report anxiety scores in the present study. However, prior studies showed no relation between symptoms of anxiety and verbal memory performance (e.g. Deckersbach et al., 2011; Brown et al., 2014).

2.4. Statistical analysis

Patient groups were compared on clinical, demographic and background neuropsychological variables using univariate analyses of variance (ANOVAs) and χ^2 tests. Univariate analyses of covariance (ANCOVAs) were used to analyze the difference between women and men with FLE and TLE in learning and delayed memory performance. p values < 0.05 were regarded as statistically significant, p values between 0.05 and 0.1 were considered as statistical trends (two-sided test). Effect sizes are reported as partial eta squared (η^2). In accordance with Cohen (1988), a η^2 of 0.01 is considered to be a small, 0.06 a medium, and 0.14 a large effect size. Data were analyzed with IBM SPSS Statistics Version 21.

3. Results

3.1. Patient characteristics

Patients were divided into four groups based on sex and localization of seizure origin (frontal lobe versus temporal lobe focus) and compared on demographic, clinical and background neuropsychological variables (see Table 1). Education was defined as years attended at primary and secondary school. As shown in Table 1, the patient groups did not differ in epilepsy duration, number of current antiepileptic drugs, years of school education, depression rating, verbal working