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Lexicon Before and After Epilepsy Surgery in Adolescents

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Objective: Poor performance on confrontation naming tasks by children and adolescents with pharmacologically intractable epilepsy has been interpreted as indicating impairments of lexicon, that is, the store of words in long-term memory. However, confrontation naming performance crucially depends not only on word knowledge but also on other functions such as fluency. We applied an alternative method to assess lexicon with the aim of tracing deficits in lexicon before and after surgery in adolescents with pharmacologically intractable epilepsy. ***Method:*** Sixteen patients and 32 age- and sex-matched controls completed the Dutch version of the controlled oral word production task. Responses were used to calculate indices of lexical fluency (retrieval efficiency), lexical breadth (vocabulary size), and lexical depth (knowledge of word properties), as well as use of search strategies. ***Results:*** Adolescents with pharmacologically intractable epilepsy had lower lexical fluency scores than healthy peers, but did not differ from them on the dimensions of lexical breadth and lexical depth. Patients demonstrated reduced use of search strategies. In fact, the difference in lexical fluency between patients and controls disappeared after controlling for Full Scale IQ (obtained using the Dutch version of the 3rd edition of the Wechsler Intelligence Scale for Children (WISC–IIINL; Kort et al., 2005; Wechsler, 2002) or—for older children—the Dutch version of the first edition of the Kaufman Adult and Adolescent Intelligence Test (KAIT; Kaufman & Kaufman, 1993; Mulder, Dekker, & Dekker, 2004) and use of search strategies. In patients, changes in the use of the antiepileptic drug carbamazepine were associated with lexical fluency. ***Conclusion:*** Adolescents with pharmacologically intractable epilepsy differ from their healthy peers mainly in lexical fluency, rather than word knowledge per se.

Keywords: epilepsy surgery, adolescents, lexicon

Lexicon—"the store of words in long-term memory" (Jackendoff, 1999, p. 60)—is often assessed using confrontation naming tasks (i.e., naming of visually presented objects or pictures; Hamberger, 2015; Ives-Deliperi & Butler, 2012). Poor confrontation naming in adolescents and children with medically intractable epilepsy (de Koning et al., 2009; Vega et al., 2015)—often with

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continued decline after epilepsy surgery (de Koning et al., 2009; Dlugos, Moss, Duhaime, & Brooks-Kayal, 1999; Vega et al., 2015)—has been interpreted as demonstrating significant impairments of lexicon. Research with other tests, however, has suggested that verbal abilities of adolescents and children with medically intractable epilepsy are generally preserved (Basheer et al., 2007; Battaglia et al., 1999).

Neuropsychologically, the store of words should be distinguished from its accessibility for naming objects (Weigl & Bierwisch, 1970). Daller, Milton, and Treffers-Daller (2007) describe a "three-dimensional [lexical] space," in which *lexical fluency* refers to how fast an individual is able to retrieve words, *lexical breadth* refers to the amount or richness of the person's lexicon, and *lexical depth* refers to the grammatical functions of words and constraints on their use. Poor performance on confrontation naming tasks therefore may not (only) be caused by inadequate vocabulary, but rather result from inefficient retrieval (i.e., poor lexical fluency) or shallow knowledge of word properties (i.e., limited lexical depth). That is, it is possible that a person knows that a name (word) corresponds to a particular type of object, yet is not able to retrieve the name in a timely fashion during a confrontation naming task.

This distinction between the lexicon itself and its accessibility raises the question whether adolescents with medically intractable epilepsy have impairments in the size of the store of words in long-term memory—*lexical breadth* in the Daller et al. (2007) model—or rather (also) in lexical fluency or lexical depth. Our primary questions were therefore (a) whether adolescents with pharmacologically intractable epilepsy differ from normally developing peers on each of these three dimensions, and (b) whether there are changes in these three dimensions after epilepsy surgery in these patients.

Because confrontation naming tasks may confound these three dimensions, we applied the Daller et al. (2007) model to a controlled oral word production task (Baron, 2004; Strauss, Sherman, & Spreen, 2006), and hypothesized that adolescents with medically intractable epilepsy differ from their peers not (or at least not only) on lexical breadth but rather on the dimensions of lexical fluency and depth. To control for possible confounders, we also traced associations between nonlexical variables (e.g., assessment number, Full Scale IQ (FSIQ; obtained using the Dutch version of the third edition of the Wechsler Intelligence Scale for Children [WISC–IIINL; Kort et al., 2005; Wechsler, 2002] or—for older children—the Dutch version of the first edition of the Kaufman Adult and Adolescent Intelligence Test [KAIT; Kaufman & Kaufman, 1993; Mulder, Dekker, & Dekker, 2004]), and use of search strategies) and—for patients—noncognitive (i.e., demographic and illness-related) variables.

Method

Participants

Patients were included in this study if they were accepted as candidates for epilepsy surgery at the University Medical Center Utrecht between September 2007 and October 2009 and were ≥12.0 and <19.0 years of age at presurgical neuropsychological assessment. For the purpose of the current study, six bilingual patients were excluded. Sixteen monolingual Dutch-speaking patients were included (for clinical and demographic information, see Table 1).

Table 1
Epilepsy (Surgery) Characteristics and Parental Education for the Patient Sample (N = 16)

Variable	Patients
Side of surgery, left/right (*n*)	11/5
Area of surgery (*n*)	
Temporal	8
Frontal	5
Central	1
Parietal	2
Etiology (*n*)	
Hippocampal sclerosis	2
Cerebral tumor	10
Focal cortical dysplasia	4
Seizure frequency at T0 (median [IQR])	>1/week (>1/week – >1/day)
Duration of epilepsy (median [IQR])	5.6 (2.8–11.0) years
Seizure freedom, yes/no (*n*)	14/2
Number of AEDs (median [IQR])	
T0	2 (2–2)
T1	2 (1–2)
T2	1.5 (1–2)
T3	.5 (0–1)
Parental education[a] (median [IQR])	3 (3–3)

Note. IQR = interquartile range; AEDs = antiepileptic drugs; T0 = at presurgical assessment; T1 = at assessment six months after surgery; T2 = at assessment 12 months after surgery; T3 = at assessment 24 months after surgery.
[a] Parental education was scored on a scale from 1 (*at most lower secondary education*) to 4 (*at least a master degree or equivalent*). A score of 3 equates to completion of a bachelor's degree or other short-cycle tertiary education (see Meekes et al., 2015, for more details).

Patients were examined before surgery as well as 6, 12, and 24 months after surgery as part of a larger study of memory and social cognition before and after childhood epilepsy surgery (Braams et al., 2015; Meekes, Braams, Braun, Jennekens-Schinkel, & van Nieuwenhuizen, 2013; Meekes et al., 2014, 2015). Demographic (handedness and parental education) and illness-related (age at surgery, side of surgery, area of surgery, etiology, age at onset, duration of the epilepsy, seizure freedom, antiepileptic drug use) variables were collected from the medical files and from detailed histories taken at each neurological examination. For each patient, two normally developing monolingual Dutch-speaking children matched for age and gender were selected from regular schools. Assessments of controls were performed according to the same protocol and at the same intervals as for patients. All children and their caregivers provided written informed consent for their participation in this study. The study was approved by the Medical Ethics Committee of the University Medical Center Utrecht.

Materials and Procedures

In the Dutch adaptation (Bouma, Mulder, Altena, & Schmand, 2012) of the controlled oral word production task (Baron, 2004; Strauss et al., 2006), participants are asked to produce as many words as they can in 60 s starting from a specific letter. The four letters (U, N, K, A) are not randomly chosen: In Dutch, K and A occur frequently in the initial position of a word, whereas U and N are only infrequently found in this position (Bouma et al., 2012).

From the resulting word lists, three measures of lexical space (fluency, breadth, and depth) were derived. In addition, we quantified clustering of words to assess the role of search strategies in effective performance on this task (Lezak, Howieson, Bigler, & Tranel, 2012).

Lexical fluency was calculated as the sum of the number of words produced in response to the four letters. Because lexical fluency scores showed a marked skewness, they were normalized using a log transformation.

Lexical breadth of the responses (the words produced by the respondent) was determined (method adapted from Vermeer, 2004) using the frequencies of occurrence in the Spoken Dutch Corpus (*Corpus Gesproken Nederlands*; Nederlandse Taalunie, 2004). We calculated the geometric means of the frequencies of responses after excluding words that belonged to the 1,000 most-frequent words in the corpus (i.e., had extremely high frequencies). Because studies on lexical richness have shown that frequency, among other factors, is largely responsible for the acquisition order of words (Goodman, Dale, & Li, 2008; Vermeer, 2001), a child can be assumed to know the most frequent words if he or she also produces infrequent words. Responses that did not occur in the corpus but were legal words based on other sources (e.g., the Dutch language dictionary; van Dale, 2005) were scored as a frequency of 1. Note that because this measure is based on word frequency, good lexical breadth (i.e., a large lexicon) corresponds to a low score (and a high score suggests a small lexicon).

For lexical depth, responses were scored as "verbs," "nouns," or "other" (adjectives, adverbs, numerals, etc., that were classed together because of their very small numbers); the number within each category was divided by the total number of responses (yielding three scores that always sum to 1). Responses that could be interpreted as belonging to multiple categories were assigned ratios based on log frequency of occurrence in the corpus. A slightly simplified example is the case of the Dutch word *kom*, which would be counted as 0.68 verbs and 0.32 nouns.[1]

Search strategies were assessed by identifying clusters, with a cluster being defined as two or more consecutive words sharing a feature. *Phonological clusters* were consecutive responses consisting of two or more identical first phonemes (e.g., ***gl**are*, ***gl**oom*, ***gl**obal*). *Semantic clusters* consisted of consecutive responses with either associated (e.g., *salute*, *soldier*) or shared (e.g., *salt*, *sugar*) meanings. Alterations of a word (e.g., *shoe*, *shoelace*, *shoemaker*) were defined as *word variations* (Lezak et al., 2004). The size of a cluster was determined by counting the number of connections within the cluster, for example, *salute, soldier* have a cluster size of 1; *shoe, shoelace, shoemaker* would have a cluster size of 2; and so forth. To obtain a search strategies score, the total number of such connections was divided by the number of connections possible within the string of a participant's responses for a given letter (e.g., if a participant produced 11 words for the letter *K*, 10 connections would be possible; if four connections were in fact found, the search strategies score would be 4/10 = 0.4). A search strategies score near 0 then indicates minimal clustering, whereas a score near 1 implies connections between almost all consecutive words.

In addition to results from the controlled oral word production task, we also obtained FSIQ using the Dutch version of the third edition of the Wechsler Intelligence Scale for Children (WISC–III^{NL}; Kort et al., 2005; Wechsler, 2002) or—for older children—the Dutch version of the first edition of the Kaufman Adult and Adolescent Intelligence Test (KAIT; Kaufman & Kaufman, 1993; Mulder, Dekker, & Dekker, 2004).

Data Analysis

Statistical analysis was performed using R 3.02 (R Core Team, 2013), including the package nlme (Pinheiro, Bates, DebRoy, Sarkar, & R Core Team, 2013) for linear mixed model analyses. Preliminary analyses in healthy controls demonstrated significant associations of lexical measures with age and gender. To retain the matching of each patient with his or her two controls, data were analyzed using linear mixed effects models with random intercepts per matching group, as well as per subject per matching group (or random intercepts per subject for analyses that included only patients, because, in such cases, there was only one subject in each matching group). Initial analyses included fixed effects for group (control [reference level] or patient) and assessment number (0 to 3), as well as their interaction. If the interaction was nonsignificant, the model was reanalyzed without the interaction term. Additional analyses explored the role of nonlexical variables (assessment number, FSIQ, and search strategies) in explaining observed differences between patients and controls. In patients, we also explored associations with noncognitive (i.e., demographic and illness-related) variables.

Likelihood ratio (LR) statistics are given when comparisons between models are presented. Given the lack of a generally accepted method to determine standardized effect sizes for each fixed effect in a mixed effects model, we report the marginal and conditional R^2 for the model as a whole (Nakagawa & Schielzeth, 2013; designated as R^2_m and R^2_c, respectively). We also report restricted maximum likelihood estimates (REMLEs) of model coefficients (i.e., unstandardized effect sizes) and their standard errors (*SE*s). These unstandardized effect sizes serve to demonstrate the size of the effect in terms of the actual measurement. For example, when we report that clustering increases with assessment number (see the Results section), the REMLE estimate is 0.016, which corresponds to a 0.016 increase in search strategies with each consecutive assessment (or, consequently, a $3 \times 0.016 = 0.048$ increase between the first and the last assessment). For analyses performed on log-transformed data, the back-transformed value of the REMLE is also given (with all other variables set to 0 or their respective reference levels). A p value <0.05 was deemed to indicate statistical significance, whereas p values ≥ 0.05 but <0.10 are reported as tendencies.

Results

Sample Characteristics

Patients did not significantly differ from controls in median age (patients = 14.5 years, range = 12.6–15.8 years; controls = 14.6 years, range = 12.9–15.7 years), $W(16, 32) = 278.5$, $p = .630$, gender (patients: eight girls, eight boys; controls: 16 boys, 16

[1] For the interested reader, the term *kom* has a frequency of 3,508 as an inflected form of the verb *komen* [to come], and a frequency of 44 as a singular form of the noun *kom* [bowl]; the calculations are therefore log(3508)/(log[44] + log[3508]) = 0.68, and log(44)/(log[44] + log[3508]) = 0.32.

girls), $\chi^2(1) = 0.00$, $p > .999$, or handedness (patients: 15 right, one left; controls: 29 right, three left), $\chi^2(1) = 0.00$, $p > .999$. Mean FSIQ (at first assessment, i.e., for patients the presurgical assessment) was significantly lower in patients than in controls (patients = 86.9, *SD* = 16.4; controls = 111.7, *SD* = 12.6), $t(24.1) = -5.30$, $p < .001$. Patients were also significantly less likely to attend regular education (patients: 12 regular, four special; controls: 32 regular, zero special), $\chi^2(1) = 5.76$, $p = .016$. One further patient had repeated a grade, but this is very common in the Dutch education system (17% of students repeats a grade in elementary school; Driessen, Leest, Mulder, Paas, & Verrijt, 2014); no data were gathered regarding repeated grades in controls.

Lexical Fluency

There was no significant interaction between group and assessment number for lexical fluency, $F(1, 142) = 0.79$, $p = .375$ (Figure 1). Lexical fluency was lower in patients than in controls, $F(1, 31) = 6.16$, $p = .019$, REMLE = −0.172, back-transformed REMLE = −5.8, *SE* = 0.069, and increased with assessment number, $F(1, 143) = 45.83$, $p < .001$, REMLE = 0.082, back-transformed REMLE = 3.1, *SE* = 0.012, $R^2_m = 0.13$, $R^2_c = 0.70$. The improvement with assessment number was significant both in controls, $F(1, 95) = 53.04$, $p < .001$, REMLE = 0.090 (3.4), back-transformed REMLE = 3.4, *SE* = 0.012, $R^2_m = 0.12$, $R^2_c = 0.72$, and in patients, $F(1, 47) = 6.30$, $p = .016$, REMLE = 0.067, back-transformed REMLE = 2.2, *SE* = 0.027, $R^2_m = 0.04$, $R^2_c = 0.64$.

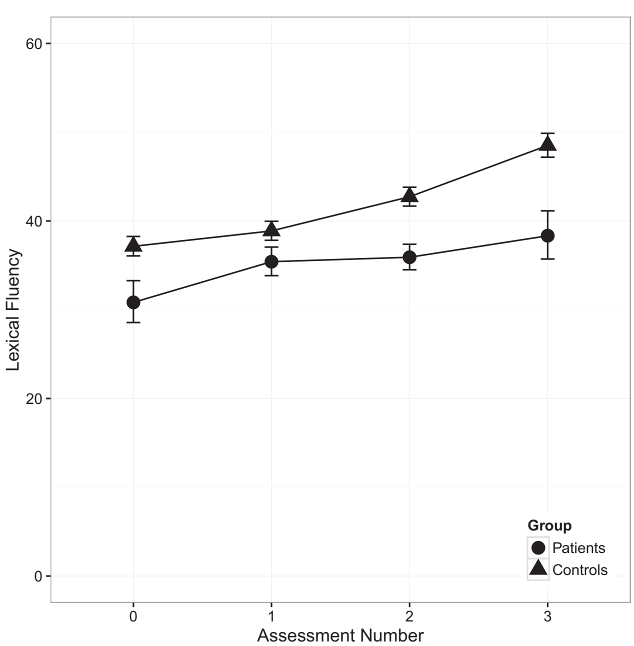

Figure 1. Lexical fluency for patients (circles; $n = 16$) and controls (triangles; $n = 32$). Error bars represent standard error of the mean. For patients, assessment number 0 = before surgery; 1 = 6 months after surgery, 2 = 12 months after surgery; 3 = 24 months after surgery; controls were tested at the same intervals.

Lexical Breadth

There was no significant interaction between group and assessment number for lexical breadth, $F(1, 142) = 2.73$, $p = .101$ (Figure 2). Patients did not differ from controls $F(1, 31) = 0.37$, $p = .550$, and lexical breadth did not change over the course of assessments, $F(1, 143) = 0.27$, $p = .603$. However, as may be observed from Figure 2, controls scored noticeably—though nonsignificantly—better than patients at the last assessment.

Lexical Depth

There were no significant interactions of group and assessment number for lexical depth (nouns: $F[1, 142] = 0.07$, $p = .790$; verbs: $F[1, 142] = 0.16$, $p = .690$; other words: $F[1, 142] = 0.00$, $p = .978$; Figure 3). Proportions of nouns, $F(1, 31) = 0.85$, $p = .363$, verbs, $F(1, 31) = 0.09$, $p = .771$, and other words, $F(1, 31) = 0.41$, $p = .524$, did not differ between patients and controls. There was also no change with assessment number (nouns: $F[1, 142] = 1.57$, $p = .212$; verbs: $F[1, 142] = 0.15$, $p = .702$; other words: $F[1, 142] = 1.20$, $p = .275$).

Search Strategies

There was no significant interaction between group and assessment number for search strategies, $F(1, 142) = 0.26$, $p = .613$ (Figure 4). Patients showed less clustering than controls, $F(1, 31) = 7.09$, $p = .012$, REMLE = −0.059, *SE* = 0.022. Clustering increased with assessment number, $F(1, 142) = 8.00$, $p = .005$, REMLE = 0.016, *SE* = 0.006, $R^2_m = 0.09$, $R^2_c = 0.37$; this increase was significant in patients, $F(1, 47) = 4.74$, $p = .035$, REMLE = 0.020, *SE* = 0.009, $R^2_m = 0.04$, $R^2_c = 0.49$, and was only a trend in controls, $F(1, 95) = 3.82$, $p = .054$, REMLE = 0.014, *SE* = 0.007, $R^2_m = 0.02$, $R^2_c = 0.23$.

Relation Between Lexical Fluency and Nonlexical Predictors

Of the three dimensions of lexical space, only lexical fluency differed significantly between patients and controls. To improve our understanding of this difference, we explored the role of three possible nonlexical predictors of lexical fluency: assessment number, search strategies, and FSIQ (search strategies and FSIQ were centered at 0.33 and 100, respectively, for these analyses, so the back-transformed REMLE estimates are valid for these values of search strategies and FSIQ).

All three variables were significantly associated with lexical fluency in controls (assessment number: $F[1, 93] = 13.71$, $p = <.001$, REMLE = 0.058, back-transformed REMLE = 2.0, *SE* = 0.016; search strategies: $F[1, 93] = 10.76$, $p = .002$, REMLE = 0.524, back-transformed REMLE = 23.2, *SE* = 0.160; FSIQ: $F[1,93] = 5.40$, $p = .022$, REMLE = 0.005, back-transformed REMLE = 0.18, *SE* = 0.002; $R^2_m = 0.22$, $R^2_c = 0.73$), in whom higher lexical fluency was associated with repeated testing, with higher IQ, and with more clustering. For patients, search strategies, $F(1, 45) = 5.56$, $p = .023$, REMLE = 0.847, back-transformed REMLE = 49.5, *SE* = 0.359, and FSIQ, $F(1, 45) = 6.72$, $p = .013$, REMLE = 0.009, back-transformed REMLE = 0.34, *SE* = 0.004, were significantly associated with lexical fluency in the full model ($R^2_m = 0.26$, $R^2_c = 0.67$), but

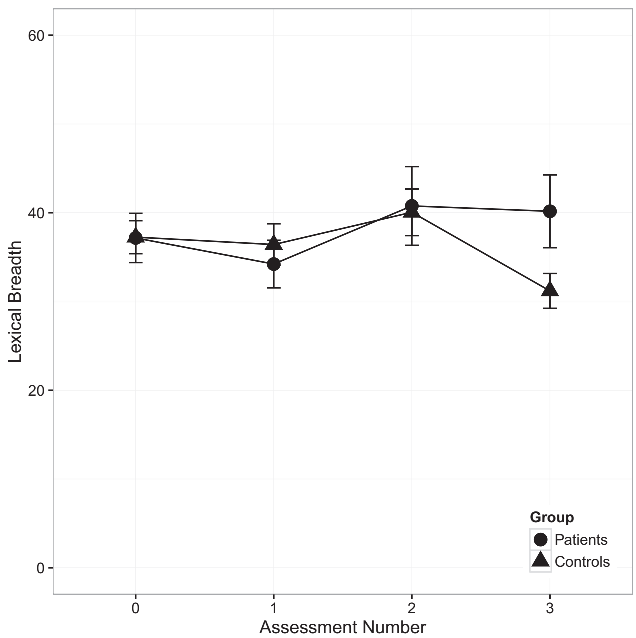

Figure 2. Lexical breadth for patients (circles; $n = 16$) and controls (triangles; $n = 32$). Error bars represent standard error of the mean. For patients, assessment number 0 = before surgery; 1 = 6 months after surgery, 2 = 12 months after surgery; 3 = 24 months after surgery; controls were tested at the same intervals. Note that lower scores indicate lower average frequency of words, that is, a larger lexical breadth or vocabulary size.

assessment number was not, $F(1, 45) = 0.71$, $p = .403$. After removal of assessment number from the model, search strategies, $F(1, 46) = 7.20$, $p = .010$, REMLE = 0.928, back-transformed REMLE = 15.9, $SE = 0.346$, and FSIQ, $F(1, 46) = 9.61$, $p = .003$, REMLE = 0.010, back-transformed REMLE = 0.11, $SE = 0.003$, were still significantly associated with lexical fluency ($R^2_m = 0.29$, $R^2_c = 0.68$).

For patients and controls combined, assessment number, $F(1, 141) = 50.73$, $p < .001$, REMLE = 0.047, back-transformed REMLE = 1.64, $SE = 0.013$, search strategies, $F(1, 141) = 13.81$, $p < .001$, REMLE = 0.582, back-transformed REMLE = 26.7, $SE = 0.157$, and FSIQ, $F(1, 141) = 24.96$, $p < .001$, REMLE = 0.006, back-transformed REMLE = 0.22, $SE = 0.001$, were all significantly associated with lexical fluency ($R^2_m = 0.28$, $R^2_c = 0.71$). Addition of a group (patient vs. control) factor ($LR_1 = 1.04$, $p = .308$), an education (regular vs. special education) factor ($LR_1 = 1.61$, $p = .204$), or the interaction between assessment number and group ($LR_2 = 1.37$, $p = .504$) did not significantly improve the model.

Noncognitive Predictors of Lexical Fluency in Patients

To assess the role of noncognitive predictors of lexical fluency, including disease variables, we performed a series of explorative analyses (in patients only). No significant relations were observed between lexical fluency and age at surgery, $F(1, 14) = 0.00$, $p = .958$; handedness, $F(1, 14) = 1.47$, $p = .0.245$; side of surgery, $F(1, 14) = 2.52$, $p = .0.135$; area of surgery, $F(3, 12) = 0.67$, $p = .585$; etiology, $F(1, 14) = 0.19$, $p = .672$; age at onset, $F(1, 14) = 1.55$, $p = .234$; duration of the epilepsy, $F(1, 14) = 1.51$, $p = .239$; parental education, $F(1, 14) = 1.14$, $p = .306$; or (for postsurgical results) seizure freedom, $F(1, 14) = 1.14$, $p = .303$. Only antiepileptic drug use was significantly associated with lexical fluency (note that because AED use varied with time, assessment number was also included in this analysis as well as the next): higher lexical fluency was associated with a lower total number of different drugs used at the time of assessment, $F(1, 46) = 4.90$, $p = .032$, REMLE = −0.119, back-transformed REMLE = −4.88, $SE = 0.054$, $R^2_m = 0.11$, $R^2_c = 0.65$. Exploring the effect of specific AEDs suggested that lexical fluency was associated with changes in carbamazepine, $F(1, 22) = 5.54$, $p = .028$, REMLE = −0.379, back-transformed REMLE = −10.35, $SE = 0.161$, $R^2_m = 0.11$, $R^2_c = 0.69$; that is, introduction of carbamazepine was associated with lower lexical fluency, and withdrawal with higher lexical fluency, but not with changes in the other AEDs (lamotrigine, oxcarbazepine, clobazam, and levetiracetam) for which the presence of the association could usefully be analyzed (topiramate, pregabaline, and lacosamide were each only used by one participant at one assessment).

Discussion

Using measures derived from a word production task, we found that—of the three dimensions of lexicon as defined in the lexical space model of Daller et al. (2007)—adolescents with pharmacologically intractable epilepsy differed from controls only in lexical fluency. Lexical fluency increased after surgery

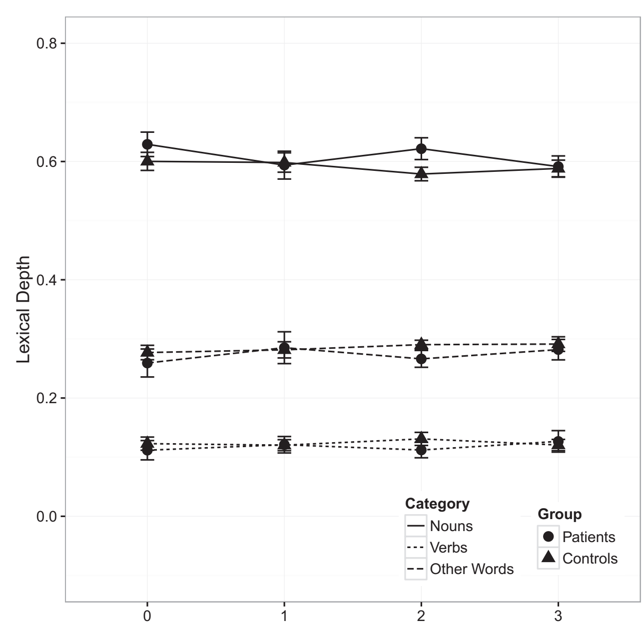

Figure 3. Proportions (possible range: 0–1) of nouns (solid lines), verbs (dashed lines), and other words (dotted lines) for patients (circles; $n = 16$) and controls (triangles; $n = 32$). Error bars represent standard error of the mean. For patients, assessment number 0 = before surgery; 1 = 6 months after surgery, 2 = 12 months after surgery; 3 = 24 months after surgery; controls were tested at the same intervals.

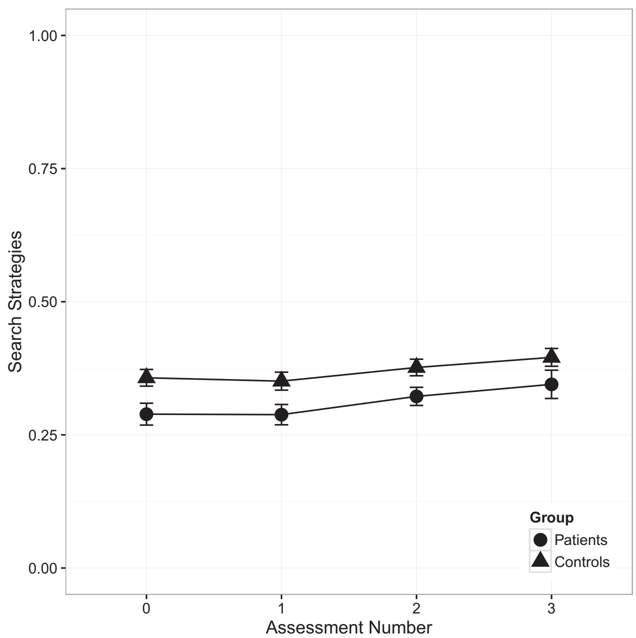

Figure 4. Search strategies (possible range: 0–1) for patients (circles; $n = 16$) and controls (triangles; $n = 32$). Error bars represent standard error of the mean. For patients, assessment number 0 = before surgery; 1 = 6 months after surgery, 2 = 12 months after surgery; 3 = 24 months after surgery; controls were tested at the same intervals.

in patients, but the improvement did not differ from that in controls. Although at the last assessment lexical breadth appeared to be somewhat better in controls than in patients, no significant differences were observed for lexical breadth or lexical depth. Patients showed reduced use of strategies to search their lexicon when compared with controls. In fact, when we controlled for FSIQ and the use of search strategies, differences in lexical fluency between patients and controls disappeared. From a set of illness-related and demographic variables, only use of antiepileptic drugs (in particular, changes in carbamazepine usage) was significantly associated with lexical fluency.

On average, epilepsy patients score lower on IQ tests than do healthy controls, especially when the epilepsy is severe. Such IQ differences probably exist before overt seizures are observed (Oostrom, Smeets-Schouten, Kruitwagen, Peters, & Jennekens-Schinkel, 2003). Hence, lower IQ in epilepsy patients may be a direct effect of the underlying etiology, rather than a result of recurrent seizures. Lexical fluency is correlated with IQ and is (therefore) lower in patients than in controls. The correlation between lexical fluency and IQ is, however, far too weak to support the conclusion that lower lexical fluency is simply a consequence of lower IQ. Instead, our analysis suggests that in patients decreased lexical fluency results from a combination of factors, such as reduced processing speed, inadequate executive function, suboptimal use of search strategies, and hampered access to lexical items. The contribution of each of these elements likely differs from patient to patient, and demonstrating exactly how they relate to the underlying brain substrate is beyond the scope of the study, but two speculative examples may serve to illustrate the basic idea. In case of a classical temporal lobe epilepsy with a left-sided seizure focus, lexical fluency may be diminished because communication between temporal areas important for semantic memory and frontal areas involved in executive function have been damaged by the lesion and/or the seizures. On the other hand, in a patient with frontal lobe epilepsy, decreased lexical fluency may result from poor executive function directly and/or from insufficient use of cognitive strategies.

The lack of significant differences in lexical breadth and lexical depth between patients and controls suggests that word knowledge is largely intact in adolescents with pharmacologically intractable epilepsy, and remains so after surgical intervention (a nonsignificant improvement of lexical breadth in controls was not matched by a similar improvement in patients). Even apart from the problems inherent in interpreting null results, these findings do not warrant the conclusion that the total store of words in patients is equal to that in controls. They do indicate, however, that word knowledge is not the limiting factor in patients' performance on this task, and suggest that the same may be true in daily life. This conclusion is congruent with the wider literature on language development in children with refractory epilepsy, which suggests that verbal abilities tend to be relatively preserved when compared with general cognitive level of these children (Basheer et al., 2007; Battaglia et al., 1999). However, studies of lexicon have observed a considerable delay in productive lexicon before surgery (de Koning et al., 2009; Vega et al., 2015), which increased after surgery (de Koning et al., 2009), in particular in children undergoing left temporal resections (Vega et al., 2015). Impairments in semantic memory have also been reported in children with pharmacologically intractable epilepsy (Messas, Mansur & Castro, 2008; Rzezak, Guimarães, Fuentes, Guerreiro, & Valente, 2011), though no deterioration has been observed after surgery (Vega et al., 2015). Although the confrontation naming and verbal fluency tasks used in previous studies (to assess lexicon and semantic memory, respectively) do require word knowledge, they crucially depend on lexical fluency as well: Usually, either a specific word has to be retrieved (confrontation naming), or many words meeting certain criteria have to be retrieved within a set time period (verbal fluency). Our analysis, based on the lexical space model (Daller et al., 2007), suggests that it is specifically this aspect of lexical fluency, rather than lexical breadth or depth, that is impaired in adolescents with pharmacologically intractable epilepsy. In other words, we suggest that these patients are limited by inefficient retrieval of required words, rather than by deficits in word knowledge per se.

We also found reduced application of search strategies by patients. Successful use of strategies, especially variations on a word (shoe—shoelace—shoemaker, etc.) can greatly increase lexical fluency scores, but tends to have at most minor effects on lexical breadth scores. Our analysis showed that differences in FSIQ and search strategies accounted for the differences in lexical fluency between patients and controls. Previous research in adults has shown that although phonemic cuing—giving the initial sound of the target word—makes a confrontation naming task easier for everyone, some patients benefit inordinately from such cuing (Busch et al., 2013). Taken together, these results support the aforementioned notion that, in this population, the problems with confrontation naming stem from slow or inefficient lexical retrieval rather than insufficient word knowledge.

Word knowledge is known to be correlated with education (Lezak et al., 2004), and hence the observed differences in education between patients and controls might lead to differences in word knowledge. However, the differences in word knowledge associated with differences in education are likely to be differences of degree rather than functional adequacy. In other words, individuals with less education may have a smaller store of words at their disposal, but what they have is sufficient for normal everyday functioning and for performance on oral word association or confrontation naming tests. Nonetheless, results of these tests would be expected to correlate with education because—as replicated in the present study—lexical fluency is correlated with IQ and executive functioning.

Lexical fluency increased over successive assessments in both patients and controls. Because the same set of letters was used at each assessment, this increase presumably reflects repeated testing in controls. The increase in patients did not differ from that in controls, and therefore we would argue that, in patients, the increase also reflects repeated testing. This is supported by previous studies from our own group suggesting that—except in the relatively rare cases in which a direct or indirect negative effect of surgery may be supposed—repeated testing improvements in epilepsy surgery patients are in line with those in controls (Meekes et al., 2013, 2014). At the time of data collection, the test did not have validated parallel versions. We therefore used the well-studied standard test; given the choice of letters for that test, it would be difficult to create four versions with similar characteristics (e.g., the Dutch alphabet only contains five true vowels). After the start of our study, an oral word-association test with parallel versions has been published (Bouma et al., 2012; Schmand, Groenink, & van den Dungen, 2008). Replication of the study using this fluency task with parallel forms would be useful to exclude the possibility that effects of repeated testing and surgery are confounded.

Besides the aforementioned variables FSIQ and use of search strategies, only the number of antiepileptic drugs was associated with lexical fluency in patients. Cognitive side effects of antiepileptic drugs are well established (Loring, Marino, & Meador, 2007), and there is now an increasing body of evidence that reduction of AEDs after successful epilepsy surgery in children is associated with improved cognitive outcome (Boshuisen et al., 2015; Meekes et al., 2013, 2015; Skirrow et al., 2011; van Schooneveld, van Erp, Boshuisen, Meekes, & Braun, 2013). The present study suggests that this may (in part) be an effect of carbamazepine, an older AED known to affect cognition—in particular, psychomotor speed (Hermann, Meador, Gaillard, & Cramer, 2010; Lagae, 2006; Loring & Meador, 2004; Park & Kwon, 2008).

Our methods for estimating the dimensions of lexical space—derived from the linguistic literature (Daller et al., 2007; Vermeer, 2004)—have not been used in previous studies of epilepsy patients. Because this is the first study to apply the three-dimensional model to exploring the lexicon in children with medically intractable epilepsy, further research is needed to assess the generalizability of our results. For example, we only included adolescents who tend to have less severe cognitive impairments than younger patients. The number of patients was small and the sample was heterogeneous with regard to disease-related variables such as etiology and side and site of surgery. Replication of our findings in larger and more homogeneous cohorts would therefore be most valuable. However, these weaknesses are balanced by a large and well-matched control sample and systematic follow-up assessments. The use of the oral word production task also had advantages. In other lexical production tasks, such as storytelling or word definition, respondents may be required to go beyond their knowledge (Turner, 1999), as the topic of a story or the word to be defined may not belong to the participant's knowledge base. Furthermore, syntactic—roughly, grammatical—abilities of the participant do not affect word production in the oral word production task. Confrontation naming tasks place strong constraints on retrieval, whereas effective performance on oral word production tasks allows a more free-ranging approach, hence limiting the required specificity of retrieval.

In summary, the present study suggests that lexical breadth and lexical depth are functionally intact in adolescents with pharmacologically intractable epilepsy, and do not deteriorate after epilepsy surgery. In other words, the store of words does not appear to be severely damaged in these patients, though it may still be somewhat smaller than in healthy peers. Lexical fluency, that is, the efficient retrieval of words from the lexicon, is decreased compared with that in healthy peers. This decrease can largely be explained from lower IQ and a reduced use of search strategies, and is neither aggravated nor ameliorated by surgery. Clinically, these results caution against interpreting commonly used tests such as confrontation naming and word association as pure measures of the lexical store. The optimal treatment for verbal impairments in adolescents with epilepsy is likely to differ from individual to individual, but our results suggest that approaches aimed at dealing with impaired retrieval are more likely to succeed than programs that aim to (re)learn word forms and meanings.

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