International Journal of Neurorehabilitation
ISSN: 2376-0281

Chung et al., Int J Neurorehabilitation Eng 2014, 1:3
DOI: 10.4172/2376-0281.1000125

Mini Review Open Access

The Potential Role of Neurocognitive Rehabilitation in Epilepsy

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Abstract

Epilepsy is a chronic dynamic medical problem requiring long-term treatment. In addition to seizures, patients with epilepsy often face a wide range of limitations in school, social situations, and employment, primarily because of cognitive impairments, especially of memory and attention. Cognitive rehabilitation therapy to restore patients' ability to deal with routine activities of daily lives has been used for years. Moreover, other studies have reported that these programs are effective in the epilepsy in memory and attention domains, and thus can be incorporated into comprehensive care programs. We reviewed studies on the two basic pragmatic approaches-retraining and compensation methods-especially the latter.

Keywords: Cognitive rehabilitation; Epilepsy

Background

Epilepsy is a common and serious neurological disorder worldwide, with an estimated prevalence rate of 0.5-1% in the general population. It is estimated that 150,000 new cases are diagnosed in the United States annually [1]. Characterized by its unpredictable seizure attacks, epilepsy is a chronic dynamic medical problem that requires long-term treatment. Furthermore, epilepsy provokes more than seizures. Patients with epilepsy face a wide range of difficulties in cognition, psychiatric status, and social functioning, and thus have limitations in school, social situations, employment, and independent living. A recent report [2] pointed out that individuals with epilepsy are at risk not only for seizures, but also for myriad comorbid health conditions. Often the comorbidities that accompany epilepsy outweigh the burden of the seizures themselves [3].

Cognition, defined as the ability to retain, process, and respond to information, depends on many physical and mental factors. It involves the ability to solve problems, communicate, memorize, and focus attention. The potential effect of epilepsy upon cognition is of interest for decades, and a lot of literatures indicate that patients with epilepsy are at a significant risk for cognitive impairments [4-9]. Studies have identified risk factors of cognitive impairments in patients with epilepsy (Figure 1). Strauss et al. [10] stated that seizure focus and age at the onset of seizures were the best indicators of intellectual decline. Seidenberg et al. [8] claimed that the duration of epilepsy is a reliable predictor of decline. Wang et al. [11] discovered that seizure frequency is a primary predictor of memory and of language function. These different results may be due to the variability of outcome measures and inclusion criteria. Etiology, seizure types, seizure frequency, duration of epilepsy, age at onset, and antiepileptic drug use may all contribute to cognitive decline [6,7,12] (Figure 1).

Most of the studies regarding cognition and epilepsy deal with patients with focal epilepsy. Temporal lobe epilepsy (TLE) is the most common focal epilepsy syndrome. Helmstaedter et al. [13] found that as time went by, 50% of the medically treated patients with TLE showed significant memory declines but had relatively non-significant changes in non-memory functions. Patients with frontal lobe epilepsy had a reduced attention span and psychomotor speed, but patients with TLE tend to have impaired memory [14]. The nature and severity of cognitive impairment is not only associated with the extent of brain damage, it also involves premorbid personality characters, psychiatric disorders, and the status and expectations of the patient [15]. Although the majority of patients with epilepsy seem to be impaired in more than one cognitive domain-memory, language, psychomotor speed, verbal episodic memory, and executive function [16] - memory and attention are the two that most frequently decline.

Neuropsychological Intervention

Neuropsychology provides information about epilepsy-related cognitive impairments. It is a useful tool for localizing epilepsy,

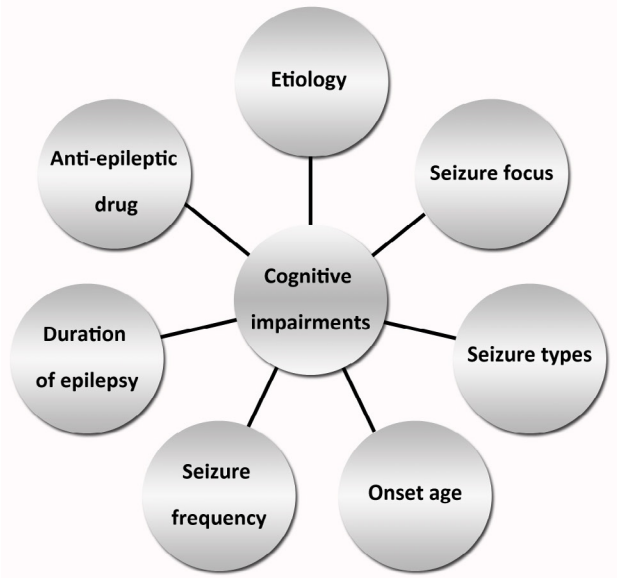

Figure 1: Risk factors of cognitive impairments in epilepsy.

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Received July 29, 2014; **Accepted** October 31, 2014; **Published** November 15, 2014

Citation: Chung YT, Hsieh IC, Lai MC, Huang CW (2014) The Potential Role of Neurocognitive Rehabilitation in Epilepsy. Int J Neurorehabilitation 1: 125. doi:10.4172/2376-0281.1000125

evaluating the lateralizing significance of its symptoms, and measuring the outcomes of epilepsy management. Neuropsychological assessments have been used in pre-surgical evaluations of cognitive function in patients with intractable epilepsy [15,17].

Cognitive impairments in patients with epilepsy were usually managed indirectly by, e.g., aggressively controlling seizures, choosing antiepileptic drugs with fewer cognitive side effects, or treating psychiatric disorders like depression. Shulman and Barr [18] suggested medical treatment: cholinesterase inhibitors, ginkgo biloba, antidepressants, and stimulants for memory deficits. However, these medical treatments lacked definite results.

Cognitive rehabilitation has been used to treat patients with epilepsy since the last decade. It is defined as "any intervention strategy or technique which intends to enable clients or patients, and their families, to live with, manage, by-pass, reduce or come to terms with cognitive deficits precipitated by injury to the brain" [19]. The goal of cognitive rehabilitation is to restore patients' ability to deal with routine activities of daily lives [19]. Specific interventions may have various approaches, including (1) reinforcing, strengthening, or reestablishing previously learned patterns of behavior; (2) establishing new patterns of cognitive activity through compensatory cognitive mechanisms for impaired neurologic systems; (3) establishing new patterns of activity through external compensatory mechanisms such as personal orthoses or environmental structuring and support; and (4) enabling patients to adapt to their cognitive disability, even though it may not be possible to directly modify or compensate for cognitive impairments, in order to improve their overall level of functioning and quality of life [20] (Table 1).

There are two main basic pragmatic approaches in cognitive rehabilitation. The first one involves increasing an individual's awareness of cognitive deficits, and tries to "retrain" the impaired cognitive function. This consists of repetitive practice of memory tasks based on the hypothesis that this will improve memory capacity (the "memory as a mental muscle" approach). This method has been proved effective in increasing attentional functioning in patients with traumatic brain injury [20]. The second one, a compensatory method, is more widely used today. Patients are taught strategies such as using external memory storage systems like agendas or diaries. Other strategies include rearranging the environment such that patients do not have to rely so much on memory to perform everyday activities; for example, including on the hospital floor colored stripes that lead to the bathroom [21].

Engelberts et al. [22] published the first randomized-controlled trial investigating the efficacy of cognitive rehabilitation in patients with focal epilepsy. Fifty patients with focal epilepsy being treated with carbamazepine were randomly divided into 3 groups: Retraining, Compensatory, and Control. The Retraining group had better performance compared with the control group in long-term memory test ($p = 0.004$). The Compensatory group also showed improvements in several memory tests ($p = 0.004$). In addition, in self-reported neuropsychological outcomes, patients in the Retraining group and Compensatory group had fewer cognitive complaints on the CFQ (CFQ score change between pre-training and follow-up: Retraining group= -2.2; Compensatory group= -3.1; control group= -0.4, $p < 0.05$ respectively), compared to the control group. Moreover, attention is also improved in both retraining method group and compensatory method group. Ponds et al. [21] reviewed the compensatory strategy used to manage memory impairments in patients with epilepsy. They averred that the compensation strategy of learning mnemonics clearly helped solve some common everyday memory problems. In 6-8 sessions scheduled every 2 weeks, patients learn to use compensatory strategies for their personally formulated treatment goals (Table 2).

1) Retraining method: reinforcing, strengthening or re-establishing previously learned patterns of behavior
2) Compensatory method: establishing new patterns of cognitive activity
3) External compensatory method: using personal orthoses or environmental structuring and support
4) Adaptation: enabling patients to adapt to their cognitive impairments

Table 1: Approaches of cognitive rehabilitation.

Helmstaedter et al. [13] investigated the effects of cognitive rehabilitation on memory outcome after temporal lobe epilepsy surgery. He included 112 patients from two epilepsy centers. Fifty-five patients from one center received rehabilitation (metacognitive neuropsychological group therapy), while 57 patients from the other center did not. Therapeutic gains of rehabilitation after surgery are significant on verbal learning and recognition ($F = 6.22$, $p = 0.001$), particularly in patients after right temporal lobe surgery. Moreover, the relative risk of deterioration in verbal learning was 3.4 times higher in patients who did not receive rehabilitation after the TLE surgery (Table 2).

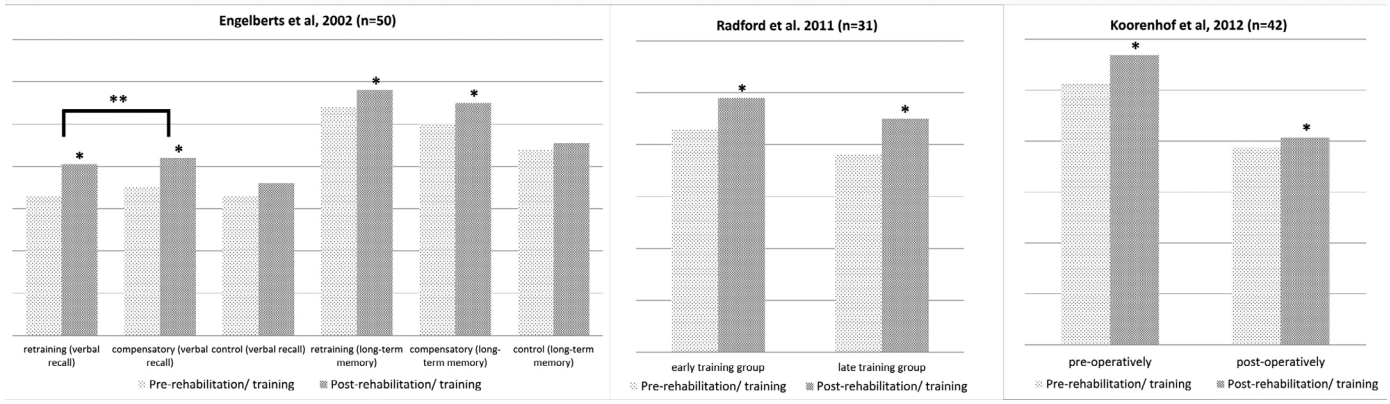
Radford et al. [23] designed a cognitive-rehabilitation training program that consisted of a 6-week, group-based, psycho educational and compensatory strategy course, for which they recruited 31 patients. This was evaluated using a waitlist crossover design and three assessments done 12 weeks apart. The patients made significant gains on tests of anterograde (Rey Auditory Verbal Learning Test, RAVLT) and appointment memory. The results of RAVLT total learning score revealed significant therapeutic benefits of training in both early training group and late training group. In addition, patients who used more strategies to overcome memory problems had fewer prospective memory difficulties in their daily lives. In this study, memory improved more in younger, less-educated, and less-depressed patients. This is consistent with a randomized controlled trial [22] in which the patients who were less educated tended to benefit more from cognitive training. Moreover, patients who had a lower baseline memory capacity but a higher level of attention had better outcomes [23]. Of the clinical variables related to epilepsy, only the number of antiepileptic drugs was associated with outcome, with smaller number associated with greater improvement [23]. Although this study lacks a control group, it provides evidence that even a short intervention can improve the memory function of patients with epilepsy (Table 2).

Koorenhof et al. [24] also investigated the short-term effect of a memory rehabilitation program on patients who underwent surgery for left temporal lobe epilepsy (LTLE). In this study, forty-two subjects are enrolled, with 22 healthy control and 20 LTLE patients. One-half of LTLE patients receive rehabilitation program pre-operatively, while the other half receive one post-operatively. The intervention uses compensatory strategies: external and internal memory supports. Outcome measures include performance on a verbal recall/ learning test and subjective ratings of memory in everyday life. In LTLE patients who received rehabilitation pre-operatively, the verbal learning score improved from 51.3±11.9 to 56.9±11. In the other LTLE group receiving rehabilitation post-operatively, the verbal learning score improved from 38.8±15.2 to 40.7±15.2. In both LTLE groups, the overall verbal learning scores improved significant after rehabilitation ($F = 16.2$, $p < 0.001$), but there was no significance between the two groups. That means, compared to post-operative memory rehabilitation, pre-

Studies	Design	Inclusion criteria	Neurocognitive intervention	Outcome Measures	Results
Engelberts et al, 2002	RCT (retraining method, compensatory method & wait-list control) Pre-, post- & 6-month follow-up testing	50 pts with focal seizures and attention impairments	• Retraining: rehearse and response • Compensatory: compensatory strategies • Individual, 1-h session, weekly for total 6 sessions	1. Computerized TAP Divided Attention Task 2. Auditory Verbal Memory Test (AVMT) 3. Stroop Color-Word Test (SCWT) Card III 4. Cognitive Failure Questionnaire (CFQ) 5. ShortForm Health Survey (SF-36)-mental compound score	Both retraining and compensatory groups show improvements in neuropsychological outcomes. The compensatory method is more effective.
Ponds et al, 2006	Cohort study	Pts with memory complaints from an Epilepsy Center	• Memory rehabilitation using compensatory strategy • Individual, every 2 week for total 6-8 sessions • One group session every 3 individual sessions	Neuropsychological evaluation, not-specified	Learning mnemonics would help patients to solve common memory problems in everyday life.
Helmstaedter et al, 2008	Non-randomized, controlled, two-center study	112 epileptic pts who had temporal lobe surgery, from 2 epilepsy centers	• Metacognitive neuropsychological group therapy, 1-h session, weekly for total 5 sessions • Cognitive exercise, average 4-5 sessions per week • Occupational therapy, 3-4 sessions per week	1. Verbal learning test (VLMT) 2. German figural design list-learning test 3. Letter cancellation test (psychomotor speed/attention)	Rehabilitation has a positive effect on verbal memory, especially those underwent right side surgery.
Radford et al, 2011	Pseudo-randomly assigned, early and late training group Pre-, 12-week & 24-week Pre-, post-, & 12 weeks	31 pts with seizure	Group-based memory intervention, 2-h session, weekly for total 6 sessions	1. Rey Auditory Verbal Learning Test (RAVLT) 2. Royal Prince Alfred Prospective Memory Test (RPA-ProMem) 3. Appointment Memory 4. Everyday Memory Questionnaire (EMQ) 5. Comprehensive Assessment of Prospective Memory (CAPM)	The objective and subjective memory outcome measures all show improvements in both early and late training group.
Koorenhof et al, 2012	pre-, 1 month later	• 42 subjects, 22 healthy controls, 20 LTLE pts • In 10/20 LTLE pts: memory training pre-operatively • In 10/20 LTLE pts: memory training post-operatively	Maximum 4-h rehabilitation over up to 3 sessions, using compensatory strategy	1. Story Recall task 2. List Learning test 3. Everyday Memory Failures Questionnaire (EMQ)	Improvements in verbal memory were observed in both groups receiving memory training pre- or post-operatively.

LTLE, left temporal lobe epilepsy; Pt, patient; RCT, randomized-controlled trial; TAP, test for attentional performance

Table 2: Summary of clinical outcomes after cognitive rehabilitation.



(*, significant change, p<0.05; **, in verbal recall test, the compensatory group shows a better improvement than the retraining group, significant , p<0.05.)

Figure 2: Improvement in memory after cognitive rehabilitation/training in patients with epilepsy in various studies.

operative intervention does not produce better outcomes. Subjective ratings of memory improvements were significant in the LTLE group (p<0.005) but not in the controls (p<0.06). Interestingly, improved verbal learning is correlated with less depression score (r = -0.58, p < 0.008) in the LTLE group. Based on this study, memory rehabilitation was effective in patients with LTLE, but the benefits did not compensate

for the memory decline after the surgery [24]. The therapeutic approach and benefits of cognitive rehabilitation in patients with epilepsy are summarized in Figure 2 and Table 2.

Conclusion

Cognitive rehabilitation has recently garnered great attention, but it needs additional controlled studies in patients with epilepsy. Other epilepsy studies have reported that cognitive rehabilitation programs, and especially those using compensation strategies, are effective in the memory and attention domains, and thus can and should be incorporated into comprehensive care programs. Training goals must be tailor-made to the needs and wishes of the patients.

Acknowledgment

This research was aided by grants from the Taiwan National Science Council (102-2314-B-006-051-MY3), National Cheng Kung University Hospital (NCKUH-10306031), and Chi-Mei Medical Center (CMNCKU10303), Taiwan.

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