Organization and Memory in Temporal Lobe Epilepsy

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Objective: Memory impairment is a common comorbidity in individuals with temporal lobe epilepsy (TLE). Further, in medication-resistant epilepsy the frontline option, neurosurgical epileptogenic zone destruction, places memory at significant risk. Research has highlighted that TLE causes whole-brain network efficiency disruption, but it is not established how this may explain pre- and post-surgical cognition. Here we examine whether white matter structural network organization predicts pre-operative memory function and/or risk for post-operative memory decline.
Participants and Methods: Patients with drug-resistant TLE were recruited from two epilepsy centers in a prospective longitudinal study. The pre-operative sample included 51 individuals with left TLE (L-TLE), 52 with right TLE (R-TLE), and 57 healthy controls who underwent T1- and diffusion-weighted MRI (dMRI), and neuropsychological tests of verbal and visual memory. Forty-four patients (n=21 L-TLE) subsequently underwent temporal lobe surgery (36 anterior temporal lobectomy; 7 stereotactic laser amygdalohippocampectomy; 1 amygdalohippocampectomy) and completed post-operative memory testing. Whole-brain connectomes were generated via diffusion tractography and analyzed using graph theory, focusing on network integration (*path length*) and specialization (*transitivity*). In the pre-operative dataset, first we compared TLE versus controls with analysis of covariance (ANCOVAs) controlling for age. Next, linear regressions examined the association between memory scores and network efficiency between L-TLE, R-TLE and controls. In the post-operative sample, bivariate correlations examined the association between pre- to post-operative memory change and 1) global network efficiency and 2) asymmetry of mesial temporal efficiency (i.e., local efficiency of the hippocampal, parahippocampal, and entorhinal nodes). Finally, efficiency metrics were entered into stepwise regressions along with established predictors of memory decline.
Results: Compared to controls, TLE showed longer path length ($p < .05$; $\eta_p^2 = .03$) and lower transitivity ($p = .01$; $\eta_p^2 = .04$). Pre-operatively, better verbal learning and memory were associated with both shorter path length (β = -0.23 to -0.32; $ps_{adjusted} < .05$) and increased transitivity (β = 0.20 to 0.31; $ps_{adjusted} < .05$). These associations were greater in L-TLE than R-TLE (i.e., a significant interaction; β = -0.29 to 0.25; $ps_{adjusted} <.05$). Post-operatively, global metrics predicted decline on list learning for L-TLEs (rs = -.57 to .58; ps < .01), and were marginal on list recall (rs = -.42 to .40; ps < .10). Leftward asymmetry of mesial temporal local efficiency predicted greater decline across most verbal memory measures for L-TLE (rs -.47 to -59; $ps_{adjusted} <.05$), but not R-TLE. Asymmetry of mesial network efficiency uniquely explained at least 20 to 43% of the variance in list learning, recall, and story learning for L-TLE, outperforming hippocampal asymmetry and pre-operative score ($ps_{adjusted} <.05$).
Conclusions: Our findings suggest that global white matter network abnormalities contribute to verbal memory impairment pre-operatively and vulnerability to decline post-operatively in L-TLE. Asymmetry of a predefined mesial temporal sub-network may help predict post-operative memory function following left temporal lobe surgery, such that greater efficiency in the to-be-resected mesial temporal network may be an important risk factor for decline. Our findings extend the importance of network approaches in TLE to include the relationships between neurobiological networks and memory function.

Categories: Epilepsy/Seizures
Keyword 1: epilepsy / seizure disorders
Keyword 2: neuroimaging: structural connectivity
Keyword 3: memory disorders
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2 Cross Cultural Application of the International Classification of Cognitive Disorders in Epilepsy (IC CoDE)*Cognitive Phenotypes in People with Temporal Lobe Epilepsy in India*

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Objective: To apply the new IC-CoDE cognitive diagnostic taxonomy (Norman et al., 2020) to a large cohort of people with temporal lobe epilepsy (TLE) in India. The IC-CoDE taxonomy of cognitive diagnoses for 1,409 English-speaking adults with TLE from seven epilepsy centres in the U.S. has been published (McDonald et al., 2022). Initial results suggest that the IC-CoDE produces stable cognitive phenotypes across centres; however, its international applicability, including the suggested impairment cut-off needs to be considered across cultures and languages to avoid misclassification. The aim of this study was to apply the IC-CoDE to a population, outside of the U.S., diverse in language representation (i.e., bi/multi-lingual), assessment tools, normative data, and educational and cultural backgrounds to determine whether the same cognitive phenotypes and their relative frequencies would emerge.
Participants and Methods: Data from 549 adults with TLE (mean age=27.14 (8.04), 60.47% males) from a tertiary referral hospital in Mumbai, India who had undergone a comprehensive neuropsychological evaluation (minimum two tests in at least 4 of the 5 cognitive domains: memory, language, executive function, attention/processing speed and visuospatial) were analysed using the IC-CoDE criteria. The base rate of impairment for individual tests was calculated using a cutoff of 1.5 standard deviations (S.D.) below the normative mean. The cognitive diagnostic criteria were applied, and the distribution and base rate of cognitive phenotypes was compared to the published taxonomy data from the U.S. (McDonald et al., 2022).
Results: In comparison to the U.S. cohort, the India group was relatively younger, lower in the education level, had a younger age at seizure onset and a shorter duration of the epilepsy. Application of the IC-CoDE taxonomy using a 1.5 S.D. cutoff revealed an Intact cognitive profile in 48% of patients, Single Domain impairment in 32%, Bi Domain impairment in 15% and Generalised impairment in 5%. These findings were mostly comparable to percentages reported in the U.S. cohorts with Intact profile (47%; c2= 0.158, p=0.690), Single Domain (29%; c2= 46.26, p<0.01), Bi Domain (16%; c2= 0.298, p=0.585) and Generalised (8%; c2= 5.347, p=0.021) impairment. However, the most common impairment in the Single Domain group for the bi/multilingual India population was Memory (38%) followed by Attention (20%) and then Language (13%), diverging from the distribution in the U.S. data with maximum impairment in Language (49%) followed by Memory (32%) in the Single Domain Group.
Conclusions: These findings demonstrate that the IC-CoDE can be applied internationally, and the broad taxonomy of cognitive diagnosis holds even in a culturally, linguistically diverse population. Differences in rates of impairments across specific domains emerged with language relatively preserved in the India bi/multilingual population, and memory more frequently impaired than observed in the multi-centre U.S. sample. These findings may reflect differences in demographics, rates of bi/multilingualism, normative data, language tools, or underlying neuropathology, which should be further explored to determine their impact on cognitive profiles.

Categories: Epilepsy/Seizures
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Keyword 3: cognitive functioning
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3 Latent Wechsler Profiles in Presurgical Pediatric Epilepsy

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