



WISC-IV Performance of Children Treated for Seizures with Monotherapy Medication

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INTRODUCTION

Research investigating the cognitive effects of specific antiepileptic drug (AED) therapy has been inconsistent; however, polytherapy has been associated with greater adverse cognitive effects than monotherapy, and although there is comparatively little research on newer AEDs, they are considered to have more favorable cognitive profiles than older AEDs (with the exception of topiramate) (Aldenkamp, De Krom, & Reijs, 2003). As medication options increase, consideration of cognitive side effects is becoming an increasingly important factor in deciding which medication may be most appropriate for a particular child. In addition, understanding how AEDs affect an individual's performance on specific measures of cognitive functioning is important when interpreting test results, particularly when comparing changes on cognitive tests over time (e.g., Is a decline in test scores related to changes in medication, and therefore differences in medication side effects, or a true regression in skill?). Most research has focused on adults. There have been a few reviews regarding the effects of AEDs on cognitive functions in pediatric populations (Bourgeois, 2004; Loring, & Meador, 2004); however, more studies are needed, particularly for newer AEDs. The purpose of this poster was to examine the effects of monotherapy on WISC-IV performance for four antiepileptic drugs: divalproex sodium, levetiracetam, lamotrigine, and oxcarbazepine. Based on a review of the literature, the following hypotheses were considered:

- H1. Children on monotherapy treatment with newer AEDs (levetiracetam, lamotrigine, and oxcarbazepine) will perform similarly on WISC-IV indices and core subtests to matched controls, while children on divalproex sodium (an older AED) will perform significantly lower on WISC-IV indices and core subtests when compared to matched controls.
- H2. Children taking divalproex sodium will perform significantly lower on WISC-IV indices and core subtests when compared to children taking levetiracetam, lamotrigine, and oxcarbazepine.

METHODS

Participants

Participants in the clinical group were selected from a larger group of children referred for neuropsychological evaluation at Children's Healthcare of Atlanta. An archival search was performed to identify children who were on monotherapy for the treatment of seizures and who were administered the WISC-IV. Medications were limited to divalproex sodium, levetiracetam, lamotrigine, and oxcarbazepine, as these are the most commonly prescribed medications among children seen within this department. Children with co-morbid neurological conditions, with the exception of ADHD, were excluded. The search yielded 80 children.

Clinical participants were matched by age, gender, ethnicity (when possible), and geographic region (all participants were from the southeast) to controls. The control group consisted of 80 children obtained, with permission from the publisher, from the standardization sample of the WISC-IV. Statistical analyses revealed no significant differences between the clinical and control groups for age, gender, geographic region, or ethnicity. Demographic characteristics were as follows:

Variable	Clinical Group	Control Group	Variable	Clinical Group	Control Group
Gender (n,%)			Age		
Female	33 (41%)	33 (41%)	Mean	11.22	10.27
Male	47 (59%)	47 (59%)	SD	8.69	2.77
Race (n,%)			Medications (Clinical Group only)		
Asian	1 (1%)		divalproex sodium	n = 16	
Black	18 (23%)	20 (25%)	levetiracetam	n = 20	
Hispanic		1 (1%)	lamotrigine	n = 19	
White	59 (74%)	59 (74%)	oxcarbazepine	n = 25	
Multiracial	2 (2%)				

RESULTS

H1a. An independent samples t-test indicated that children treated for seizures with monotherapy (n = 80) performed significantly worse on all WISC-IV factor index scores, as well as most core subtests (except Picture Concepts), compared to controls (n = 80). (See Table 1).

Table 1: WISC-IV Index Scores of Clinical Group and Standardization Controls

WISC-IV Index	Epilepsy Group		Control Group		t	p-value
	Mean	SD	Mean	SD		
Verbal Comprehension Index	90.78	18.47	100.70	15.12	-3.175	<.001
Perceptual Reasoning Index	90.59	18.23	98.91	16.82	-3.002	<.01
Working Memory Index	88.70	16.50	102.09	16.90	-5.070	<.001
Processing Speed Index	84.89	16.51	99.08	15.06	-5.674	<.001

H1b. When specific medications were examined, findings indicated that all four medication types were associated with significantly poorer performance on the Processing Speed Index (PSI), and three out of four medications (divalproex sodium, levetiracetam, and oxcarbazepine) were associated with lower scores on the Working Memory Index (WMI) when compared to controls. (See Table 2).

Table 2: WISC-IV Scores of Clinical Group by Medication and Standardization Controls.

Divalproex sodium	Clinical Group (n = 16)		Control Group (n = 16)		t	p-value
	Mean	SD	Mean	SD		
WISC-IV Index Scores						
Verbal Comprehension Index	82.00	19.68	95.75	11.81	-2.396	<.05
Working Memory Index	78.00	18.16	99.75	13.41	-3.854	<.01
Processing Speed Index	76.94	16.04	96.38	20.10	-3.024	<.01

Vocabulary*, Comprehension*, Digit Span**, Letter-Number Sequencing**, and Coding** subtests were significantly lower for children taking divalproex sodium compared to controls. (*p<.05, **p<.01, ***p<.001)

Levetiracetam	Clinical Group (n = 20)		Control Group (n = 20)		t	p-value
	Mean	SD	Mean	SD		
WISC-IV Index Scores						
Verbal Comprehension Index	94.40	19.82	108.40	17.03	-2.396	<.05
Perceptual Reasoning Index	94.15	19.14	106.10	17.09	-2.083	<.05
Working Memory Index	88.70	16.63	108.35	17.80	-3.608	<.01
Processing Speed Index	88.85	16.66	102.10	13.72	-2.746	<.01

Comprehension**, Block Design*, Digit Span**, Letter-Number Sequencing**, Coding*, and Symbol Search* subtests were significantly lower for children taking levetiracetam compared to controls. (*p<.05, **p<.01, ***p<.001)

Lamotrigine	Clinical Group (n = 19)		Control Group (n = 19)		t	p-value
	Mean	SD	Mean	SD		
WISC-IV Index Scores						
Processing Speed Index	85.37	20.05	98.16	13.43	-2.310	<.05

The Symbol Search subtest was significantly lower for children taking lamotrigine compared to controls (p<.05).

Oxcarbazepine	Clinical Group (n = 25)		Control Group (n = 25)		t	p-value
	Mean	SD	Mean	SD		
WISC-IV Index Scores						
Working Memory Index	93.12	13.93	104.84	18.06	-2.569	<.05
Processing Speed Index	86.44	12.66	99.08	14.02	-3.346	<.01

Letter-Number Sequencing*, Coding***, and Symbol Search* subtests were significantly lower for children taking oxcarbazepine compared to controls. (*p<.05, **p<.01, ***p<.001)

H2. A one-way ANOVA indicated that WMI scores for children taking divalproex sodium (mean = 78.00; SD = 18.16) were significantly worse than those taking oxcarbazepine (mean = 93.12; SD = 13.93) [F (3, 76) = 3.354, p<.05]. This reflected significantly lower Letter-Number Sequencing subtest scores (p<.05).

DISCUSSION

These findings indicate that children on monotherapy AED treatment (regardless of medication type) obtain lower scores on certain WISC-IV indices, particularly the WMI and PSI, when compared to controls. In addition, children taking divalproex sodium obtain significantly lower WMI scores than children taking oxcarbazepine. This latter finding is consistent with research demonstrating that older AEDs tend to be associated with greater cognitive side effects than newer AEDs. While WMI and PSI scores were generally within the low average to average range for children taking levetiracetam, lamotrigine, and oxcarbazepine, they were within the borderline range for children taking divalproex sodium.

It is important to note that multiple factors, including underlying brain pathology, psychosocial issues, and seizure variables (e.g., age of onset, seizure type, seizure frequency), may impact cognition; however, given the increasing number of available medications, a greater understanding of the side effect profile for specific medications will help clinicians minimize the possible side effects caused by medications that negatively impact learning. While there is a definite need for prospective, well-controlled studies examining the effects of AEDs on children's performance across measures of IQ and other cognitive tests, the above analyses investigating four commonly prescribed AEDs on WISC-IV performance supports the need to evaluate cognitive skills prior to initiating, adding to, or changing an AED regimen. This would allow clinicians to monitor and track cognitive side effects and determine whether adjustments in medication or academic accommodations are needed.

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