

## Neuropsychological Assessment and Quality of Life in Patients with Refractory Temporal Lobe Epilepsy Related to Hippocampal Sclerosis

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### ABSTRACT

**Introduction:** Epilepsy is a disorder that results in abnormal activity in a group of neurons that may have significant impact on the normal cognitive processes and behavior. Temporal lobe epilepsy (TLE) is the most frequent form of partial epilepsy in adults, and hippocampal sclerosis (HS) the most common neuropathologic finding in patients with medically refractory TLE. Patients with TLE often present cognitive difficulties that may be determined by the effects of epileptic discharges and side of the lesion. And its consequence is that patients have poor effects on quality of life (QOL). **Purpose:** We report the relationship between neuropsychological assessment and QOL under the hypotheses that patients with worst results in neuropsychological assessment have poorer QOL assessed by the QOLIE-31. **Results:** Regarding seizure frequency, 23 (46%) had had 1-5, 20 (40%) 6-10 and 7 (14%) more than 10 seizures/month. In relation to seizure types, 5 (10%) had had auras, 37 (74%) complex partial seizures and 8 (16%) partial evolving to generalized tonic-clonic seizures (GTCS). Neuropsychological evaluation had a positive correlation with QOLIE-31 domains. QOL evaluations had the worst scores in QOLIE-31 were in Cognitive Function (45.0) and Social Function (46.0). The best was Overall QOL (62.0). **Conclusion:** People with epilepsy have great impact on their QOL not only because of daily seizures but because of the impact seizures cause in their cognitive functions. TLE is an example of how refractory epilepsy can exterminate any possibilities of work, study and live in a society that discriminates someone with epilepsy who also presents cognitive decline.

**Key words:** temporal lobe epilepsy, neuropsychology, quality of life, cognitive decline.

### RESUMO

*Avaliação neuropsicológica e qualidade de vida em pacientes com epilepsia refratária do lobo temporal relacionada com esclerose hipocampal*

**Introdução:** Epilepsia é um distúrbio decorrente de atividade anormal de um grupo de neurônios, causando grande impacto no processo cognitivo e comportamental do indivíduo. A epilepsia do lobo temporal (ELT) é o tipo de epilepsia parcial mais comum e a esclerose hipocampal (EH) o substrato neuropatológico mais freqüentemente encontrado em pacientes com epilepsia refratária. Pessoas com ELT apresentam declínio cognitivo que pode ser determinado pela localização das descargas e da lesão. E, além disso, também apresentam limitação na qualidade de vida (QV) pelas crises diárias. **Objetivo:** Avaliar a relação entre a avaliação neuropsicológica e QV com a hipótese de que pacientes com piores resultados na primeira têm pior QV determinada pelo QOLIE-31. **Resultados:** Quanto à freqüência de crises, 23 pacientes (46%) tiveram até 5 crises, 20 (40%) de 6 a 10 e 7 (14%) mais de 10 por mês. Quanto ao tipo de crises, 5 (10%) apresentaram apenas auras, 37 (74%) crises parciais complexas e 8 (16%) crises parciais complexas com generalização secundária. Os resultados da avaliação neuropsicológica tiveram correlação positiva com os domínios do QOLIE-31. Nos domínios Aspectos Sociais com testes de função executiva, Preocupação com as Crises e

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Received Aug 10, 2006; accepted Sept 22, 2006.

Qualidade de Vida Global com testes de memória verbal e Bem-estar Emocional com os testes utilizados para cálculo do QI. **Conclusão:** Pessoas com epilepsia têm grande impacto na QV não apenas pelas limitações causadas pelas crises diárias, mas também pelo que estas causam em suas funções cognitivas. ELT é um exemplo de como uma epilepsia refratária pode acabar com qualquer possibilidade dessas pessoas procurarem um emprego, estudarem e viverem em uma sociedade que as discrimina pelo fato de ter epilepsia e um declínio cognitivo comprovado.

**Unitermos:** epilepsia do lobo temporal, neuropsicologia, qualidade de vida, processo cognitivo.

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## INTRODUCTION

Epilepsy is a disorder that results in abnormal activity in a group of neurons that may have significant impact on the normal cognitive processes and behavior of the affected individual<sup>(1)</sup>. Temporal lobe epilepsy (TLE) is the most frequent form of partial epilepsy in adults, and hippocampal sclerosis (HS) is the most common neuropathologic finding in patients with medically refractory TLE<sup>(2,3)</sup>.

Patients with TLE often present cognitive difficulties that may be determined by the effects of epileptic discharges and side of the lesion<sup>(4,5,6)</sup>, age at seizure onset, seizure frequency, antiepileptic drug treatment and surgery<sup>(1)</sup>.

Neuropsychological testing remains the best method of characterizing and quantifying the nature and degree of cognitive dysfunction arising from epilepsy<sup>(7)</sup>. This evaluation comprises a comprehensive measurement of cognitive functioning that includes intelligence, memory, frontal executive skills, attention, visuospatial abilities, language and motor skills<sup>(7)</sup>.

Epilepsy is also well-known to have poor effects on quality of life (QOL). Patients with epilepsy endure driving restrictions and social stigma, they often fear their next seizure, and are exposed to adverse medication side effects. All these factors contribute to impaired health-related quality of life (HRQOL)<sup>(8,9,10,11,12,13)</sup>.

QOL is conceptually composed of physical, emotional, social, spiritual, occupational and economic dimensions, as well as health-related aspects pertaining to a specific disease<sup>(14)</sup>. Calman<sup>(15)</sup> suggested that epilepsy is both, medical diagnosis and social label, and the latter aspect can be handicapped in patients with epilepsy, for example by prejudicing job applications and imposing other psychosocial restrictions.

Difficulties in working, interpersonal, familial and social relationships, the perception of stigma, the discrimination by others have been associated with interictal depressive state influencing negatively QOL of people with epilepsy. Depression has a high prevalence (20-55%) in epilepsies, being considered the most important

factor in the judgment of the patient concerning his QOL<sup>(16,17)</sup>.

In this paper we report the relationship between neuropsychological assessment and QOL under the hypotheses that patients with worst results in neuropsychological assessment have poorer QOL assessed by the QOLIE-31.

## METHODS

### Casuistic

This study involved 50 pre-surgical patients with diagnosis of refractory TLE related to unilateral mesial temporal sclerosis (MTS) from the Epilepsy Section of the Hospital São Paulo, Universidade Federal de São Paulo. The eligible consenting patients were older than 18 and capable of answering the verbal administration of the instruments.

Those with concomitant co-morbidity (e.g. other chronic illness) likely to affect the state of health and also those with Intelligence Quotient (IQ) score less than 70, were excluded.

### Instrument evaluation

Neuropsychological assessment of the patients had the following tests: Block Design, Vocabulary, Rey Auditory Verbal Learning Test (RAVLT), Logical Memory (LM) and Visual Reproduction (VR) (delayed recall), Stroop Test, and Trail Making Test. The assessment was divided into two days. All the instruments were administrated in a face-to-face interview. QOL was assessed through the QOLIE-31.

The Block Design is a subtest of Wechsler Adult Intelligence Scale – Revised (WAIS-R) and measures visuospatial organization and planning. The Vocabulary is a subtest of WAIS-R, measures verbal functions (expressive word knowledge), which correlate very highly with Full Scale IQ. The RAVLT provides measures of immediate memory, efficiency of learning, effects of interference and recall following short and long delay periods. In this paper we used the total score of the five lists. Logical Memory subtest of Wechsler Memory

Scale – Revised (WMS-R) is a measures verbal episodic memory functions and in this paper we only used the delayed recall, that tends to be more sensitive to the variables that affect verbal learning than immediate recall. Visual Reproduction subtest of WMS –R is a test of visual memory and visual retention using presented complex figures. In this paper we only used the delayed recall. Stroop Test measures effectiveness of concentration and control of inhibition (executive function). The Trail Making Test measures motor speed, attention functions and mental flexibility.

Data of IQ score were obtained by scale scores from subtests Block Design and Vocabulary. These scores were not included in statistical analyses when compared with QOLIE-31.

QOL was assessed by QOLIE-31 which an epilepsy-specific instrument to evaluate QOL which includes 30 items organized into seven subscales: Seizure Worry (5 items), Emotional Well-Being (5 items), Energy/Fatigue (4 items), Social Functioning (5 items), Cognitive Functioning (6 items), Medication Effects (3 items), Overall Quality of Life (2 items) and an additional item assessing overall health status<sup>(18)</sup>. The raw scores are rescaled from zero to 100 with higher values reflecting better QOL.

## RESULTS

### Characteristics of the sample

Regarding seizure frequency, 23 (46%) had had 1-5, 20 (40%) 6-10 and 7 (14%) more than 10 seizures. In relation to seizure types, 5 (10%) had had auras, 37 (74%) complex partial seizures and 8 (16%) partial evolving to generalized tonic-clonic seizures (GTCS). Socio-demographic characteristics are shown in Table 1.

**Table 1.** Socio demographic characteristics of patients with refractory temporal lobe epilepsy

	Number (N=50)	Percentage (%)
Male	25	50
Female	25	50
<b>Mean age</b>	38	
<b>Educational level</b>		
Primary school	35	70
Secondary school	14	28
Higher education	1	2
<b>Age of onset</b>		
Until 10 years old	10	20
11 to 20 years old	37	74
21 to 30 years old	3	6

### Instrument evaluation

Table 2 shows the mean scores the patients obtained in all neuropsychological tests. Neuropsychological evaluation had a positive correlation with QOLIE-31 domains depicted in Table 3.

**Table 2.** Mean scores from neuropsychological evaluation in patients with refractory temporal lobe epilepsy

Neuropsychological Tests	Scores
Vocabulary	8.5
Block Design	11.52
Visual Reproduction (delayed recall)	28.1
Logical memory (delayed recall)	17.04
RAVLT	43.56
Trail Making Test A	54.28
Trail Making Test B	104.7
Stroop Test I	16.92
Stroop Test II	18.95
Stroop Test III	30.18

**Table 3.** Correlation between QOLIE-31 and Neuropsychological evaluation

Neuropsychological evaluation	QOLIE-31						
	SW	OQOL	EWB	E/F	C	ME	SF
Vocabulary	0.508*	0.779*	<b>0.023*</b>	0.102*	0.751*	0.475*	0.185**
Block Design	0.292*	0.721*	<b>0.023**</b>	0.624*	0.986*	0.425*	<b>0.034**</b>
RAVLT	<b>0.034**</b>	<b>0.018**</b>	0.481*	0.341*	0.642*	0.524*	0.925*
Stroop Test	0.267*	0.952*	0.631*	0.214*	0.619*	0.733*	<b>0.006**</b>
Logical Memory	<b>0.026*</b>	0.884*	0.255*	0.856*	0.350*	0.965*	0.226*

Superscript refers to the type of statistical tests.

\* Pearson's correlation.

\*\* Multiple correlation ( $p < 0.005$ ).

QOL evaluations had the worst scores in QOLIE-31 were in Cognitive Function (45.0) and Social Function (46.0). The best was Overall QOL (62.0). Table 4 shows all the mean scores.

**Table 4.** Mean scores from QOLIE-31 in patients with refractory temporal lobe epilepsy

QOLIE-31 Domains	Scores
Seizure Worry	59.0
Overall Quality of Life	62.0
Emotional Well-Being	55.0
Energy/Fatigue	59.0
Cognitive Function	45.0
Medications Effects	50.0
Social Function	46.0

## DISCUSSION

Neuropsychological assessment and QOL are directly correlated in epilepsy because cognitive decline have great impact on patient's daily life. Memory complaints are common among epilepsy patients especially in those with refractory TLE related to HS. It brings consequences to their social, familial, marital and employment status.

Memory is the process that the knowledge is retained through time and the most part that we know about the world and civilization. Therefore, learning process and memory are essential to our own growing as persons. Memory impairment leads us to lose our own history and the relationship with those whom we are related to<sup>(7)</sup>.

Perrine et al.<sup>(19)</sup> found that although mood was the strongest predictor of QOL, neuropsychological performance also predicted self-reported cognitive functioning and overall QOL.

In this series, as for clinical characteristics, seizure frequency as well as seizure types had a strong correlation with QOLIE-31 domains of Emotional Well-Being and Social Function. These characteristics have been considered the most significant predictors of QOL in some studies since patients with more severe seizures presented significantly poorer QOL<sup>(8,12,18,20)</sup>. There were no correlation between QOLIE-31 and duration of epilepsy. In the literature, regarding neuropsychological assessment, there has been strong correlation between seizure frequency as well as seizure types and duration of epilepsy and cognitive impairment<sup>(21,22,23,24,25,26,27)</sup>.

The influence of socio-demographic variables in QOL has yielded contrasting results. Whereas for some,

these variables were the most strongly associated with poor QOL<sup>(28,29,30)</sup>, in our study, in accordance with others<sup>(12,31)</sup>, there was no consistent association between employment status, educational level and QOL scores ( $p > 0.005$ ).

In relation to cognitive function, Oyegbile<sup>(26)</sup> demonstrated that socio-demographic characteristics, such as, educational level had correlation with cognitive decline. Higher education, greater occupational attainment, or increase participation in mindful activities may benefit from increase plasticity or neuroprotection that may serve to delay or attenuate disease effects.

The type and anatomic location of brain pathology have crucial impact on cognitive deficit, such as verbal memory deficit which is more commonly associated with left-sized mesial epileptogenic zone. A significant relationship is also suggested between performance tests and memory difficulties in TLE patients, corresponding to objective deficits. Self-reported memory has been considered an important predictor of QOL, and therefore, correlates with performance on memory tests, suggesting that memory improvement by specific training may help to improve QOL. However, we did not find a relationship between cognitive function domain from QOLIE-31 and neuropsychological evaluation. As much as they seem obvious, data from literature have not always been found to universally correlate<sup>(1,32,33,34,35)</sup>.

There were correlations between QOLIE-31 domains and neuropsychological tests. Patients had worse results in test than measures verbal functions (RAVLT an LM) and these tests had correlation with Seizure Worry from QOLIE-31. RAVLT worse results also correlated with Overall QOL. Gotman<sup>(7)</sup> reported that verbal memory deficits are related to the impact of refractory epilepsy in patient's lives. These difficulties brought impact on daily life once interfering in learning, professional and social process. Nevertheless, people with epilepsy know that seizures can impact their cognitive functions; in consequence, they worry more about seizures and loss of memory.

Tests used to calculate the IQ had a positive correlation with Emotional Well-Being domain of QOLIE-31. Moore and Baker<sup>(36)</sup>, suggested that intellectual decline and psychosocial adjustment are related to intractable epilepsy as found in our series. Patients with less intellectual resources have less capacity of facing social difficulties in consequence of the disturbance, creating an emotional impact.

Tests than measures Executive Function had a positive correlation with Social Aspects from QOLIE-31. Executive Functions, such as, critic, planning, judgment, decisions,

adaptation and social adjustment. Difficulties with these functions cause impact on social aspects of patient's lives, once these functions are extremely important to social adaptations and living.

## CONCLUSION

People with epilepsy have great impact on their QOL not only because of daily seizures but because of the impact seizures cause in their cognitive functions. TLE is an example of how intractable epilepsy can exterminate any possibilities of work, study and live in a society that discriminates someone with epilepsy who also presents cognitive decline.

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