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Cognitive and EEG Fluctuation in Benign Childhood Epilepsy with Central-Temporal Spikes: A Case Series

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Abstract

Aware of parental reports of academic variability, we investigated month-to-month fluctuations in cognitive abilities and EEG status by repeated measures testing in six children with Benign Epilepsy with Central-Temporal Spikes (BECTS). All showed greater than normal test-retest variability. Daytime EEG abnormalities were also variable. Short-term fluctuations in cognitive function appear common in children with BECTS, potentially impacting academic performance.

1. INTRODUCTION

Benign epilepsy with central-temporal spikes (BECTS), or benign rolandic epilepsy, is the most common idiopathic partial epilepsy of childhood (Heijbel, Blom, & Bergfors, 1975). BECTS is characterized by central-temporal sharp waves and sleep-onset partial somatosensory/motor seizures, beginning 3–10 years of age and resolving by age 16 years. Although most children with BECTS have normal intelligence, previous studies have reported impairments in various cognitive domains (Baglietto et al., 2001; Croona, Kihlgren, Lundberg, Eeg-Olofsson, & Eeg-Olofsson, 1999; D'Alessandro et al., 1990; Northcott et al., 2006). However, no consistent cognitive phenotype has emerged.

Parents report day-to-day inconsistencies in children's cognitive and academic performance, but short-term fluctuations in cognitive function have not been studied. It is possible that within-patient variability in cognitive function contributes to the heterogeneity of impairments found in previous research. Moreover, failure to recognize cognitive variability in children with BECTS could lead to underestimating their risk for academic difficulties.

Prior attempts to relate EEG findings in BECTS to the presence of neuropsychological impairment have yielded inconsistent results (Nicolai et al., 2007). However, the stability of EEG findings in BECTS is not known. The purpose of this case series was to investigate short-term (month-to-month) variability of cognitive function and EEG findings in six children with BECTS.

2. METHODS

2.1 Participants and Screening

The six BECTS participants were ages 7–11 years (Table 1). All were in the active stage of BECTS (Commission on Classification and Terminology of the International League Against Epilepsy, 1989). Mean age of diagnosis was 8.4 years (range 6–9 years). No medications were adjusted during the study. Based on parental report, all participants had one or more night-time seizures within eight months prior to enrollment but were seizure-free for at least one month before testing. Average Full Scale IQ was 112 (SD±14), as measured by the Wechsler Abbreviated Intelligence Scale for Children. No participant met criteria for ADHD as determined by the Behavior Assessment System for Children (BASC) (Reynolds & Kamphaus, 1992) questionnaire and the parental interview (American Psychiatric Association, 1994). Subjects also participated in a concurrent study of auditory function (Boatman et al., 2008). Written parental consent was obtained for all participants in compliance with the Johns Hopkins Medicine Institutional Review Board.

2.3 Cognitive Testing

All participants underwent repeat neuropsychological testing at 4–5 week intervals. Five participants completed three testing sessions; one participant completed two sessions. A battery of 15 neuropsychological tests was administered (Table 2) to assess multiple cognitive functions, including selective and sustained attention (visual, auditory), executive function, auditory-verbal learning, visual-spatial skills, auditory and verbal memory, receptive and expressive language, and motor function. At the first visit, parents completed the BASC and were interviewed by a neuropsychologist (CAS) regarding behavioral and academic performance.

The same neuropsychological tests were administered in fixed order at each session by a clinical neuropsychologist (CAS). Different test versions, when available (WJ-III, Rey Complex Figure, RAVLT, MAE, TEA-Ch), were administered at consecutive sessions to reduce familiarity and practice effects.

2.4 EEG Recordings

All participants underwent awake, 20–30 minute EEGs at each visit, prior to neuropsychological testing. EEGs were recorded using standard clinical technique. At each session, parents confirmed no seizures occurred the previous evening.

2.5 Data Analysis

Neuropsychological raw test scores were converted to age-normed z-scores based on published norms. The likelihood of test-retest changes were computed using published test-retest coefficients. Specifically, $a = (var(y_1) + var(y_2)) \cdot (1 - corr(y_1 y_2))$, where a = the z-score related to the difference between the first (y_1) and second (y_2) measurement. Variances $var(y_1)$ and $var(y_2)$ each equal 1 (each measurement is expressed as an age-normed z-score). $corr(y_1 y_2)$ is the published test-retest coefficient. Test-retest differences of >2SD (i.e., <5% likelihood of occurring) were considered to be significant.

EEGs were reviewed independently by three pediatric epileptologists (EPV, JBE, WHT) using standard clinical viewing parameters in a bipolar longitudinal montage. Records were examined for central-temporal abnormalities: spike rate, asynchronous spike foci and presence of a slow-wave focus (reviewed in Nicolai et al., 2007). Spike rate was averaged across the entire recording and coded using a five-category index (no spikes; <1 spike/min; 1–5 spikes/min; 6–10 spikes/min; >10 spikes/min). Inter-rater agreement in coding EEG spike rate yielded a kappa statistic of 0.856, indicating very good agreement.

3. RESULTS

3.1 Neuropsychological Findings

All participants demonstrated scores more than 1 standard deviation (SD) below the mean on at least one test. Within each session, up to 33% of patients (range 17–33%) showed moderate-to-severe impairments on at least one test (≥2 SD below the normative mean), and up to 67% of patients (17–67%) were mildly impaired on at least one test (≥1 SD below the mean).

Score changes of a magnitude consistent with ≤5% likelihood occurred for every subject, for each session, and, independently, for every test (Table 3). The TOVA (ADHD index score) test of attention was the most variable, with unexpectedly large within-subjects changes occurring in all session-to-session comparisons, however the direction of change was not always the same as for other cognitive tests. Creature Count, RAVLT recognition memory and Rey Complex Figure copy had the least variability, with only one unexpectedly large session-to-session change occurring out of the 11 pairs of testing sessions.

3.2 EEG Findings

A total of 15 serial EEGs were obtained. All participants had at least two EEGs (Table 1). No clinical or electrographic seizures were observed. Twelve EEGs (80%) were classified as abnormal, in all cases due to features typical of BECTS. All participants had at least one abnormal EEG during the study, and two (33%) maintained abnormal EEGs across all sessions.

Of the nine repeat EEGs, four (44%) showed a change in status from the previous recording (normal-to-abnormal, abnormal-to-normal) (Table 4). Six repeat EEGs (67%) showed changes in spike rate category. Side of EEG spiking changed in two subjects (Subjects 4, 6), focal slowing was inconsistent on three subjects' repeat EEGs (Subjects 1, 2, 4), and presence of an asynchronous focus was inconsistent in one repeat EEG (Subject 5). In summary, 100% of repeat EEGs had at least one change from the immediately preceding EEG; moreover, all participants had EEGs that changed by one or more central-temporal features associated previously with cognitive impairment in BECTS (Nicolai et al., 2007).

3.3 Neuropsychological correlation with EEG

We cannot comment on whether fluctuations in EEG correlate with the variability in neuropsychological testing, due to limitations in statistical power. However, visual inspection of the data showed no apparent trends.

4. DISCUSSION

Our BECTS participants showed considerable short-term (month-to-month) variability in their neuropsychological and EEG findings. Specifically, all month-to-month comparisons showed greater-than-expected changes in at least one neuropsychological test, based on published test-retest coefficients. All subjects had at least one month-to-month comparison with at least five test scores in the comparison demonstrating greater-than-expected changes. Additionally, all subjects showed impairments (scores >1SD below the normative mean) in at least one neuropsychological domain. The test of attention showed the most variability, which is perhaps not surprising, given that attention is generally recognized to fluctuate with stress, sleep disturbances, affective state and alertness. Similarly, all repeat EEGs showed significant change from the previous session when the EEGs were examined for features previously implicated as being significant for characterizing inter-individual differences in BECTS.

One implication of the EEG and neuropsychological findings is that future studies on BECTS should take into account the degree of intra-individual variability, and future researchers may need to be cautious about basing the characterization of a subject on a single EEG or neuropsychological measurement. Additionally, the findings of neuropsychological variability may in part explain the elusiveness of a cognitive phenotype in BECTS. Finally, the cognitive findings may have practical clinical implications: first, children with BECTS who perform well on a single neuropsychological evaluation may have deficits if re-evaluated even a short time later; second, short-term cognitive variability may be a feature of BECTS. This interpretation would be consistent with anecdotal reports from parents, who note day-to-day fluctuations in children with BECTS. Clinicians, educators and family member should be aware of the possibility that children with BECTS may demonstrate cognitive variability. Neuropsychological assessment should take into consideration any parental or teacher report of cognitive and academic variability, and repeated testing may be helpful to document the difference between “good” and “bad” days.

There are a number of limitations to this study. The first is the small sample size. The second is the lack of a control group. The published test-retest coefficients may not have been derived using an experimental design consistent with the approach taken in this study, and it was impractical in this dataset to correct for multiple comparisons. Nevertheless, the fact that 65 of 163 (40%) neuropsychological test × session comparisons showed greater-than-expected changes suggests that the assertion of excessive variability may be valid. The use of a control group would address concerns related to the use of published normative values. Finally, a major limitation of this study is the lack of overnight EEGs preceding the testing sessions. There is considerable evidence linking sleep quality to cognitive abilities. Moreover there is evidence relating t nocturnal inter-ictal and ictal findings to cognitive performance the following day in BECTS (Nicolai et al., 2007). Future larger studies that address the issue of the relationship between neuropsychological and EEG variability and are sufficiently powered to make comparisons between the two should record overnight EEGs prior to cognitive testing sessions. In summary, this case series suggests that cognitive performance and EEG findings may vary considerably over the short-term in children in the active phase of BECTS and thereby adversely impact educational opportunities and quality of life for these children.

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Table 1

Subject Demographics and Testing

DEMOGRAPHICS						TESTING					
Subject	**Sex**	**Age at Testing (yr.mo)**	**Age at Diagnosis (yr.mo)**	**FSIQ**	**AED**	**Session 1**		**Session 2**		**Session 3**	
						Cognitive	**EEG**	**Cognitive**	**EEG**	**Cognitive**	**EEG**
1	M	10.0	7.10	97	CBZ	Y	N	Y	Y	Y	Y
2	F	11.9	9.8	109	CBZ	Y	N	Y	Y	Y	Y
3	M	11.1	9.2	105	VPA	Y	Y	Y	Y	N	N
4	F	7.1	6.7	116	NONE	Y	Y	Y	Y	Y	Y
5	F	11.9	8.0	107	CBZ	Y	Y	Y	Y	Y	Y
6	M	9.9	9.3	137	CBZ	Y	Y	Y	Y	Y	Y
Mean (± SD)		*10.3 (±1.8)*	*8.4 (±1.3)*	*111.8 (±13.8)*							

Abbreviations: AED (anti-epilepsy drug); CBZ (carbamazepine); VPA (valproate); FSIQ (full-scale intelligence quotient); M (male); F (female).

Table 2

Neuropsychological Battery

Test Name Abbreviation	Full Name	Domain	Citation
TOVA	Test of Variables of Attention (ADHD score)	Attention	Leark, Greenberg, Kindschi, Dupuy, & Hughes, 2007
TEA-Ch SCORE!	Test of Everyday Attention for Children, SCORE! Subtest	Auditory Attention	Manly, Robertson, Anderson, & Niparko, 1999
TEA-Ch CC-TS	Test of Everyday Attention for Children, Creature Count Subtest, Total Score	Executive Functioning Set Shifting	Manly, Robertson, Anderson, & Niparko, 1999
JLO	Judgment of Line Orientation	Visual-Spatial Perception	Benton, Varney, & Hamsher, 1978
RCFC	Rey-Osterrieth Complex Figure copy	Visual-Spatial Organization & Planning	Osterrieth, 1944; Rey, 1942
RCFR	Rey-Osterreith Complex Figure Recall	Visual-Spatial Memory	Osterrieth, 1944; Rey, 1942
RAVLT-A7	Rey Auditory Verbal Learning Test (List 7 Score)	Verbal Memory (recall)	Schmidt, 2004
RAVLT-RECOG	Rey Auditory-Verbal Learning Test, Recognition score	Verbal Memory (recognition)	Schmidt, 2004
WJ-III UD	Woodcock-Johnson-III Understanding Directions	Language: Comprehension	Woodcock, McGrew, & Mather, 2001
MAE-SR	Multilingual Aphasia Examination—Sentence Repetition	Language: Repetition; Working Memory	Benton, Hamsher, & Sivan, 1994
Pegboard	Grooved Pegboard	Motor Speed and Dexterity	Lafayette Instruments
FT	Finger Tapping	Motor Speed	Lafayette Instruments

Table 3

Session-to-Session Changes in Neuropsychological Z-Scores for Each Subject, for Each Test

Subj	Sessions	TOVA	SCORE!	CC-TS	JLO	RCFC	RCFR	RAVLT-ACQ	RAVLT-A7	RAVLT-RECOG	WJ-III UD	MAE- SR	Pegboard- Left	Pegboard- Right	FT-Left	FT-Right
1	1 → 2	**0.84**	**−3.33**	0.67	0.38	**2.67**	**5.09**	−1.01	−1.04	0	0.53	**−0.5**	0.27	**0.8**	0.59	0.65
	2 → 3	**0.96**	**2**	0.33	**0.57**	−1.31	**−1.75**	0.7	0.69	0.29	**−1.07**	**−0.65**	0.47	0.53	**1.07**	**1.79**
2	1 → 2	**1.92**	**−1**	−0.67	0.19	0.8	**1.36**	**1.6**	0.5	1.25	0.4	**1.05**	0.2	0.53	−0.36	−0.66
	2 → 3	**−3.66**	**1**	2	**−0.54**	1.66	−0.23	−0.54	−0.5	−0.84	−0.53	−0.26	0.33	0.4	**0.92**	−0.21
3	1 → 2	**−1.67**	**−3.67**	−0.67	**1.16**	0.13	−0.16	−0.93	−0.5	−1.25	0.47	**0.5**	0.2	−0.4	**1.32**	**1.35**
4	1 → 2	**−1.59**	0	0.67	−0.02	0.95	0.6	−0.94	−1.5	0	0.27	0	−0.2	0.4	0.55	0.46
	2 → 3	**2.52**	0	0	**0.66**	0.25	0.62	−0.76	**−1.53**	0.29	0.13	**−2.86**	**1.6**	**1.07**	**1.7**	**1.55**
5	1 → 2	**−4.84**	**−3**	−0.33	**1.58**	0.75	**1.35**	−0.2	−0.71	1.25	−0.13	**−2.42**	0	**1.87**	−0.49	**−1.06**
	2 → 3	**4.57**	0.33	**2**	−0.4	−0.34	**−1.28**	**1.8**	**−1.42**	0.37	**1.26**	**1.01**	−0.4	−0.2	0.26	−0.04
6	1 → 2	*	**−1.33**	1.33	**−0.98**	0	**1.36**	0	−0.87	0	−0.07	−0.06	**1.13**	**1.53**	**2.26**	**3.65**
	2 → 3	*	**2.33**	1	**0.98**	0.29	0.68	0.69	0	**−1.67**	0.07	**−1**	0.2	**0.8**	−0.61	**−2.54**
Test-Retest Coeff.		0.80	0.76	0.57	0.90	0.47	0.79	0.70	0.62	0.60	0.76	0.91	0.86	0.86	0.77	0.78
Sig. Change		**±0.80**	**±0.96**	**±1.72**	**±0.40**	**±2.12**	**±0.84**	**±1.20**	**±1.52**	**±1.60**	**±0.96**	**±0.36**	**±0.56**	**±0.56**	**±0.92**	**±0.88**

Notes: Test-Retest Coeff. = published test-retest coefficient; Sig. Change = Z-score change which has ≤ 5% probability of occurring, based on published test-retest coefficient. NT = Not tested for one of the sessions. NA = Not applicable. L = Left; R = Right; B = Bilateral.

Neuropsychological session-to-session change values marked in **bold** are those in which variability was considered significant.

* TOVA could not be scored for Subject 6 in any of the three sessions due to high Intra-session trial-by-trial response variability.

Table 4

Session-to-Session Changes in EEG Features for Each Subject, for Each Test

Subject	Sessions	Spike Rate	Spike Side	Asynchronous Focus	Slowing
1	2 → 3	**11.5 → 0**	L → NA	N → N	**Y → N**
2	2 → 3	0 → 0	NA	N → N	**N → Y**
3	1 → 2	**0 → 4.2**	NA → R	N → N	N → N
4	1 → 2	**2.3 → 0**	**L → NA**	N → N	**Y → N**
	2 → 3	**0 → 4.8**	**NA → R**	N → N	**N → Y**
5	1 → 2	**0.8 → 3.8**	B → B	Y → Y	N → N
	2 → 3	**3.8 → 0.8**	B → B	**Y → N**	N → N
6	1 → 2	0.7 → 0.2	**B → R**	N → N	Y → Y
	2 → 3	0.2 → 0.8	**R → L**	N → N	Y → Y

Note: EEG session-to-session change values marked in **bold** are those in which the change was significant: i.e., change from one category to another.