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The impact of Cognitive Reserve (CR) on the neuropsychological performance of pre-surgical patients with Temporal Lobe Epilepsy (TLE): A case series

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Introduction

Epilepsy, a condition characterized by recurrent and unprovoked seizures, is among the most commonly diagnosed chronic neurological disorders [1]. Seizures are excessive bursts of electrical activity generated within distinct cortical regions and networks that may acutely influence an individual's cognitive, behavioral, and/or psychological state, though more persistent changes in these areas of functioning may occur with repeated seizures [1]. Temporal Lobe Epilepsy (TLE) is widely considered to be the most prevalent diagnosed form of focal epilepsies [2,3]. Individuals with a diagnosis of TLE may experience diminutions in cognitive functioning, typically within the domains of language and memory [4,5]. Such cognitive disturbances could be attributed to seizure-related damage occurring at the cellular level within temporal lobe structures, including the hippocampus and amygdala [5]. Individuals with a TLE diagnosis may experience drug-resistant seizures that persist despite treatment with two Antiepileptic Drug (AED) schedules [3,6]. In these cases, neurosurgical intervention is the treatment of choice for controlling or reducing the frequency of seizures, with the ultimate goal of improving overall quality of life [7]. When determining the optimal surgical intervention, the lateralization and localization of seizure foci are guided by multiple factors, including neuropsychological evaluation findings.

Precise interpretation of neuropsychological data necessitates consideration of pre-existing intellectual parameters, including Cognitive Reserve (CR). CR theory postulates that an individual's capacity for cognitive adaptation in the context of neuropathology is reliant on premorbid factors, intrinsic intellectual abilities and accumulated body of knowledge [8]. Other factors, such as occupational status and accomplishments, routine physical exercise, and active participation in leisure activities, are also considered critical components of an individual's CR [9]. There is also evidence that multilingualism contributes

to CR through the augmentation of neural network efficacy and gray matter in cortical areas [9-12].

In the context of a pre-surgical epilepsy workup, a high level of Cognitive Reserve (CR) may obscure interpretation of the neuropsychological data used for lateralization and localization of neuropathology, as well as for neurosurgical decision-making purposes. Neuropsychological evaluations also serve to establish a baseline for outcome comparison, as patients presenting with a decline in cognition prior to a neurosurgical intervention are at an elevated risk for further cognitive deterioration post-operatively when compared to patients with intact cognitive capabilities [13-15].

The potential impact of CR on the neuropsychological performance of patients diagnosed with TLE has not been fully explored or systematically researched. The authors posit that high levels of CR predating seizure onset may impact neuropsychological findings that can factor into determining candidacy for neurosurgical interventions. Thus, the CR phenomenon within epilepsy patients merits further exploration, as neuropsychological data may less likely lateralize and localize as well as prognosticate in expected ways due to the influence of CR.

Methods

Two cases of patients with drug-resistant TLE are presented to illustrate the potential impact of CR on the manifestation of expected neurocognitive profiles. Both cases were evaluated with a neuropsychological battery appropriate for patients with a diagnosis of epilepsy, as part of a comprehensive, multi-disciplinary epilepsy workup to determine candidacy for neurosurgical intervention. (Table 1) presents the full classification of the cases' testing scores per cognitive domain that indicated at least intact or better functioning when compared to a standardized population.

Results

Case 1

53-year-old, ambidextrous, tri-lingual (Spanish, Mandarin and English), East Asian female, with a medical history significant for drug-resistant, lesional, left-hemispheric localized TLE. In terms of neurodiagnostic findings, a 24-hour ambulatory electroencephalogram (aEEG) was notable for left fronto-temporal lobe slowing. Reported seizure semiology included feelings of dread, seeing "stars" for several seconds, head and eye deviation to the right side and difficulties with verbalization. Brain Magnetic Resonance Imaging (MRI) demonstrated mild hippocampal asymmetry (left smaller than right) and possible small right inferior cerebellopontine cistern arachnoid cyst. In terms of her academic history, the patient earned a graduate degree in the humanities. With regards to occupational history, the patient operates a self-made online store, authors books for children and translates written material between her spoken languages. Following seizure onset, the patient reported a decline in her ability to sustain attention, memory lapses and word-finding difficulties.

This patient was believed to have high CR based on her ability to master three distinct languages, her vocational functioning prior to seizure emergence and her achieved strong score on a screening measure of literacy that assesses pre-morbid abilities. Her composite score on an abbreviated measure of intellectual functioning was firmly intact, and within expectations when compared to a normative sample. Analysis of the patient's neuropsychological data revealed strengths on measures of verbal learning and memory, visual learning and memory, visuospatial abilities and executive functioning. She did not exhibit the expected deficits on metrics of learning and memory that are consistent with a TLE population. Furthermore, the patient displayed intact functioning on measures of working memory and attention. She evinced inconsistencies on metrics of executive functioning involving abstract reasoning, inhibitory behavioral control and mentally shifting between two distinct categories. Weaknesses were observed on measures of processing speed. In terms of language functioning, she did not display anticipated deficits on metrics of verbal fluency, as her performance was solidly intact and consistent with a normative sample. The patient performed poorly on a measure of confrontation naming when responding in English; however, her score improved significantly to reveal intact functioning when permitted to provide answers in either Mandarin or Spanish.

Case 2

21-year-old, right-handed, English-speaking, White female, with a medical history significant for drug-resistant, non-lesional, left-hemispheric localized TLE. In terms of neurodiagnostic findings, continuous EEG (cEEG) recorded at the time of her neuropsychological evaluation showed that the patient's seizures originated in the left temporal region, while prior EEG recordings by an outside hospital captured onset from the right posterior temporal-occipital juncture. Reported seizure semiology reported included left-sided twitching, left head-turn, tonic contraction of upper extremities progressing to tonic-clonic involvement of all four limbs, breathing difficulties, seeing rainbow spirals, hearing buzzing noises, tongue biting, feelings of dread and urinary incontinence. The patient was a senior in college and reported having consistent elevated academic performance throughout her schooling prior to seizure onset, in which she was required to take medical leave. Following seizure emergence, the patient reported memory decline, word-finding difficulties, and an increased tendency to lose personal items.

The patient was considered to have a high level of CR based on her exceptional level of academic functioning, as measured by a strong Grade Point Average (GPA) prior to seizure emergence, as well as her strong performances on a screening measure of literacy assessing pre-morbid abilities and on an abbreviated measure of intellectual functioning. Analysis of the patient's neuropsychological data revealed strengths on measures of verbal fluency and visuospatial perception. Intact functioning was observed on measures of verbal learning and memory, confrontation naming, basic attention, complex attention, working memory and executive functioning. Importantly, she did not demonstrate deficits in verbal memory and language that are commonly exhibited by the TLE population. With regards to visual learning and memory, the patient's ability to learn and spontaneously recall simple geometric shapes was stronger as compared to a complex geometric figure. The patient also demonstrated varied performance on metrics of processing speed and fine motor dexterity.

Discussion

This case series sought to address the paucity of research regarding the potential effects of CR on cognitive functioning in pre-surgical epilepsy evaluations by examining the cases of two TLE patients who underwent neuropsychological assessment to determine neurosurgical candidacy. CR theory is applicable to Case 1, as the patient was able to master three distinct languag-

Table 1: Neuropsychological testing score interpretations per cognitive domain.

Cognitive domain	Case 1	Case 2
Test of premorbid functioning	High Average	Above Average
Abbreviated scale of intelligence	Average	High Average
Basic attention	Low Average	Average
Complex attention	Average	Average
Working memory	Average	Average
Mental set-shifting	Low Average – Average	Low Average – High Average
Inhibitory control	Low Average	Average
Abstract reasoning	Average – Above Average	Average – Exceptionally High
Processing Speed	Low Average – Average	Low Average – Average
Non-contextual verbal learning	Average	High Average
Non-contextual verbal memory	High Average	Average
Contextual verbal learning	Average	Average
Contextual verbal memory	Average	Average
Visual learning	Average	Low Average – High Average
Visual memory	Average – High Average	Low Average – High Average
Verbal fluency	Low Average – Average	High Average – Above Average
Confrontation naming	*Average	Average
Visuospatial perception	Average – High Average	High Average

*Describes the patient's performance when permitted to provide responses in English, Mandarin or Spanish.
American Academy of Clinical Neuropsychology (AACN) labeling of performance test scores [16]. Standard Scores and percentiles correspond to the following classifications: Exceptionally High = 130 and above (≥ 98th %ile); Above Average = 120-129 (91st - 97th %ile); High Average = 110-119 (75th- 90th%ile); Average = 90-109 (25th - 74th%ile); Low Average = 80-89 (9th- 24th %ile); Below Average = 70-79 (2nd- 8th %ile); Exceptionally Low = <70 and below (<2nd %ile).

es, had cognitively complex vocational tasks across time prior to seizure onset and performed well on a test of premorbid functioning. CR theory is also applicable to Case 2, as the patient had a strong academic functioning prior to seizure emergence in addition to achieving high scores on measures of premorbid functioning and on an abbreviated measure of intelligence.

The seemingly elevated degree of CR in both cases may have manifested in their performance on neuropsychological testing, as their scores indicated fully intact functioning or strengths across cognitive domains. Significantly, neither case evinced the expected cognitive impairments that are typical of the TLE population, particularly with respect to the domains of memory, language [4,5]. With regards to memory, both Case 1 and Case 2 evinced a functional capacity to learn and spontaneously recall non-contextual verbal information (i.e., a list of randomized words), contextual verbal information (i.e., a short story) and visually presented information (i.e., a complex geometric figure). In terms of language functioning, both cases displayed intact abilities on metrics of verbal fluency and confrontation naming; of note, Case 1 performed at commensurate with a standardized sample of age-related peers when permitted to provide answers in all of her known languages including English, Mandarin and Spanish. Each case demonstrated skilled capabilities within the general domain of executive functioning that include inhibitory control, abstract reasoning as well as planning and organization.

Conclusion

The factors underlying neurosurgical profiles with definitive localization and lateralization of neuropathology differ from patient-to-patient (i.e., handedness, duration of epilepsy, structural lesion, language(s) spoken). This case series suggest that CR should also be considered as a performance modifier when interpreting unexpected intact neuropsychological data that does not align with expected deficits given localization and laterality of seizure foci, particularly in the context of neurosurgical candidacy determination in a TLE population. Evidence that individual patient factors prior to seizure onset can potentially mask the impact of seizures on cognitive functioning in specific cognitive domains of memory and language, which may typically be exhibited by patients with TLE. Therefore, a patient's lifestyle, intellectual abilities and functional capacity prior to developing a seizure disorder, should be taken into consideration when determining surgical candidacy analyzing pre-surgical neuropsychological data in order to determine biological bases of seizure-related pathology and forecasting post-operative cognitive functioning.

This highlights the critical need to establish an expert consensus in applying the concept of CR within the context of determining neurosurgical candidacy. Such a consensus may allow neuropsychologists, and other experts on a neurosurgical team, to stratify the seizure type and to discern whether laterality is potentially obscured by an individual's level CR. Furthermore, neuropsychologists can also be knowledgeable about applying knowledge about the effects of CR to presurgical TLE evalua-

tions, including recommendations to the surgical team and prognostic trajectory of the surgical candidate's cognition. More research on the topic of CR on patients with drug-resistant epileptic conditions, including those diagnosed with TLE or another localized-related epilepsy, is warranted as neuropsychological assessment is a critical variable in the decision-making process of neurosurgical teams when determining candidacy.

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