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Associations between cognition and employment outcomes after epilepsy surgery

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ABSTRACT

Objectives: Previous studies have shown that younger age, higher education, and seizure freedom after epilepsy surgery are associated with employment. However, very few studies have investigated associations with cognition and employment status in epilepsy surgery patients.
Methods: This retrospective study consists of 46 adult patients, who underwent resective epilepsy surgery in the Helsinki University Hospital between 2010 and 2018 and who had been assessed by a neuropsychologist prior to surgery and 6 months after surgery using a systematic test battery. In addition to neuropsychological evaluation, neurologists assessed the patients prior to surgery and followed up the patients up to 24 months after the surgery and evaluated work status of the patients. Logistic regression models were used to assess the effects of cognition on changes in employment status, while controlling for age and education.
Results: Out of the 46 patients 38 (82.6%) were seizure free and 7 (15.2%) had their seizures reduced 2 years postsurgically. From prior to surgery to 2 years postsurgery, use of antiseizure medication was reduced in most of the patients, mean reduction of the dosage being 26.9%. Employment status improved in 10 (21.7%) patients, remained unchanged in 27 (58.7%) and worsened in 3 (6.5%). An additional 6 patients were already not working prior to surgery. Subsequent analyses are based on the subsample of 37 patients whose employment status improved or remained unchanged. Mistakes in executive function tasks ($p = 0.048$) and working memory performance ($p = 0.020$) differentiated between the group whose employment status remained similar and those who were able to improve their employment status. Epilepsy surgery outcome or changes in antiseizure medication (ASM) use were not associated with changes in employment status.
Conclusions: In the subsample of 37 patients, errors in executive function tasks and poorer working memory differentiated patients whose employment status did not change from those patients who could improve their employment status. Problems in executive function and working memory tasks might hinder performance in a complex work environment. When assessing the risks and opportunities in returning to work after surgery, difficulties in working memory and executive function performance should be taken into consideration as they may predispose the patient to challenges at work.

1. Introduction

Epilepsy surgery needs to be considered among patients with drug-resistant epilepsy (DRE) in order to reduce or eliminate seizures and to support adequate functioning of the patients with epilepsy (PWE). Successful epilepsy surgery allows for reduced antiseizure medication (ASM) dosage [1], and freedom from or less frequent seizures, although some patients may show complications [2,3]. Epilepsy surgery may also alleviate some psychiatric symptoms, although some studies report de novo psychiatric symptoms after epilepsy surgery [4].

Being seizure free is strongly associated with better employment status. Hamiwka et al. [5] have reported improvement in full-time employment in up to 40% of epilepsy surgery patients and Wilson and Coleman [6] showed that a majority of studies (75%) report improvements in employment after epilepsy surgery. Full- or part-time preoperative employment, seizure freedom post-

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operatively and younger age at surgery predicted better employment outcome postoperatively in a 10-year follow-up study [7].

The effects of epilepsy surgery on cognitive skills are less well studied, and may be linked with reduction or stopping of ASM [8,9]. Based on a systematic review, more patients see gains instead of losses of function in objective neuropsychological tests [10] at least in some cognitive skills, such as verbal fluency. This is dependent on locus of epilepsy and location of resection, and left temporal lobe resection may expectedly result in poorer language outcomes with much smaller risk in patients who undergo right-sided temporal surgery [10]. In addition, the effects of epilepsy surgery on cognition depend on whether self-reports or neuropsychological tests are used [10]. Subjectively many patients report gains and losses in cognitive abilities, but this may not be in line with objective measures of cognition.

The association between cognitive functioning and employment status after epilepsy surgery has been studied rarely and with mixed results [11]. Full scale IQ was slightly and positively associated with employment status 2 years postsurgically only in univariate analyses, suggesting that the impact of IQ on employment was mostly explained by other factors [12]. Consistent with this, lower IQ was associated with poorer employment status, but this is likely due to earlier epilepsy onset and epilepsy severity, which explain both poorer IQ and employment status [13]. It is not known which domains of cognition other than IQ influence employment status or improvement in employment status in epilepsy surgery patients.

To address what cognitive functions are associated with change in employment status from presurgery to 2 years postsurgery, we collected registry data from epilepsy surgery patients referred to surgery in the Helsinki University hospital. Our primary goal was to assess if cognitive functioning, epilepsy surgery outcome, ASM use, or demographic factors would be associated with improvements in employment status. We expected that younger age, presurgical employment status, and higher educational attainment would be associated with improvements in employment postsurgically. We also assessed changes in ASM use and psychiatric symptoms from presurgery to postsurgery and expected to see reductions in both.

2. Material and methods

2.1. Patients, study design, and setting

Helsinki University hospital (HUS) is the largest tertiary hospital in Finland, located in the Helsinki metropolitan area. It is one of the two University hospitals in Finland providing epilepsy surgery. The primary special catchment area of HUS comprises a population of more than 2,000,000. Additionally, patients from other areas of Finland (population ca. 5,500,000) are referred to HUS for presurgical evaluation and resective epilepsy surgery.

We conducted a retrospective registry study on those adult (18 years of age or older) PWE who were operated between 2010 and 2018 ($N = 106$) in HUS and were assessed both presurgically and postsurgically (6 months) with a standardized neuropsychological epilepsy surgery test battery taken into use in 2009 by one of the authors (T.N., PhD, neuropsychologist). This yielded a total of 46 patients.

The test battery was administered mainly in Finnish, but patients with Swedish ($n = 1$) or English ($n = 1$) as their mother tongue were also included. Patients with other native languages were excluded ($n = 13$) as well as those who were assessed by a neuropsychologist but not using the full standardized test battery ($n = 47$).

The Institutional Board of Helsinki University Hospital approved the study protocol.

2.2. Data collection and variable selection

Data were collected from patients' medical records and neuropsychological test forms. In line with the Epilepsia Helsinki follow-up protocol, neurologists assessed the patients presurgically and followed them up for up to 24 months. The cognitive variables were collected from neuropsychological test forms from presurgical and postsurgical assessments. Outcome variables were collected from medical reports 24 months after the surgery by a neurologist (L.K.).

The collected data are divided into three categories:

1. **Demographic and clinical variables** were sex, age at surgery and epilepsy onset, years of education, etiology and locus of epilepsy, ASM medication used and employment status at the time of surgery and 24 months postop, and psychiatric disorders presurgically and 24 months postsurgery.
2. **Cognitive variables** were collected from neuropsychological test forms from presurgical and 6 months postsurgical assessments and are summarized in Table 1. When different test versions were administered, scores were scaled to match. **Executive functions** were measured using two tests: Trail Making A and B, Stroop word reading and color naming, but also by summing together all the uncorrected and self-corrected errors in executive function tests the patients did (TM-A and B, Stroop tests, perseveration errors in word fluency subtests). Stroop color naming was not used for postop analyses due to too many missing values.
3. **Outcome variables** were change in employment status, epilepsy surgery outcome, and change in ASM use.

Change in employment status was categorized into four groups: improved status (e.g. from part-time to full-time work, from sick leave to part-time work or studies), no significant change, worsened status (e.g. change from full-time or part-time work to sick leave, from full-time to part-time work, from studying to having studies on hold), and not at work (e.g. retired or unable to work both presurgically and postsurgically).

Epilepsy surgery outcome was assessed using Engel scores at 24 months postop and were grouped into three categories: seizure free (Engel categories 1A, 1B, 1C, and 1D), seizures reduced by at

Table 1
Cognitive variables used in the study.

Reasoning	WAIS similarities WAIS block design WAIS coding WAIS digit span forward WAIS digit span backward
Memory	WMS-III or WMS-R Logical memory, immediate and delayed recall WMS-III or WMS-R Visual reproduction, immediate and delayed recall WMS-III, RAVLT, or MNEST-1A Word list, immediate and delayed recall
Basic verbal processes	Phonemic word fluency Semantic word fluency Boston naming test
Executive function	Trail making A Trail making B Stroop word reading Stroop color naming

least 50% (Engel categories 2A, 2B, 2C, 2D, 3A, and 3B), and no change (Engel categories 4A, 4B, and 4C).

Change in ASM use was counted as a percentage of change in the amount of ASM prescribed (in daily mg). For example, if the patient was on levetiracetam (500 mg × 2), oxcarbazepine (1050 + 750 mg), and zonisamide (150 + 200 mg), and zonisamide was reduced to 100 mg × 2 postop while other medications were unchanged, total change would be 14% (43% reduction in zonisamide divided by the number of medications, three). In cases where the types of ASMs were changed from presurgery to postsurgery (3 cases), the approximate change percentage was determined by author L.K. (MD, PhD, specialist in neurology).

2.3. Statistical analyses

All statistical analyses were conducted using IBM SPSS version 25 (IBM, Armank, New York, USA). The not at work group and worsened employment status groups were excluded from all group comparisons as only three patients had worsened work status (mostly due to new or preexisting psychiatric symptoms) and would have had large leverage on the models. Please see Supplementary data for specific details on the statistical analyses.

Changes in ASM use from presurgery to 24 months postsurgery was investigated using two-tailed *t*-test. Effects of ASM use on changes in employment (no change vs improved) was studied using one-way ANOVA.

Effects of demographic and clinical variables (operated hemisphere, temporal vs extratemporal) on change in employment status was analyzed using Chi square tests (χ^2). Logistic regression models were used to assess the effects of cognitive variables (presurgical, postop, change from presurgery to postsurgery) on changes in employment status (no change vs improved). Only individual variables whose regression coefficient differed from zero with a *p*-value of 0.1 or less, or the odds ratio was between 0.8 and 1.2 were used. Backward elimination using likelihood ratio (with the criterion of $p = 0.1$ for removal) was used to remove variables from the final model. Age and years of education were forced to be included in the models, as they are expected to be highly correlated with cognitive variables. For logistic regression model effect sizes, Nagelkerke's R^2 are reported. Akaike's Information Criteria (AIC) was used to evaluate model fit in terms of underfitting and overfitting, which assess goodness of fit of the model but penalizes for adding explanatory variables to the model (smaller AIC indicates a better model). To assess the risk of underfitting versus overfitting, models with all possible combinations of cognitive variables were analyzed and are reported in Supplementary Material 2.

We tested post hoc if cognitive variables differed between temporal and extratemporal and left-hemispheric vs right-hemispheric epilepsy loci using two-tailed *t*-tests. We also analyzed post hoc if change in ASM use or epilepsy surgery outcome (Engel score classified into three categories) was associated with cognitive variables using Spearman correlation. These results are reported in Supplementary Material 1.

Results are given as number of cases and percentage or mean and standard deviation (SD), where *p* values <0.05 were considered significant.

3. Results

The demographic and clinical characteristics of the study group are listed in Table 2.

3.1. Epilepsy surgery outcome and psychiatric symptoms

Out of all 46 patients 38 (82.6%) were seizure free and 7 (15.2%) had their seizures markedly reduced. Regarding psychiatric symptoms, increase in mild symptoms was observed and two de novo cases of psychotic symptoms were found; however, reactive symptoms related to epilepsy were reduced (Table 3).

3.2. Changes in ASM use

Presurgical ASM use of all 46 patients and ASM use 24 months postsurgery are reported in Table 4. ASM dosage was statistically significantly ($t(45) = -4.016$, $p < 0.001$) reduced from presurgery to 24 months postsurgery. Mean reduction of the dosage was 26.91%, standard deviation 45.45%, range −100% to +150%. ASM dosage increased in only 6 patients due to continuation of the seizures.

3.3. Changes in employment status

Following epilepsy surgery, there was no change in employment status for 27 patients (58.7%), whereas 10 (21.7%) improved their employment status (Table 5). Only these 37 patients are included in further analysis.

Epilepsy surgery outcome or changes in ASM use were not associated with change in work status (no change, improved) ($p = 0.417$, $p = 0.526$, respectively).

Table 2
Demographic and clinical characteristics of patients with epilepsy included in the analyses. The whole sample ($N = 46$) and the group used in the analyses ($N = 37$, patients with improved or unchanged employment status) are reported separately. M = male, F = female.

Variable	All patients ($N = 46$)			Patients with improved or unchanged employment status ($N = 37$)		
	N	Mean	Range	*N*	Mean	Range
Age at surgery (years)		33.97	21–67		33.11	21–57
Sex	20 M, 26 F			15 M, 22 F		
Years of education		12.76	6–20		13.24	9–20
Age at epilepsy onset (years)		17.85	3–39		19.46	4–39
Etiology of epilepsy:						
Cortical dysplasia	14 (30%)			8 (22%)		
Tumor	12 (26%)			11 (30%)		
Encephalocele	6 (13%)			6 (16%)		
Hippocampal sclerosis	5 (11%)			4 (11%)		
Other	9 (20%)			8 (21%)		
Locus of epilepsy:						
Left	29 (63%)			26 (67%)		
Right	17 (37%)			13 (33%)		
Temporal	33 (72%)			28 (72%)		
Extratemporal	13 (28%)			11 (28%)		

Table 3
Epilepsy surgery outcome and psychiatric comorbidities (presurgery – 24 months postsurgery).

Epilepsy surgery outcome (all patients):		$N = 46$
seizure free (Engel categories 1A, 1B, 1C, and 1D)		38 (82.6%)
seizures reduced by at least 50% (Engel categories 2A, 2B, 2C, 2D, 3A, and 3B)		7 (15.2%)
no change (Engel categories 4A, 4B, and 4C)		1 (2.2%)
Psychiatric symptoms	**presurgery**	**24 months postsurgery**
Reactive symptoms related to epilepsy	3 (6.5%)	0 (0%)
Psychotic symptoms	1 (2.2%)	3 (6.5%)
Mild or moderate depression or other mild symptoms	4 (8.7%)	8 (17.4%)
Severe depression, anxiety, or other symptoms requiring psychiatric care	5 (10.9%)	5 (10.9%)
No psychiatric symptoms mentioned in medical records	33 (71.7%)	30 (65.2%)

Table 4
ASM use of patients. The number of patients is reported (median dosage in brackets).

ASM	Prescribed presurgery	Prescribed at 24 months postsurgery
Levetiracetam	28 (2000 mg)	23 (2000 mg)
Lacosamide	11 (400 mg)	9 (400 mg)
Valproate	11 (1500 mg)	6 (1400 mg)
Oxcarbazepine	18 (1800 mg)	17 (1500 mg)
Zonisamide	14 (275 mg)	8 (100 mg)
Pregabalin	8 (375 mg)	5 (400 mg)
Clobazam	8 (10 mg)	3 (17 mg)
Lamotrigine	11 (300 mg)	11 (350 mg)
Clonazepam	1 (2 mg)	0
Gabapentin	2 (3150 mg)	2 (3150 mg)
Phenytoin	1 (400 mg)	1 (350 mg)
Carbamazepine	9 (800 mg)	8 (800 mg)
Perampanel	1 (6 mg)	0
Eslicarbazepine	1 (1600 mg)	0
Topiramate	1 (200 mg)	1 (150 mg)

Table 5
Changes in employment status from presurgical period to 24 months postsurgery.

Change in employment status (all patients):	46 (100%)
Improved	10 (21.7%)
No change	27 (58.7%)
Worsened	3 (6.5%)
Not at work (e.g. retired prior to surgery)	6 (13%)

3.4. Effects of cognitive abilities on improvement in employment status

Analyses on effects of cognitive variables on improvement in employment status were done using a subsample of 37 patients. No presurgical cognitive variables were associated with improvement in employment in our models (see Supplementary data).

Analyses on association of 6 months postop cognitive variables with improved employment status showed that four cognitive variables were associated with improved employment status: block design, word list immediate recall, number of self-corrected executive function mistakes, and number of uncorrected executive function mistakes (see Supplementary data). The final model included five variables: age, education in years, word list immediate recall, the number of uncorrected executive function mistakes, and block design. The number of corrected executive function mistakes was removed during backward elimination. The fit of the final model was clearly better than the model with intercept only when evaluated using AIC. Variance explained was adequate (Nagelkerke's $R^2 = 0.681$). See Table 6 for details of the model.

For changes in cognitive variables, the regression model included 6 variables: age, years of education, Block design, Phonemic word fluency, number of self-corrected executive function mistakes, and number of uncorrected executive function mistakes. Phonemic word fluency and the number of uncorrected executive function mistakes were removed during backward elimination. The final model fit was slightly better than that of the model with intercept only. Variance explained was adequate (Nagelkerke's $R^2 = 0.402$). See Table 7 for details of the model.

Table 6
Backward elimination regression models of 6 months postop cognitive variables to improvement in employment. Statistically significant effects are marked in **bold**.

Model		AIC	Likelihood ratio
Final model: Age, Education in years, Block design, Word list immediate recall, Number of uncorrected executive function mistakes		31.770	$\chi^2(5) = 23.411$, $p < 0.001$
Intercept only		45.181	
Without Age		31.981	$\chi^2(1) = 2.210$, $p = 0.137$
Without Education in years		38.696	$\chi^2(1) = 8.926$, $p = 0.003$
Without Block design		33.122	$\chi^2(1) = 3.352$, $p = 0.067$
Without Word list immediate recall		42.062	$\chi^2(1) = 12.292$, $p < 0.001$
Without Number of uncorrected executive function mistakes		41.999	$\chi^2(1) = 12.229$, $p < 0.001$
Parameter estimates			
Variable	*B*	Significance	Odds ratio
Age	−0.084	$p = 0.177$	0.919
Education in years	**0.916**	$\mathbf{p = 0.020}$	**2.499**
Block design	−0.094	$p = 0.130$	0.911
Word list immediate recall	**0.384**	$\mathbf{p = 0.020}$	**1.469**
Number of uncorrected executive function mistakes	**1.939**	$\mathbf{p = 0.048}$	**6.952**

Table 7
Backward elimination regression models of changes in cognitive variables to improvement in employment. Statistically significant effects are marked in **bold**.

Model		AIC	Likelihood ratio
Final model: Age, Education in years, Block design, Number of corrected executive function mistakes		41.180	$\chi^2(4) = 12.001$, $p = 0.017$
Intercept only		45.181	
Without Age		41.562	$\chi^2(1) = 2.382$, $p = 0.123$
Without Education in years		39.701	$\chi^2(1) = 0.521$, $p = 0.471$
Without Block design		44.580	$\chi^2(1) = 5.400$, $p = 0.020$
Without Number of corrected executive function mistakes		45.873	$\chi^2(1) = 6.693$, $p = 0.010$
Parameter estimates			
Variable	*B*	Significance	Odds ratio
Age	−0.071	0.135	0.931
Education in years	0.138	0.477	1.148
Block design	−0.116	0.061	0.891
Number of corrected executive function mistakes	**0.683**	**0.027**	**1.980**

3.5. Operated hemisphere and epileptic locus and employment status

Posthoc, we compared whether the operated hemisphere (right vs left) or operated locus (temporal vs extratemporal) showed performance differences in cognitive performance testing.

Change in work status was not significantly affected by the operated hemisphere ($p = 0.238$) or whether the epilepsy was temporal or extratemporal ($p = 0.570$). In temporal lobe resection patients poorer surgery outcome was associated with poorer 6 months postop performance in Coding ($\rho = -0.357$, $p = 0.041$), word list immediate recall ($\rho = -0.349$, $p = 0.046$), and word list delayed recall ($\rho = -0.361$, $p = 0.039$).

Improvements in block design ($t(44) = -2.074$, $p = 0.044$) and delayed word list recall ($t(44) = -2.249$, $p = 0.030$) performance were significantly greater in patients operated on the right hemisphere.

Patients operated on extratemporal locus performed better in delayed visual reproduction ($t(44) = -2.552$, $p = 0.015$), presurgical number of uncorrected executive function mistakes ($t(44) = 2.366$, $p = 0.022$), and postop Boston Naming Test performance ($t(44) = -2.033$, $p = 0.048$) than temporal lobe resection patients, whereas, patients operated on temporal locus performed better in phonetic word fluency ($t(44) = 2.489$, $p = 0.017$).

Changes in performance were larger in temporally than extratemporally resected patients in phonetic word fluency ($t(44) = 2.171$, $p = 0.035$) and in number of corrected executive function mistakes ($t(44) = 2.235$, $p = 0.031$).

4. Discussion

To our knowledge, this is the first study investigating the detailed effects of cognitive factors on improvement of employment status after resective epilepsy surgery. Our findings indicated that better working memory (word list immediate recall) and better executive functions (fewer number of executive function errors) were associated with improvement in employment status. We show that resective epilepsy surgery is generally associated with good outcomes regarding employment status, seizure reduction and medication reduction. For most patients, employment status stayed the same or improved in two-year follow-up. Employment status worsened for only three patients, two of which were probably due to de novo psychotic symptoms postop.

4.1. Changes in employment status

Employment status improved for 26% of the patients, in line with other studies [14]. However, we found no association between surgery outcome and improvement in employment, even though this association has been reported previously in several studies [[15], see also [7]]. This may be due to the fact that most patients in our study were either seizure free or had their seizures effectively reduced. As the number of patients with poor surgery outcome is small, only very large effects become statistically significant. While surgery outcome is probably the best predictor for employment after epilepsy surgery, in studies with mostly only good outcomes this is not necessarily seen. This can be especially pronounced in our data, as for most of our patients (72%) the locus of epilepsy was in the temporal lobes and epilepsy surgery may elicit the best outcomes in patients with temporal epilepsy [16].

4.2. Effects of cognitive abilities on improvement in employment status

We found that both 6 months postoperative short-term memory and uncorrected mistakes in executive function tasks and increase in the number of corrected mistakes in executive function tasks from presurgery to postsurgery were associated with improvement in employment when controlling for age and years of education. For example, working memory allows the person to perform various tasks more efficiently without the need to resort to external memory aids, which is likely to make work less straining. Regarding executive functions, the ability to monitor own tasks allows mistakes to be detected, reducing the need to check and re-evaluate tasks after their completion, potentially reducing work strain. While few studies have been conducted in epilepsy surgery patients, returning to work has been studied extensively in other patient groups, such as stroke and patients with traumatic brain injury (TBI) [17,18]. For example, studies in groups with an acquired brain injury have indicated that executive functions are relevant for employment outcomes [19,20], but so is the number of cognitive domains in which deficits are observed in [21].

Comparison between our results and earlier findings are somewhat challenging due to different outcome variables. In the current study, most of the patients were already at work and their work status did not change in 24 postsurgical months ($n = 27$). Our analyses focused on factors that predicted improvement in employment status as the group whose employment status worsened was too small. On the basis of the studies that have focused on return to work, either to full-time or part-time employment after a neurological event, factors such as global cognitive functioning [18] or the number of domains in which cognitive deficits are found [21] seem to be one of the most robust factors that are associated with employment. Especially improving one's work status can be taxing, either by taking on a more challenging position or switching from part-time to full-time employment. Especially if executive functions are not adequate, it may be challenging or stressful to increase work demands, regardless of whether they are related to working time or task demand. Consistent with this, previous studies have suggested a link between executive functions and work performance [22].

Another important aspect of the current study is that executive function is analyzed as an aggregate measure instead of utilizing test scores from a single test only. As Baxendale [23] points out, changes or associations in one measure only, especially when analyzed using univariate analyses, are not likely to be beneficial in a clinical setting. However, across several tasks, cognitive difficulties may become apparent as common features (e.g. mistakes) are summed together. As executive function deficits may be common in patients with epilepsy [24], executive function mistakes averaged across multiple tests may be a more ecologically valid measure of the underlying executive function deficit as performance may vary across different tests.

In addition to executive functions, working memory performance word list task after the surgery was also associated with improvement in employment. Performance in this task is likely to be largely dependent on working memory performance. While working memory is important for many tasks, which strain the individuals' limited processing capability, and is considered a fundamental cognitive process [25] and important part of executive functioning [26], we only found this effect in the word list task, not in digit span tasks. This could be a random effect or result from the study population as the majority of the patients had left-hemispheric epilepsy surgery (24 left-hemispheric, 13 right-hemispheric) as these patients are likely to have at least small deficits in the language domain [27]. As a single test score, it is interesting and warrants further study, but may not be clinically relevant on its own, at least in comparison to the executive function findings.

We found no associations with cognitive functioning prior to epilepsy surgery and improvement in employment. While those associations have been previously reported, it is possible that preoperative cognitive performance may simply be a proxy for epilepsy severity as it did not emerge as a significant predictor in multivariate models used to predict postsurgical employment status [12].

Finally, even though employment status improves in epilepsy surgery patients, and this may partly be mediated by cognitive functioning, long-term follow-up studies are needed. Even if epilepsy surgery helps patients with DRE return to work, their careers may become shorter than in those without epilepsy as they have less cognitive reserve to cope with accumulating challenges that result from aging. Indeed, epilepsy surgery patients tend to retire and move from full-time to part-time employment sooner than the general population [7].

4.3. Changes in ASM use

The amount of medication the patients were taking was significantly reduced as the result of surgery, as expected [9,28]. The effect of ASM on cognition may vary depending on types of medication used [29]. As adverse effects from ASM often lead to lower quality of life, it seems plausible that improved cognitive abilities resulting from reduction in ASM are likely to mediate the improved quality of life seen in epilepsy surgery patients [30]. In contrast, incomplete seizure control was associated with poorer performance in some cognitive tests, as expected [31]. This result supports the benefits of epilepsy surgery.

4.4. Epilepsy surgery outcome and psychiatric symptoms

Our general findings on the outcome of epilepsy surgery are consistent with previous studies [25]. Altogether 38 (82.6%) were seizure free and 7 (15.2%) patients had their seizures reduced 2 years after the surgery. No great decrease in psychiatric symptoms, such as depression, was seen over the 2-year follow-up, even though such results have been reported previously [32]. Although epilepsy is associated with psychiatric symptoms, such as anxiety or depression, our results suggest that a large majority of PWE have no severe psychiatric symptoms. However, patients without severe psychiatric symptoms may still exhibit subclinical psychiatric difficulties, which required no psychiatric care and therefore were unseen in the present sample. Thus, no possible alleviation of subclinical psychiatric symptoms was seen in our retrospective setting. Consistent with previous studies, we noticed some de novo psychotic symptoms [4].

Epilepsy surgery outcome was not associated with changes in cognitive functioning to a large degree in our study. It is likely that effects will be evident in longer follow-up studies [9], as seizures no longer deteriorate cognitive skills.

4.5. Study limitations

A disadvantage of the present study is that it is not conducted as a multicenter study, resulting in a small sample size. Although this limits the sample size, it allows for the use of a standardized neuropsychological test battery and standardized follow-up protocol used by neurologists. The use of standardized neuropsychological test battery also results in a smaller number of missing values.

The interpretation of our results is limited by small sample size, which increases the risk of overfitting the model to the data. While odds ratios of most cognitive variables remained stable regardless of the model chosen (see Supplementary data), fluctuation was observed for the executive function mistakes at 6 months postop, but not for changes in corrected executive function mistakes from preop to 6 months postop. It is possible that some, but not all, effects of executive function in improvement on employment result from overfitting errors.

5. Conclusions

Our findings suggest that especially executive functions are associated with improvement in employment in epilepsy surgery patients. While a similar finding was observed for verbal working memory, it may be less robust and partly due to the prevalence of left-hemispheric surgery patients in our data. However, it is an integral part of executive functions, and thus consistent with the executive function findings.

From a clinical perspective, our data suggest that postoperative neuropsychological assessments of epilepsy surgery patients should utilize aggregate measures across several tests to reveal subtle difficulties. For the patient with epilepsy's wellbeing, even small difficulties in executive function may make challenging jobs more demanding than they are for individuals without epilepsy and result in poorer quality of life in general. These findings could help clinicians to better assess possible risks associated with returning to work after epilepsy surgery, focus neuropsychological rehabilitation optimally, and better screen patients that are less likely to return to work after epilepsy surgery. Consistent with previous studies, we also suggest that epilepsy surgery is likely to improve the patients' quality of life by, for example, allowing for reduction in ASM dosage.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

As the data are from patient registry, the current ethical permission and legislation do not allow for data sharing or processing outside of Helsinki University Hospital servers.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2022.108709.

References

[1] Schiller Y, Cascino GD, So EL, Marsh WR. Discontinuation of antiepileptic drugs after successful epilepsy surgery. Neurology 2000;54(2). 346-346.

[2] Wiebe S, Blume WT, Girvin JP, Eliasziw M. A randomized, controlled trial of surgery for temporal-lobe epilepsy. N Engl J Med 2001;345(5):311–8.

[3] Malmgren K, Edelvik A. Long-term outcomes of surgical treatment for epilepsy in adults with regard to seizures, antiepileptic drug treatment and employment. Seizure 2017;44:217–24.

[4] Desai S, Shukla G, Goyal V, Srivastava A, Srivastava MVP, Tripathi M, et al. Changes in psychiatric comorbidity during early postsurgical period in patients operated for medically refractory epilepsy—a MINI-based follow-up study. Epilepsy Behav 2014;32:29–33.

[5] Hamiwka L, Macrodimitris S, Tellez-Zenteno JF, Metcalfe A, Wiebe S, Kwon CS, et al. Social outcomes after temporal or extratemporal epilepsy surgery: a systematic review. Epilepsia 2011;52(5):870–9.
[6] Wilson SJ, Coleman H. Long-term educational and vocational outcomes of adults after epilepsy surgery. In: Malmgren K, Baxendale S, Cross JH, editors. Long-term outcomes of epilepsy surgery in adults and children. Cham: Springer International Publishing; 2015. p. 135–50.
[7] Edelvik A, Flink R, Malmgren K. Prospective and longitudinal long-term employment outcomes after resective epilepsy surgery. Neurology 2015;85(17):1482–90.
[8] Brunbech L, Sabers A. Effect of antiepileptic drugs on cognitive function in individuals with epilepsy. Drugs 2002;62(4):593–604.
[9] Téllez-Zenteno JF, Dhar R, Hernandez-Ronquillo L, Wiebe S. Long-term outcomes in epilepsy surgery: antiepileptic drugs, mortality, cognitive and psychosocial aspects. Brain 2007;130(2):334–45.
[10] Sherman EMS, Wiebe S, Fay-McClymont TB, Tellez-Zenteno J, Metcalfe A, Hernandez-Ronquillo L, et al. Neuropsychological outcomes after epilepsy surgery: systematic review and pooled estimates. Epilepsia 2011;52(5):857–69.
[11] Bujarski KA, Wozniak G, Kobylarz EJ. Cognitive impairment predicts social disability in persons with epilepsy. J Epileptol 2014;22(2):89–97.
[12] Thorbecke R, May TW, Koch-Stoecker S, Ebner A, Bien CG, Specht U. Effects of an inpatient rehabilitation program after temporal lobe epilepsy surgery and other factors on employment 2 years after epilepsy surgery. Epilepsia 2014;55(5):725–33.
[13] Dulay MF, York MK, Soety EM, Hamilton WJ, Mizrahi EM, Goldsmith IL, et al. Memory, emotional and vocational impairments before and after anterior temporal lobectomy for complex partial seizures. Epilepsia 2006;47(11):1922–30.
[14] Chin PS, Berg AT, Spencer SS, Sperling MR, Haut SR, Langfitt JT, et al. Employment outcomes following resective epilepsy surgery. Epilepsia 2007;48(12):2253–7.
[15] Zarroli K, Tracy JI, Nei M, Sharan A, Sperling MR. Employment after anterior temporal lobectomy. Epilepsia 2011;52(5):925–31.
[16] Téllez-Zenteno JF, Dhar R, Wiebe S. Long-term seizure outcomes following epilepsy surgery: a systematic review and meta-analysis. Brain 2005;128(5):1188–98.
[17] Van Velzen JM, Van Bennekom CAM, Edelaar MJA, Sluiter JK, Frings-Dresen MH. Prognostic factors of return to work after acquired brain injury: a systematic review. Brain Inj 2009;23(5):385–95.
[18] Edwards JD, Kapoor A, Linkewich E, Swartz RH. Return to work after young stroke: a systematic review. Int J Stroke 2018;13(3):243–56.
[19] Nybo T, Sainio M, Müller K. Stability of vocational outcome in adulthood after moderate to severe preschool brain injury. J Int Neuropsychol Soc 2004;10(5):719–23.
[20] Fride Y, Adamit T, Maeir A, Ben Assayag E, Bornstein NM, Korczyn AD, et al. What are the correlates of cognition and participation to return to work after first ever mild stroke? Top Stroke Rehabil 2015;22(5):317–25.
[21] Kauranen T, Turunen K, Laari S, Mustanoja S, Baumann P, Poutiainen E. The severity of cognitive deficits predicts return to work after a first-ever ischaemic stroke. J Neurol Neurosurg Psychiatry 2013;84(3):316–21.
[22] Ownsworth T, Shum D. Relationship between executive functions and productivity outcomes following stroke. Disabil Rehabil 2008;30(7):531–40.
[23] Baxendale S. The impact of epilepsy surgery on cognition and behavior. Epilepsy Behav 2008;12(4):592–9.
[24] Äikiä M, Hyppönen J, Mervaala E, Kälviäinen R. Cognitive functioning in progressive myoclonus epilepsy type 1 (Unverricht-Lundborg Disease, EPM1). Epilepsy Behav 2021;122:108157.
[25] Jones G, Justice LV, Cabiddu F, Lee BJ, Iao L-S, Harrison N, et al. Does short-term memory develop? Cognition 2020;198:104200.
[26] Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD. The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. Cogn Psychol 2000;41(1):49–100.
[27] Lee TM, Yip JT, Jones-Gotman M. Memory deficits after resection from left or right anterior temporal lobe in humans: a meta-analytic review. Epilepsia 2002;43(3):283–91.
[28] Park K-I, Lee SK, Chu K, Jung K-H, Bae E-K, Kim J-S, et al. Withdrawal of antiepileptic drugs after neocortical epilepsy surgery. Ann Neurol 2010;67(2):230–8.
[29] Eddy CM, Rickards HE, Cavanna AE. The cognitive impact of antiepileptic drugs. Ther Adv Neurol Disord 2011;4(6):385–407.
[30] Seiam AHR, Dhaliwal H, Wiebe S. Determinants of quality of life after epilepsy surgery: systematic review and evidence summary. Epilepsy Behav 2011;21(4):441–5.
[31] Helmstaedter C, Kurthen M, Lux S, Reuber M, Elger CE. Chronic epilepsy and cognition: a longitudinal study in temporal lobe epilepsy. Ann Neurol 2003;54(4):425–32.
[32] Reuber M, Andersen B, Elger CE, Helmstaedter C. Depression and anxiety before and after temporal lobe epilepsy surgery. Seizure 2004;13(2):129–35.