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Atypical handedness in mesial temporal lobe epilepsy

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A B S T R A C T

Objective: The main aim of our study was to investigate the handedness of patients with mesial temporal lobe epilepsy (MTLE). We also sought to identify clinical variables that correlated with left-handedness in this population.
Methods: Handedness (laterality quotient) was assessed in 73 consecutive patients with MTLE associated with unilateral hippocampal sclerosis (HS) using the Edinburgh Handedness Inventory. Associations between right- and left-handedness and clinical variables were investigated.
Results: We found that 54 (74.0%) patients were right-handed, and 19 (26%) patients were left-handed. There were 15 (36.6%) left-handed patients with left-sided seizure onset compared to 4 (12.5%) left-handed patients with right-sided seizure onset ($p = 0.030$). Among patients with left-sided MTLE, age at epilepsy onset was significantly correlated with handedness (8 years of age [median; min-max 0.5–17] in left-handers versus 15 years of age [median; min-max 3–30] in right-handers ($p < 0.001$).
Conclusions: Left-sided MTLE is associated with atypical handedness, especially when seizure onset occurs during an active period of brain development, suggesting a bi-hemispheric neuroplastic process for establishing motor dominance in patients with early-onset left-sided MTLE.

1. Introduction

The left and right hemispheres differ in their functional organization and specialization. The left hemisphere is typically responsible for processes involved in language and verbal memory. Left-sided language dominance is present in nearly all right-handers as well as the majority of left-handers. Damage to the left hemisphere in utero or during early childhood is often associated with network reorganization, resulting in atypical lateralization of hemispheric functions such as language, verbal memory, and motor dominance (handedness) [1]. For example, several authors have demonstrated atypical lateralization of language and memory functions in patients with left-sided mesial temporal lobe epilepsy (L-MTLE) [2–7]. Based on this work, it appears that the crucial variable determining the likelihood of cerebral reorganization is the age at epilepsy onset; i.e., the lower the age of epilepsy onset, the greater the probability of atypical lateralization of function [6].

In addition to atypical hemispheric dominance for language and verbal memory associated with L-MTLE, there is a correlation between left-sided cerebral damage or seizure onset and atypical handedness [8–14]. For example, in 1959, Penfield and Roberts reported that 27% of 246 patients with epilepsy and focal left-sided brain injury were left-handed compared to only 8% of 276 patients with epilepsy and focal right-sided brain injury [10]. What remains unclear is the extent to which frontal lobe pathology, with or without frontal lobe seizure onset, is a pre-requisite for atypical handedness in patients with epilepsy, given the localization of motor control in the frontal lobe. In light of the growing evidence that MTLE is a brain network disease, with widespread extra-temporal anatomic and functional alterations [15], we hypothesized that MTLE would be associated with atypical handedness. We further speculated that atypical handedness would be associated with L-MTLE, reflecting the increased likelihood of atypical handedness lateralization associated with left-sided lesions, and early age of seizure onset, given the known correlation between young age and atypical hemispheric function [1,16]. The main aim of our study was therefore to assess handedness in patients with MTLE. We also sought to identify clinical variables that correlated with left-handedness in this population.

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2. Methods

We retrospectively analyzed handedness in 73 consecutive adult patients (41 females, 32 males) with drug-refractory MTLE associated with unilateral hippocampal sclerosis (HS). Handedness was assessed with the Edinburgh Handedness Inventory [17]. A laterality quotient (LQ) which ranged from −100 to 100 was calculated for each patient as described previously [17]. Patients with LQ from 100 to 0 were defined as right-handers. Patients with LQ from 0 to −100 were defined as left-handers. All patients underwent investigation for epilepsy surgery, including brain MRI, neuropsychological tests, and interictal/ictal semi-invasive video-EEG monitoring with sphenoidal electrodes, including ictal semiology analysis. Positron emission tomography (PET), interictal/ictal single photon emission tomography (SPECT), subtraction ictal SPECT co-registered to MRI (SISCOM) and invasive EEG (SEEG) were performed only in a subset of patients based on their clinical data and expert consensus. The inclusion criteria differ between surgically and medically treated patients. In medical group, only patients with unilateral temporal seizure onset and anatomically concordant HS on MRI were included. The HS was radiologically defined as unilateral hippocampal atrophy and increased signal in the hippocampus [18]. We excluded patients with suspicion of dual pathology, including bilateral HS, and bilateral seizure onset. In surgical group, we included only patients who underwent anteromesial temporal lobe resection, the presence of HS was confirmed histopathologically and was classified as having Engel 1a outcome at one year postsurgical follow-up [19]. Demographic data, including age at epilepsy onset, duration of epilepsy, performance of surgery, number of seizures per month, occurrence of generalized tonic-clonic seizures (GTCS), and type or age of initial precipitating injury were obtained by medical chart review.

The statistical analysis utilized Fisher's exact test or Mann-Whitney test according to their condition of validity. For all tests, a p value <0.05 was considered statistically significant.

All patients gave their informed consent prior to participation in the study and study approval was granted by the ethical committee at St. Anne's University Hospital.

3. Results

Among 73 enrolled patients with MTLE (46 [63%] patients underwent surgery, 27 [37%] were treated medically), HS was lateralized to the right in 32 (43.8%) patients and to the left in 41 (56.2%) patients. We did not find any statistically significant differences in demographics between patients with R-MTLE and L-MTLE (Table 1). Overall, 54 (74.0%) patients were right-handed and 19 (26%) patients were left-handed. The proportion of left-handers was statistically significantly higher in patients with L-MTLE than in patients with R-MTLE: 15 (36.6%) patients with L-MTLE were left-handed compared with 4 (12.5%) patients with R-MTLE ($p = 0.030$, Fig. 1).

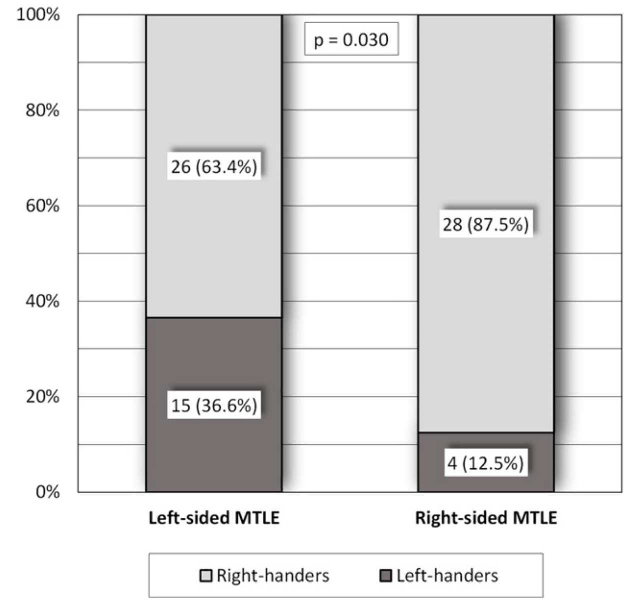

Fig. 1. Difference in left-handers representation between patients with left- and right-sided MTLE MTLE – mesial temporal lobe epilepsy.

We then assessed for clinical variables that correlated with handedness in patients with L-MTLE, and, separately, in patients with R-MTLE (Table 2). This revealed that in patients with L-MTLE MTLE, age of epilepsy onset correlated with handedness (Fig. 2). Left-handed patients with L-MTLE had an earlier age of epilepsy onset (median 8 years of age, min-max 0.5–17) compared with right-handed patients with L-MTLE (median 15 years of age, min-max 3–30; $p < 0.001$). No other clinical variables, including the presence of initial precipitating injury, correlated with handedness in patients with L-MTLE, and there were no clinical variables associated with handedness in the patients with R-MTLE.

Table 1
The comparison of demographic data between patients with right- and left-sided MTLE.

	Right-sided MTLE (n = 32)	Left-sided MTLE (n = 41)	p-Value
Age at epilepsy onset Median (min-max)	13.5 (0.5–41)	13 (0.5–30)	1.000
Duration of epilepsy Median (min-max)	15 (5–20)	15 (6–26)	1.000
Surgery Y/N n(%)	30 (93.8)/2(6.2)	38 (92.7)/3 (7.3)	1.000
Number of seizures per month ≥5 seizures/<5 seizures n(%)	26 (81.3)/6 (18.7)	34 (82.9)/17 (17.1)	1.000
GTCS Y/N n(%)	14 (43.8)/18 (56.3)	16 (39.0)/25 (61.0)	0.811
Initial precipitating injury n (%)	9 (28.1)	19 (46.3)	0.147

GTCS – generalized tonic-clonic seizures, MTLE – mesial temporal lobe epilepsy, N – no, Y – yes.

Table 2
Comparison of demographic data between left- and right-handers, analysis done separately for left-sided MTLE and right-sided MTLE.

Left- sided MTLE			
	Left-handers (n = 15)	Right-handers (n = 26)	p-Value
Age at epilepsy onset Median (min-max)	8 (0.5–17)	15 (3–30)	<0.001
Duration of epilepsy Median (min-max)	16 (6–26)	16 (8–25)	0.103
Surgery Y/N n(%)	13 (86.7)/2 (13.3)	25 (96.2)/1 (3.8)	0.543
Number of seizures per month ≥5 seizures/<5 seizures n(%)	11 (73.3)/4 (26.7)	23 (88.5)/3 (11.5)	0.390
GTCS Y/N n(%)	9 (34.6)/17 (65.4)	7 (46.7)/8 (53.3)	0.517
Initial precipitating injury n (%)	7 (46.6)	12 (46.2)	1.000
Right-sided MTLE			
	Left-handers (n = 4)	Right-handers (n = 28)	p-Value
Age at epilepsy onset Median (min-max)	19 (1.5–30)	13.5 (0.5–41)	1.000
Duration of epilepsy Median (min-max)	15 (10–20)	14.5 (5–25)	0.129
Surgery Y/N n(%)	3 (75)/1 (25)	27 (96.4)/1 (3.6)	0.238
Number of seizures per month ≥ 5 seizures/< 5 seizures n(%)	4 (100)/0 (0)	22 (78.6)/6 (21.4)	0.566
GTCS Y/N n(%)	2 (50)/2 (50)	12 (42.9)/16 (57.1)	1.000
Initial precipitating injury n (%)	9 (32.1)	0 (0)	0.303

GTCS – generalized tonic-clonic seizures, MTLE – mesial temporal lobe epilepsy, N – no, Y – yes.