Can Neuropsychological Rehabilitation Determine the Candidacy for Epilepsy Surgery? Implications for Cognitive Reserve Theorizing

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Published date: July 18, 2017; Accepted date: October 04, 2017; Published date: October 10, 2017

Abstract

Objective: The purpose of this study was to explore the effectiveness of a neuro-optimization intervention to determine the suitability for surgery in a patient suffering from left medial temporal lobe epilepsy (MTLE) and hippocampal sclerosis (HS). The rehabilitation program was aimed at amplifying cognitive resources and improving memory functioning, particularly in the non-dominant healthy hemisphere.

Method: A preoperative neuro-optimization program, inspired by the functional reserve model and the right hemisphere’s verbal processing potential, was adopted. This neuro-optimization program targeted global cognitive and metacognitive enhancement with an emphasis on memory functions of the right temporal lobe, i.e., the functional upgrade of the healthy right hippocampus and related structures to assist memory after surgery.

Results: After a 32-weeks neuro-optimization program, the patient once again underwent intracarotid amobarbital test (IAT). This time his right hemisphere memory functioning yielded a borderline score, allowing us to consider surgery. Immediately after surgery, the patient was seizure free and did not show any clinically significant memory impairment. At six months post-surgery he had largely preserved memory optimization gains.

Conclusion: Preoperative optimization interventions aiming at enhancing cognition, in general and memory of the healthy hemisphere, in particular, may contribute to a positive memory outcome after left selective amygdalohippocampectomy.

Keywords: Medial temporal lobe epilepsy; Preoperative cognitive intervention; Neuro-optimization; Cognitive Reserve; Amygdalohippocampectomy

Introduction

In the context of neurorehabilitation the concept of cognitive reserve, i.e., the inherent potential of the brain in order to cope with damage, represents a key concept. In the domain of MTLE surgery, the concept of cognitive reserve has been applied in two different models of hippocampal functioning, i.e. functional reserve vs. hippocampal adequacy, in relation to the risk for memory decrements following temporal lobectomy (TL). The hippocampal functional reserve model claims that the size of memory loss is related to the spare capacity of the contralateral temporal lobe to support memory functions after resection of the affected (ipsilateral) lobe. IAT injections contralateral to the side of epileptogenesis typically lead to memory impairment, whereas normal memory performance is seen in the healthy hemisphere following injections to the pathologic one [13,14,17,21,23,27,19]. Some researchers found no significant relationship between the functional reserve of the contralateral-healthy temporal lobe as assessed by the IAT and memory changes following TL.

On the other hand, there is rising evidence that the functional adequacy of the tissue to be resected determines the nature and extent of postoperative memory loss. It has been repeatedly observed that patients, whose mnemonic abilities were sufficiently intact before surgery, are adversely affected following TL [6,22,1,16]. In line with these findings, studies on memory functioning derived from IAT injections contralateral to the seizure focus indicated that patients with good memory before surgery were at much greater risk for memory loss than those who performed poor at baseline [2,10]. A weak point of the functional adequacy model, however, is that it does not predict mild material-specific memory deficits following TL. Although the contralateral temporal lobe alone does not determine the probability of memory loss following TL, this is not to say that its functional capacity should be ignored, especially if we consider ample clinical evidence documenting the devastating consequences for memory following bilateral hippocampal damage [24].

There is strong evidence of an inverse relation between the risk of postoperative memory impairments and the functional adequacy of the surgical temporal lobe, mostly seen with respect to verbal memory and left MTLE patients, rather than the functional reserve of the contralateral hemisphere [1,10,18,14,12].

In light of the above, we present the case of a patient with refractory left MTLE and hippocampal sclerosis, who participated in a 32 weeks...
he was put on polytherapy (topiramate, valproic acid, lacosamide) and
around, mastication, tonic contractions of the right arm, simple
the proved ability of the right hemisphere to process lexical-semantic
memory
treating neurologist for a neuropsychological evaluation as a likely
negative family history for epilepsy. According to his personal history,
compared to postoperative interventions [11].To our knowledge no
render them suitable surgical candidates.
Cognitive rehabilitation program
The neuro-optimization intervention was divided into two parts: one aimed at enhancing the patient's global cognitive and meta-
cognitive [26] functioning, with an emphasis on right hemisphere
memory; the other part introduced the patient to the use of external
aids and strategic compensatory approaches in dealing with everyday
life tasks. The patient participated in the program for 1 h twice a week.
Right hemisphere training
Imagery mediated verbal recall has been considered to enhance
right hemisphere's contribution to verbal memory. As a result, the
patient is instructed to form and memorize images of verbal material
in order to remember (e.g. words) and later recall it by simply naming
the stored image.
Neurosurgical procedure
Our patient underwent a left temporal craniotomy. A transcortical
selective amygdalohippocampectomy, including the parahippocampal
gyrus, was performed, sparing the posterior one third of the
hippocampus.
Discussion
The aim of this work was to verify the effectiveness of a pre-surgery
neuro-optimization program in amplifying cognitive resources and
improving memory functioning, particularly in the non dominant
healthy hemisphere, in order to contain the adverse effects of temporal
resection.
AG showed a slight improvement in memory for abstract words and
pictures, and a larger and stable improvement in (RAVLT) delayed
recall, as well as in his higher level attention and executive functions
(TMT-B). This improvement is consistent with our initial hypothesis
predicting that contralateral temporal functions strengthening can
effectively support memory after surgery.
To sum up, our patient's post surgery overall memory profile was
slightly lower than his post rehabilitation one (before surgery), but still
considerably higher with respect to his baseline performance (pre-
rehabilitation performance).
Among others, our intervention led to improved right hemisphere
memory functioning, as shown by patient's post-rehabilitation IAT,
making patient suitable candidate for surgery (Table 1).

Case Report
At first assessment AG was 29 year old and had been referred by the
treating neurologist for a neuropsychological evaluation as a likely
candidate for epilepsy surgery. He is a right handed man with a
negative family history for epilepsy. According to his personal history,
at the age of three months he was hospitalized for 24 h, due to an
episode of loss of consciousness which lasted about five to ten minutes;
similar episodes were noted by his parents with a frequency of every
five to six months. At the age of six, another episode of loss of
consciousness occurred accompanied by fever, and that was the first
time that encephalitis was diagnosed. Since then, teachers have
described AG as distractible and unfocused, with concentration
difficulties in class.

The epileptic episodes typically began with an unpleasant
abdominal feeling, followed by obscuration of consciousness. Such
episodes lasted for about 10-15 min with a frequency of one every 15
days, until the age of 17 years. At that age he was hospitalized, because
of a secondary generalized seizure episode and placed on
ocarbazepine 300-300-300 mg. Since AG continued to have seizures,
he was put on polytherapy (topiramate, valproic acid, lacosamide) and
later on other medication regiments (i.e., phenobarbital, primidone,
pregabalin, tiagabine hydrochloride, zonisamide, phenytoine,
ethosuximide), but with no therapeutic effect.

At the time of evaluation, AG's ictal symptoms included looking
around, mastication, tonic contractions of the right arm, simple
movements of left arm and aphasia. His seizures lasted about 1 min,
followed by postictal blurring, drowsiness and sleep. The patient's MRI
was suggestive of a left sided hippocampal sclerosis, while his
electroencephalographic recordings (EEG) were not sufficiently
specific to shed light on his pathology. Upon admission to the hospital,
AG was receiving carbamazepine 700-600-700 mg, topiramate 25-0-50
mg, levetiracetam 1000-0-1000 mg, with a seizure frequency of 2-4
episodes per month.

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AG was receiving carbamazepine 700-600-700 mg, topiramate 25-0-50
mg, levetiracetam 1000-0-1000 mg, with a seizure frequency of 2-4
episodes per month.

Insights to our rehabilitation program formulation were given by
the proved ability of the right hemisphere to process lexical-semantic
information and mediate verbal memory through its ability to process
highly imageable words. This latter notion is known as of imagery
mediated verbal recall and constituted the basis for our right-
hemisphere training program aimed at enhancing verbal mediation to
support verbal memory after surgery. Jones [7], confirming Patten et
al. [20], reported that both healthy individuals and left TLE patients
improve their performance in a verbal paired-associate task by using
the strategy of imagery mediated verbal recall, while right TLE patients
do not. Accordingly, further evidence [8,9] suggested the critical role of
the right temporal lobe in processing verbal material with high
imageability, such as recalling concrete words. This is further
 corroborated by evidence that right TLE patients may face verbal
memory difficulties when to be remembered material presents a strong
imagery component [25].
The relatively limited literature in the domain of cognitive
rehabilitation for epilepsy surgical patients has mainly focused on
postoperative memory training [15,5,7], while there is only one study
dealing with preoperative memory rehabilitation in patients with
indication for surgery, which failed to find better memory outcomes as
compared to postoperative interventions [11].To our knowledge no
studies to date have addressed preoperative cognitive rehabilitation in
epilepsy patients for whom surgery is contraindicated with the aim to
render them suitable surgical candidates.

J Neurol Neurophysiol, an open access journal
ISSN:2155-9562
Volume 8 • Issue 5 • 1000446
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Our case points to the important clinical implications stemming from the notions of cognitive reserve and functional hemispheric asymmetry, in order to plan preoperative rehabilitation programs before epilepsy surgery.

Further neuropsychological research in the context of epilepsy surgery is required to address the complex concept of reserve and how the brain responds to preoperative rehabilitation challenges (Figure 1) and (Figure 2).

**Table 1:** Comparisons of neuropsychological performance of AG patient with control groups performed at baseline, 6 months post-treatment and 6 months post-surgery using the procedure of Crawford and Garthwaite [27] for comparing a single case with a control population. All comparisons were made using a one-tailed level of significance*.

**Conflict of Interest**

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements) or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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**Table 1:**

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<th>Verbal Fluency</th>
<th>Semantic</th>
<th>Phonological</th>
<th>RAVLT</th>
<th>IAT</th>
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**Figure 1:** Preoperative MRI scans. A. Coronal T1WI MRI scans. B. Coronal T2WI MRI scans. The arrow shows sclerosis in the hippocampus of the left temporal lobe.

**Figure 2:** Postoperative MRI scans. A. Axial T1WI MRI scans. B. Coronal T2WI MRI scans. The arrow shows a small basal ganglia ischemic lesion induced by surgery.
Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Patient Consent

The patient has consented to submission of this case report to the journal.

References