Everyday cognition in temporal lobe and frontal lobe epilepsy

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ABSTRACT – The purpose of this pilot study was to compare the performance of patients with temporal lobe epilepsy (TLE) and frontal lobe epilepsy (FLE) on cognitively-based daily living tasks. The hypothesis was that patients with TLE would demonstrate relatively more impairment on a test of everyday memory, while patients with FLE would demonstrate relatively more impairment on a test of everyday executive function. The five Daily Living subtests of the Neuropsychological Assessment Battery (NAB) were administered to twenty-five patients with TLE and nine patients with FLE. The two groups were matched on all demographic variables. The hypothesis was not confirmed: the TLE and FLE patient groups did not demonstrate a double dissociation in memory and executive daily functioning. Rather, both groups were significantly impaired in daily memory functioning, while their executive daily functioning test scores were within normal limits. Relative deficits were also noted in attention in the TLE group and in language in the FLE group, suggesting that despite having focal lesions, functional impairments may be seen in a broad range of daily activities in these patient groups. Generalizability of the findings is limited due to the small number of subjects and because the everyday cognition measures employed may not have been adequately sensitive. Future studies are needed with larger sample sizes to provide a better understanding of how cognitive impairment in epilepsy is associated with deficits in daily functioning.

Key words: cognition, memory, everyday function, temporal lobe epilepsy, frontal lobe epilepsy

A number of recent studies have focused on specific patterns of cognitive dysfunction in patients with temporal lobe epilepsy (TLE) and frontal lobe epilepsy (FLE). Although there is overlap in some aspects of cognitive functioning, FLE patients do show deficits on some tasks that differentiate them from patients with TLE. Specifically, FLE patients demonstrate more impairment in motor coordination, response inhibition, and set-shifting compared to patients with TLE (Helmstaedter et al., 1996; McDonald et al. 2005a; McDonald et al. 2005b; McDonald et al. 2005c; Culhane-Shelburne et al., 2002; Riva et al., 2005). In contrast, the cognitive deficits most frequently observed in patients with TLE include learning and memory dysfunction due to the direct effect of the temporal lobe epileptic focus (Chelune, 1995). While these studies address differences between these patient groups on formal neuropsychological testing, we know little about how the location of the seizure focus affects everyday
functioning. Elucidation of the relationships between frontal lobe and temporal lobe seizure activity and daily living skills would have both theoretical and clinical implications.

Evaluation of real-world, everyday functioning has not been systematically evaluated in epilepsy patients, despite recognition that this is an important aspect of assessment for both chronic and surgical patients (Hauser, 1987; Sander, 2005). The methods of assessing everyday functioning in epilepsy are limited. Quality of life (QOL) measures provide information regarding certain aspects of patient functioning, but are limited because inaccurate self-assessment and emotional factors may impact the validity of self-report measures for assessing everyday functioning in epilepsy patients (Banos et al., 2004; Cramer et al., 2003).

Impairment in everyday cognition is frequently observed in patients with neurocognitive impairment. Studies of patients with varying neurological disorders including dementia and movement disorders show deficits in aspects of everyday functioning that correlate with cognitive dysfunction (Boyle et al., 2003; Cahn-Weiner et al., 2007, 2003; Tomaszewski Farias et al., 2008). Comparable studies in patients with epilepsy have not been conducted to date, although it might be expected that deficits in certain cognitively-based daily living skills would correlate with circumscribed lesions. Specifically, hippocampal volume has been shown to be a significant predictor of daily functioning in patients with dementia (Cahn-Weiner et al., 2007).

The primary objective of this pilot study was to examine cognitively-based daily living skills in patients with FLE and TLE. The Neuropsychological Assessment Battery (NAB) is a modular neuropsychological assessment tool in which each cognitive domain assessed includes a daily living task. Our hypothesis was that patients with TLE and FLE would exhibit different patterns of cognitively-based daily living skills deficits that would correlate with the site of epileptogenesis. Specifically, FLE patients were expected to show relatively more impairment on an everyday task of executive function than everyday tests measuring other cognitive domains. In contrast, TLE patients were expected to show relatively more impairment on an everyday test of memory as compared to everyday tests examining other cognitive domains.

Methods

Subjects

Twenty-five patients with TLE and nine patients with FLE were recruited from the University of California, San Francisco Epilepsy Center and the University of California, San Diego Epilepsy Center for this study. Subjects were diagnosed by a board-certified neurologist with expertise in epileptology. The study was approved by the Institutional Review Board (IRB) of both institutions and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All participants provided written consent prior to enrollment in the study. Patients were classified according to EEG monitoring, seizure semiology, and detailed neuroimaging (MRI, SPECT, and/or PET). Subjects with either an epileptic focus or radiological evidence of dysfunction outside the frontal or temporal regions were excluded. The two groups were matched on all demographic variables (see below).

The sample of FLE participants consisted of five patients with unilateral right FLE, and four patients with unilateral left FLE. Of the FLE group, six patients showed structural lesions on neuroimaging, whereas the remaining three FLE patients exhibited no identifiable structural lesion. Lesions included cavernous malformation (n = 1), DNET (n = 2), cystic lesion (n = 1), encephalomalacia (n = 1), and venous anomaly (n = 1). Eight of the patients were right-handed and one was ambidextrous. The FLE group consisted of 4 females and 5 males. The mean age of the FLE subjects was 36.8 ± 8.6 years, mean educational level was 12.8 ± 1.6 years, and mean seizure duration was 15.0 ± 11.9 years.

In the TLE subjects, the diagnosis was based on clinical semiology, neuroimaging, and presence of ictal and interictal temporal lobe epileptiform activity as monitored by video-EEG telemetry. Eighteen of the patients exhibited mesial temporal sclerosis (MTS) on MRI. Three patients had evidence of cortical dysplasia; the other structural findings included cavernous malformation (n = 1), hamartoma (n = 1), and ganglioglioma (n = 1). One patient had no MRI evidence of abnormality but had EEG confirmation of temporal lobe seizure onset. The sample of TLE patients consisted of 11 patients with unilateral right TLE, and 14 with unilateral left TLE. Four of the patients with TLE were left-handed, and two were ambidextrous. The TLE group consisted of 14 females and 11 males. The mean age of the TLE subjects was 33.6 ± 11.4 years, mean educational level was 14.2 ± 2.7 years, and mean seizure duration was 23.7 ± 11.4 years.

All patients in the FLE and TLE groups were taking one to three anticonvulsant medications at the time of the evaluation. Medications included valproic acid, phenytoin, felbamate, carbamazepine, clonazepam, levetiracetam, lamotrigine, primidone, topiramate, oxcarbazepine, and zonisamide.

Materials and procedure

The five Daily Living tests from the Neuropsychological Assessment Battery (NAB) (Stern et al., 2003) were administered to all subjects. The Daily Living subtests from the NAB provide domain-specific assessment of five different functional areas that are highly congruent with analogous real-world behavior and serve as proxy measures for daily

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functioning (table 1). The executive function Daily Living test measures judgment through a series of questions about home safety, health, and medical issues likely to be encountered in everyday situations. The Daily Living test of the memory module employs information that individuals often must remember in their daily lives, such as a name, address, phone number, and medication instructions. The spatial module includes a map reading test incorporating visuospatial skill, spatial/directional and right-left orientation, and visual scanning. The language module assesses auditory comprehension, reading comprehension, writing, simple calculations, and speech output through a utility bill-payment task. The attention module utilizes a driving scenes test designed to assess the useful field of view, working memory, visual scanning, and attention to detail. A composite everyday cognition measure was derived by averaging the T-scores of the five NAB Daily Living subtests. T-scores falling more than one standard deviation below the mean are considered impaired (Stern et al., 2003).

Patients were also administered a standard comprehensive neuropsychological battery of tests assessing attention, memory, language, visuospatial skills, and executive functioning. Because only the NAB Daily Living subtests were the focus of this investigation, the additional NAB measures were not administered.

### Results

#### Group performances on everyday cognition

Figure 1 displays T-scores (mean = 50, SD = 10) for the TLE and FLE groups on the NAB Daily Living subtests. The TLE group showed significant impairment relative to normative data (i.e., > 1 SD below the mean) on the Daily Living tests of memory and attention while the FLE group showed relative impairment on the Daily Living tests of memory and language. Independent samples t-tests revealed no significant group differences on any of the five NAB Daily Living subtests. Because of the difference in sample size of the two groups, non-parametric statistics were also run to compare the groups; there were no significant differences between the FLE and TLE groups. The two groups also did not differ significantly on the composite measure of everyday cognition. An additional analysis examined the frequency with which patients performed two or more standard deviations below published demographically-corrected means on the individual NAB Daily Living subtests. This analysis revealed that the frequency of significantly impaired performance in the two patient groups was comparable, with chi-square analyses demonstrating no group differences on any of the NAB Daily Living subtests.

### Relationship of everyday cognition to neuropsychological test performance and demographic variables

We conducted additional analyses to examine the relationships between everyday cognition, neuropsychological test

<table>
<thead>
<tr>
<th>Module</th>
<th>Daily Living test name</th>
<th>Primary functions assessed</th>
<th>Example of test item</th>
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</thead>
<tbody>
<tr>
<td>Executive</td>
<td>Judgment</td>
<td>Judgment and decision making capacity about issues and situations likely to be encountered in daily living</td>
<td>Answer questions pertaining to home safety, health, and medical issues</td>
</tr>
<tr>
<td>Memory</td>
<td>Daily living memory</td>
<td>Explicit learning and delayed free recall and recognition of verbal information likely to be encountered in daily living</td>
<td>Recall and recognition of previously-presented medication instructions and a person’s name, address and phone number</td>
</tr>
<tr>
<td>Language</td>
<td>Bill payment</td>
<td>Auditory language comprehension, reading comprehension, writing, simple calculations, and speech output</td>
<td>Following commands requiring oral and written responses related to a utility bill</td>
</tr>
<tr>
<td>Spatial</td>
<td>Map reading</td>
<td>Visuospatial skill, spatial/directional and right-left orientation, and visual scanning</td>
<td>Answer questions about and follow directions on a city map</td>
</tr>
<tr>
<td>Attention</td>
<td>Driving scenes</td>
<td>Visual working memory, visual scanning, attention to detail, and selective attention</td>
<td>Identifying changes to a driving scene relative to a previous driving scene</td>
</tr>
</tbody>
</table>
performance, and demographic characteristics of the patients. A representative test from each cognitive domain was selected: for attention, the digit span from the Wechsler Memory Scale-III (Wechsler, 1997); for executive functioning, the Controlled Oral Word Association test (Benton and Hamsher, 1989); for memory, Logical Memory delayed recall from the Wechsler Memory Scale – III (Wechsler, 1997); for language, the Boston Naming test (Kaplan et al., 1983), and for visuospatial abilities, the copy condition of the Rey-Osterrieth Complex figure test (Osterrieth, 1944). Both parametric and nonparametric tests revealed no significant differences between the two groups (table 2). A correlation matrix was generated for the entire group of subjects. None of the demographic variables (e.g. age, seizure duration, education) correlated significantly with the everyday cognition measure. Of the neuropsychological measures of interest, only the logical memory delayed recall measure demonstrated a significant association (r = 0.42, p < 0.05) with the composite score of everyday cognition (figure 2).

### Discussion

To gain a better understanding of the impact that cognition has on everyday functioning in epilepsy, we examined the performance of two epilepsy patient groups, TLE and FLE. Based on previous studies demonstrating dissociations in cognitive performance between these groups, our hypothesis was that a double dissociation in everyday cognition would be observed, whereby TLE patients would exhibit more prominent deficits in everyday memory and FLE patients would exhibit more prominent deficits in everyday executive function. The results did not confirm this hypothesis, however, and the two subject groups did not differ significantly on any of the NAB Daily Living subtests. Instead, both patient groups exhibited impairment relative to normative data on the Memory test. Impairments in memory functioning in patients with FLE have been reported but the source of the deficits may differ depending on the underlying etiology (McDonald et al., 2006). The finding of relative difficulty on this test of everyday functioning is consistent with what has been reported in the literature, namely, that patients with chronic focal epilepsies experience significant problems in everyday memory (Ponds et al., 2006).

That neither group showed significant impairment on the Daily Living Executive Function subtest was unexpected, particularly since dysexecutive function is reported in both patient groups (Hermann and Seideberg, 1995, McDonald et al., 2008, 2005a, 2005b, 2005c). The specific deficits reported involve problems with shifting cognitive sets, abstraction, and inhibition. Such deficits may not be adequately tapped by the Judgment subtest, which requires an individual to respond to questions regarding everyday safety and medical decision making. One possible explanation for our findings is that the NAB is insufficiently sensitive to the specific deficits that are associated with FLE and TLE, as only one component of executive function was tapped by this test. Advances are being made towards better definitions and measurements of everyday cognition in neurological patient groups. The recently published everyday cognition battery (Farias et al., 2008) may be more sensitive to deficits in everyday cognition as it measures a broader range of problems associated with neurological illness.

<table>
<thead>
<tr>
<th>Function domain – neuropsychological test</th>
<th>FLE (n = 9)</th>
<th>TLE (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention – digit span (range 0-30)</td>
<td>15.7 (4.4)</td>
<td>15.9 (4.4)</td>
</tr>
<tr>
<td>Language – Boston Naming test (range 0-60)</td>
<td>47.4 (7.2)</td>
<td>47.0 (9.9)</td>
</tr>
<tr>
<td>Executive function – lexical fluency (range &gt; 0)</td>
<td>25.9 (10.8)</td>
<td>31.5 (12.5)</td>
</tr>
<tr>
<td>Memory – Logical Memory Delayed Recall (range 0-50)</td>
<td>17.8 (7.5)</td>
<td>14.5 (10.1)</td>
</tr>
<tr>
<td>Visuospatial – Rey-Osterrieth Figure copy (range 0-36)</td>
<td>28.3 (5.1)</td>
<td>30.9 (4.6)</td>
</tr>
</tbody>
</table>
We were interested in the relationship between individual neuropsychological test measures and everyday cognition, as recently published literature has suggested that some test measures are better predictors of everyday functioning than others. Specifically, literature from dementia populations has suggested that measures of executive function, in particular, are predictive of daily living skills (Cahn-Weiner et al., 2002; Cahn-Weiner et al., 2007). Memory has also been found to be a significant predictor of daily functioning in some studies (Tomaszewski Farias et al., 2008). The correlational analyses conducted with the combined group of patients suggests that verbal delayed recall is significantly associated with general everyday cognition; none of the other neuropsychological test scores correlated significantly with the composite measure. This finding may be interpreted as suggesting that, despite cognitive impairments observed across multiple domains in these two patient groups, memory dysfunction may be the greatest contributor to everyday cognitive problems. It is possible that the everyday tasks assessed by the NAB tap memory functions, even if the proposed function is another cognitive domain. This is particularly true of the Attention module, in which immediate recall of specific spatial elements is necessary for successful performance. While it is possible that the larger proportion of TLE subjects in this analysis may have contributed to this finding, both groups were similarly impaired on the everyday memory and neuropsychological memory tests.

In summary, the findings of this pilot study suggest that there are no prominent differences in everyday cognition between patients with TLE and FLE. Both patient groups exhibit relative impairments in everyday memory, but a selective impairment was not observed in the FLE group on a test of judgment, thought to reflect everyday executive function. There are a number of limitations which should be emphasized. First, the small sample sizes and differences in sample sizes between our two groups makes generalization difficult. Second, we were not able to examine the effect of aging specifically on everyday cognition. It is possible that everyday functioning is impacted differentially throughout the lifespan, with some everyday tasks being more difficult as aging exerts its effects on cognition. For example, even in healthy community dwelling elderly individuals, executive function appears to be a strong predictor of independence in activities of daily living (Cahn-Weiner et al., 2002). The small sample sizes also precluded our investigation of laterality, which is also likely to affect performance on individual cognitive measures. In addition, patients with FLE are heterogeneous in etiology, presence or absence of a cerebral lesion, and location of seizure onset, representing a significant challenge to studying the cognitive and behavioral characteristics of this patient group (Patrikelis et al., 2009). With a larger group of FLE subjects, subgroups could be studied that show unique profiles of executive dysfunction that would be better detected with the everyday functioning measures used in this study. Due to the challenge of obtaining a sizeable group of these patients, however, this would likely require a multicenter effort. Finally, the current study did not examine the influence that mood and subjective experience have on everyday functioning. Future studies with larger sample sizes are needed to improve understanding of the selective relationships that seizure origin may have on everyday cognition.

Disclosures.
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