Effects of breastfeeding in children of women taking antiepileptic drugs

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ABSTRACT

Background: Breastfeeding is known to have beneficial effects, but there is concern that breastfeeding during antiepileptic drug (AED) therapy may be harmful to cognitive development. Animal and human studies have demonstrated that some AEDs can adversely affect the immature brain. However, no investigation has examined effects of breastfeeding during AED therapy on subsequent cognitive abilities in children.

Methods: The Neurodevelopmental Effects of Antiepileptic Drugs Study is an ongoing prospective multicenter observational investigation of long-term effects of in utero AED exposure on cognition. Between 1999 and 2004, we enrolled pregnant women with epilepsy who were taking a single AED (carbamazepine, lamotrigine, phenytoin, or valproate). We recently reported on differential AED effects on age 3 year cognitive outcomes. In this report, we focus on the effects of breastfeeding during AED therapy on age 3 cognitive outcomes in 199 children.

Results: A total of 42% of children were breastfed. IQs for breastfed children did not differ from nonbreastfed children for all AEDs combined and for each of the 4 individual AED groups. Mean adjusted IQ scores (95% confidence intervals) across all AEDs were breastfed = 99 (96–103) and nonbreastfed = 98 (95–101). Power was 95% to detect a half SD IQ effect in the combined AED analysis, but was inadequate within groups.

Conclusions: This preliminary analysis fails to demonstrate deleterious effects of breastfeeding during AED therapy on cognitive outcomes in children previously exposed in utero. However, caution is advised due to study limitations. Additional research is needed to confirm this observation and extend investigations to other AEDs and polytherapy. ***Neurology*® 2010;75:1954–1960**

GLOSSARY

AED = antiepileptic drug; **NART** = National Adult Reading Test; **NEAD** = Neurodevelopmental Effects of Antiepileptic Drugs; **TONI** = Test of Nonverbal Intelligence; **WASI** = Wechsler Abbreviated Scale of Intelligence.

Breastfeeding is known to be beneficial for the infant and mother.[1] Breastfeeding is associated with reduced risk of severe lower respiratory tract infections, atopic dermatitis, asthma, acute otitis media, nonspecific gastroenteritis, obesity, type 1 and 2 diabetes, childhood leukemia, sudden infant death syndrome, and necrotizing enterocolitis. Several studies have suggested that breastfeeding may have positive effects on subsequent cognitive development, but this remains controversial.[1] In mothers, breastfeeding is associated with a reduced risk for type 2 diabetes, breast cancer, ovarian cancer, and maternal postpartum depression.

Animal studies have demonstrated that some AEDs can produce widespread neuronal apoptosis in the neonatal brain, which is dose-dependent, occurs at therapeutically relevant blood levels, and requires only brief exposure.[2-8] The effect may be due to reduced expression of neurotrophins and levels of protein kinases that promote neuronal growth and survival. Thus,

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AEDs might produce similar adverse effects in children exposed in utero or in the neonatal period. In fact, some AEDs have been associated with reduced cognitive abilities in children exposed in utero.[9-11] Thus, concern exists that breastfeeding during AED therapy might be harmful to the child. However, no investigation has examined the effects of breastfeeding during AED therapy on subsequent cognitive abilities in children. Since neonatal exposure to AEDs via breast milk is voluntary, data are needed for mothers to make informed decisions. Here, we examine the effects of breastfeeding during AED therapy in an ongoing prospective investigation of neurodevelopmental effects of AEDs on cognitive outcomes in children of mothers with epilepsy.

METHODS

Design. The Neurodevelopmental Effects of Antiepileptic Drugs (NEAD) study is a prospective observational study examining possible behavioral teratogenesis of AEDs. We enrolled pregnant women with epilepsy, who were on 1 of the 4 AED monotherapies (i.e., carbamazepine, lamotrigine, phenytoin, or valproate) from October 1999 through February 2004, across 25 epilepsy centers in the United States and United Kingdom. We recently reported on preliminary findings of cognitive outcomes in the children at 3 years of age.[11] Here we test the hypothesis that breastfeeding during AED therapy is detrimental to the child's cognitive development.

Standard protocol approvals and patient consents. Institutional review boards at each center approved the study, and written informed consent was obtained prior to enrollment.

Participants. Pregnant women with epilepsy on carbamazepine, lamotrigine, phenytoin, or valproate monotherapy were enrolled. These 4 AED monotherapies were the most frequently employed during the enrollment time period. Other AEDs were not included because of insufficient numbers. Polytherapy was not included because of its association with poorer outcomes.[12] A nonexposed control group was not included at the direction of an NIH review panel. Mothers with IQ below 70 were excluded to avoid floor effects and because maternal IQ is the major predictor of child IQ in population studies.[13] Other exclusion criteria included positive syphilis or HIV serology, progressive cerebral disease, other major disease (e.g., diabetes), exposure to teratogenic agents other than AEDs, poor AED compliance, drug abuse in the prior year, or drug abuse sequelae.

Procedures. Information was collected on potentially confounding variables, including maternal IQ, age, education, employment, race, seizure/epilepsy types and frequency, AED dosages, compliance, socioeconomic status,[14] UK/US site, preconception folate use, use of alcohol, tobacco, or other drugs during pregnancy, unwanted pregnancy, abnormalities/complications in the present pregnancy or prior pregnancies, enrollment and birth gestational age, birthweight, breastfeeding, and childhood medical diseases. Children were classified as breastfed if they were currently breastfeeding at the time of the 3-month follow-up phone call after delivery. Cognitive outcomes were evaluated by assessors (blinded to AED) using the Differential Ability Scales[15] (conducted at 36–45 months/old); standardized scores were calculated. Separate investigations with very similar designs in the United States and United Kingdom were merged after initiation. Maternal IQs were determined by different measures due to the later merger; these measures included the Test of Nonverbal Intelligence (TONI)[16] in 267 mothers, Wechsler Abbreviated Scale of Intelligence (WASI)[17] in 18, and National Adult Reading Test (NART)[18] in 18. Training and monitoring of neuropsychological evaluations were conducted to assure quality and consistency. Face-to-face training on all neuropsychological test batteries was performed annually. Each assessor was required to identify errors in a videotaped test session and provide appropriate correction for errors in administration and scoring. In addition, assessors submitted their own videotape and record forms using each test instrument to the Neuropsychology Core Director for review, feedback, and approval. If assessors failed, they submitted additional video assessment for approval prior to testing children in the study.

Statistical analysis. The primary analysis in this substudy included 199 children, for whom there were both cognitive assessment at age 3 and data on breastfeeding. Two children with complete data were excluded from this sample because their mothers either switched AED or stopped using AEDs while breastfeeding. In the primary analysis, the breastfed and nonbreastfed groups were compared across all AEDs with respect to child cognitive outcomes at age 3. Secondary analyses examined the following: 1) effects of breastfeeding within each AED group; 2) sensitivity of results to baseline differences in covariates; and 3) sensitivity of results to missing data. Analyses were performed at the NEAD Data and Statistical Center using SAS 9.2.

Linear regression models were used to examine breastfed/nonbreastfed group differences in IQ adjusting for AED group, maternal IQ, standardized AED dose, maternal and gestational age at delivery, and preconception folate. These covariates were found to be significantly related to the age 3 outcomes in our prior analysis.[11] A nonparametric Kruskal-Wallis test was used to compare duration of breastfeeding across AED groups.

Since the women were not randomized to AED in this observational study, baseline differences between AED groups might obscure a negative effect of an AED taken during breastfeeding. Propensity scores methods are well-accepted tools to examine this possibility. Thus, subgroup analyses were conducted in which subgroups were defined by propensity scores.[19,20] Propensity scores are predicted probabilities of receiving a treatment (or in this case, being breastfed) based on baseline covariates. Covariates are approximately equally distributed within subgroups defined by propensity scores. Propensity scores were estimated using predicted probabilities from a logistic regression model with breastfeeding status (yes/no) as outcome. Variables related to breastfeeding were predictors in the propensity score model along with variables significantly related to age 3 IQ.[21] The predictors in the propensity score model included AED group, maternal IQ, maternal and gestational age, preconception folate, tobacco use during pregnancy, education, socioeconomic status, employment status, unwanted pregnancy, race, and convulsions during pregnancy (yes/no). Given the resulting distributions of estimated propensity scores in the 2 groups (breastfed and nonbreastfed), subjects were partitioned into 2 subgroups depending on whether their estimated propensity score was above or below the median estimated propensity score. Within each of the 2 resulting subgroups, covariates were balanced between the breastfed and nonbreastfed groups ($p > 0.05$, t test for continu-

Table 1 Baseline characteristics of 194 mothers according to breastfed category for the 199 children

	Breastfed	Nonbreastfed	Statistical difference[a]
Mothers, n (%)[b]	82 (42)	112 (58)	0.03
Maternal IQ, mean (95% confidence interval)	104 (100–108)	95 (92–98)	0.0001
Maternal age, mean (95% confidence interval)[c]	31 (30–32)	30 (28–31)	0.02
Standardized dose, mean (95% confidence interval)[d]	37 (33–41)	38 (34–42)	0.72
Gestational age, wk, mean (95% confidence interval)[c]	39 (38–39)	39 (38–39)	0.48
Folate, n (%)[e]	56 (68)	59 (53)	0.03
UK site, n (%)	15 (18)	32 (29)	0.10
Epilepsy types, n (%)[f]			
Localization related	49 (60)	72 (64)	0.52
Idiopathic generalized	23 (28)	33 (29)	0.83
Generalized tonic-clonic seizures[g]	10 (12)	7 (6)	0.15
Convulsions, n (%)[h]			
None	63 (84)	77 (75)	0.17
>5 Convulsions	2 (3)	4 (4)	0.65

[a] Chi-square test of equal proportions for categorical variables; *t* test for continuous variables.
[b] Maternal racial/ethnic distributions were 79% white, 11% Hispanic, 5% black, and 5% other.
[c] Age at delivery.
[d] Average dose for pregnancy. See Methods for description of how dosages were standardized.
[e] Preconception folate use.
[f] Three epilepsy types: localization related, idiopathic generalized, and generalized tonic-clonic unknown if partial or generalized. Maternal seizure types included 62% localization-related epilepsy (simple partial, complex partial, or secondary generalized tonic-clonic), 29% generalized epilepsy (absence, myoclonic, tonic-clonic, or tonic seizures with initial bilateral cerebral involvement as indicated by EEG or clinical syndrome), and 9% generalized tonic-clonic (uncertain if partial or generalized). The localization-related epilepsies were 42% symptomatic and 58% cryptogenic. All generalized epilepsies were idiopathic (4% juvenile myoclonic, 5% absence, 21% positive family history but without an identified specific genetic abnormality, and 70% not otherwise classified).
[g] Uncertain if localization related or generalized.
[h] Convulsions = n (%) of mothers without convulsions or >5 during pregnancy; seizure frequency during pregnancy not available for 17 mothers.

ous variables or χ^2 test for categorical variables), permitting us to compare mean IQ outcomes between the breastfed group and the nonbreastfed group.

To investigate sensitivity of primary results to missing data (missing age 3 outcome or missing breastfeeding data), analyses were also conducted using the intent-to-treat sample (n = 309 live births including 6 twin pairs). To account for missing data, a third breastfeeding category was created for "breastfeeding data missing" to compare to the breastfed and nonbreastfed groups. Data were available for breastfeeding in 249 (81%). Age 3 outcomes were missing in 77 (25%). Two were excluded from the analysis because the mother stopped AED or switched AED while breastfeeding, resulting in an analysis sample size of n = 307. Monotone data Markov Chain Monte Carlo methods were used in secondary analyses to impute missing age 3 outcomes.[22-24] Missing age 3 outcomes were imputed from available age 2 outcomes (n = 26 of 77) and from baseline variables related to outcome or likelihood of missing outcome data (n = 51 of 77). Baseline variables in the imputation model included AED, dose, maternal IQ and age, gestational age at delivery, preconception folate, socioeconomic status, and US/UK site. Least squares mean IQs were estimated for the breastfed and nonbreastfed groups adjusting for maternal IQ, AED group, maternal age, dose, gestational age, and folate. Standard errors and confidence intervals of all estimates incorporated imputation uncertainty.

RESULTS The primary analysis included 194 mothers and 199 children (5 sets of twins). Baseline characteristics of the breastfed and nonbreastfed groups and differences between groups are depicted in table 1. The statistical results for the primary analysis of all AEDs combined are presented in table 2. No effect of breastfeeding was seen on IQ outcomes at age 3. Follow-up analyses for each AED group individually also found no effect of breastfeeding on IQ. Table 3 summarizes the sample sizes, adjusted mean IQs, 95% confidence intervals, and statistical comparisons for all AEDs combined and for each AED group. Overall, 42% of children were breastfed; median time breastfeeding across all AEDs was 6 months (range 3–24 months). The percent breastfed for each AED group were as follows: CBZ = 44%, LTG = 46%, PHT = 42%, and VPA = 32%, which did not differ statistically across AEDs (p = 0.61). AED groups also did not differ in breastfeeding duration (p = 0.70). Mean adjusted IQ scores (95% confidence intervals) across all AEDs were as follows: breastfed = 99 (96:103) and nonbreastfed = 98 (95:101). Power was 95% to detect a half SD IQ effect in the combined AED analysis, but was inadequate within groups. Note that the mean IQ scores in table 3 differ from those presented in our prior publication[11] because the primary analyses differed. The present IQ results are divided by breastfed/nonbreastfed and are based on a subset of 199 children for whom there were both cognitive assessment at age 3 and data on breastfeeding. The prior publication presented IQs based on an intent-to-treat analysis of the full 307 live births. Nevertheless, the differential pattern across AEDs is the same with the lowest IQs associated with in utero valproate exposure.

The propensity score analysis suggests that the results are not due to differences in baseline variables related to either the child IQ outcome or breastfeeding status (table 4). The analysis examining sensitivity of results to missing data demonstrates that the results cannot be explained by incomplete data. A summary of missing data for age 3 IQ and for breastfeeding for each AED group is given in table e-1 (on the *Neurology*® Web site at www.neurology.org). In the intent-to-treat sample, which included 307 of the originally enrolled children, missing outcomes were imputed and a third breastfeeding category was created for missing breastfeeding data. The adjusted mean IQs (95% confidence intervals) are as follows:

Table 2 Statistical results for effects of breastfeeding and other factors on age 3 child IQ based on regression models for the age 3 completer population with data on breastfeeding (n = 199)

	F value	Degrees of freedom	Coefficient[a] for variable in model	*p* Value for variable in model
Breastfed	0.48	1	1.63	0.49
Maternal IQ	15.47	1	0.28	0.0001
Maternal age	6.15	1	0.56	0.01
Antiepileptic drug group	2.91	3	(4 categories: *p* value only)	0.04
Antiepileptic drug dose	3.93	1	−0.12	0.05
Gestational age	8.11	1	1.38	0.005
Folate	6.82	1	6.57	0.01

[a] Coefficients represent the incremental effect on the IQ outcome of a one unit increase in the covariate, at fixed values of all other covariates in the model.

breastfed = 100 (96–103); nonbreastfed = 97 (94–100); missing breastfeeding data = 97 (92–102).

DISCUSSION The present study did not demonstrate any deleterious effects of breastfeeding during AED therapy on cognitive outcomes in children who were previously exposed to AEDs during their mother's pregnancy. Similar to our prior report,[11] IQ at age 3 years in children of women with epilepsy is related to maternal IQ, maternal age, gestational age, preconception folate use, and type of AED exposure. Fetal valproate exposure was associated with lower IQ in a dose-dependent manner, consistent with other studies that indicate a special teratogenic risk for valproate.[12] Children exposed in utero to valproate are at risk for both congenital malformations and cognitive impairment.[9-12,25,26] The recent American Academy of Neurology guidelines recommend that if possible, valproate should be avoided during the first trimester of pregnancy to decrease the risk of major congenital malformations and avoided throughout pregnancy to prevent reduced cognitive outcomes.[12]

Table 3 Adjusted mean age 3 IQ by antiepileptic drug (AED) group

AED group	Breastfed	No.	Age 3 IQ[a]	95% Confidence intervals[b]
All AEDs	Yes	84	99	96-103
	No	115	98	95-101
Carbamazepine	Yes	26	103	97-108
	No	32	98	93-103
Lamotrigine	Yes	30	104	97-110
	No	36	104	98-110
Phenytoin	Yes	17	91	84-98
	No	23	99	93-105
Valproate	Yes	11	93	82-105
	No	24	90	83-98

[a] Mean age 3 years IQs adjusted for maternal IQ, maternal age, dose, gestational age, and folate. Means were also adjusted for AED group in the "all AEDs" category.
[b] None of the breastfed vs nonbreastfed comparisons was significant.

Strengths of our study include its prospective design, blinded cognitive assessments using standardized measures, and detailed monitoring of multiple potential confounding factors. However, caution is advised due to study limitations, which include a relatively small sample size, loss of enrolled subjects to analysis, lack of randomization, lack of an unexposed control group during pregnancy, lack of details to fully quantitate the amount of breastfeeding, absence of AED concentrations in breast milk or in children's serum, and relatively young age of the children at this planned interim analysis. In addition, the present study does not address any potential deleterious effects of AED exposure through breast milk in the newborn not previously exposed in utero.

Because the NEAD study is not a randomized trial, it is possible that an adverse effect of breastfeeding during AED therapy might be obscured by confounding factors related to baseline characteristics, which might affect the child's IQ. For example, maternal IQ was higher in the breastfeeding group, and preconception folate use was also higher in the breastfeeding group. Further, a larger portion of patients on valproate had generalized epilepsy. However, no adverse effects of breastfeeding were found in analyses adjusting for these and other baseline characteristics, including the propensity score subgroup analyses.

Rather than epilepsy or seizures, most AED prescriptions are written for pain or psychiatric indications. Our study did not include women who were prescribed AEDs for these other indications, but there is concern that their children are at the same risk, since one study found that incidence of malformations in these children is similar to that of children of women taking AEDs for epilepsy.[27]

Why would adverse cognitive outcomes be associated with in utero exposure for some AEDs (e.g., valproate), but not for exposure to breastfeeding? Susceptibility to AED exposure may be greater for the fetal than neonatal brain, but animal studies would suggest that this is not the case. The adverse effects on the immature brain seen with some AEDs are dose dependent. The blood levels achieved in the child during breastfeeding are likely to be substantially lower than those achieved during pregnancy,[28] and thus, may be inadequate to produce the adverse effects. Alternatively, adverse effects produced from in utero exposure may mask any further smaller effects obtained during breastfeeding. In addition, the proposed benefits of breastfeeding on newborn cognitive development[1] could offset potential deleterious effects of continued AED exposure. Although not significant, fewer mothers on valproate breastfed, but the mean IQ of children of women with epilepsy

Table 4 Means and 95% confidence intervals by breastfeeding status and propensity score subclass[a]

Breastfed	Propensity score subclass	No.	Mean child	95% Confidence interval
Yes	Below median	22	93	86–100
	Above median	62	107	102–112
No	Below median	77	92	89–96
	Above median	38	103	97–109

[a] Subjects in each propensity score subclass are distributed similarly in terms of the baseline variables related to the outcome or to breastfeeding (i.e., AED group, maternal IQ, maternal and gestational age, preconception folate, tobacco use during pregnancy, education, socioeconomic status, employment status, unwanted pregnancy, race, and convulsions during pregnancy [yes/no]). The above median group includes women who were more likely to breastfeed given their baseline covariates, while the below median group includes women who were less likely to breastfeed given their baseline covariates (e.g., the women in the above median group had higher IQ, were slightly older, and were more likely to take preconception folate). The 2 above median subgroups are similar in their baseline characteristics, but differ in their actual breastfed status. Thus, differences in these 2 subgroups should be related to breastfeeding if all relevant covariates were measured. The same applies to comparison of the 2 below median subgroups.

on valproate who breastfed was not less than the mean among those who did not breastfeed while taking valproate (see table 3). Other baseline differences between the breastfed and nonbreastfed groups may have obscured breastfeeding effects, but as noted previously propensity score analyses did not provide evidence for this hypothesis.

Further studies are needed to confirm our preliminary analysis and to extend investigations to other AEDs and to AED polytherapy. In addition, it is critical that research be conducted to understand the underlying mechanisms of adverse AED effects on the immature brain and to define the risks associated with AEDs in the neonate for treatment of seizures where the AED blood levels are higher.

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DISCLOSURE

Dr. Meador serves on the editorial boards of *Neurology®*, *Behavior & Neurology*, *Epilepsy and Behavior*, *Epilepsy Currents*, *Epilepsy.com*, and the *Journal of Clinical Neurophysiology* and on the Professional Advisory Board for the Epilepsy Foundation; received travel support from Sanofi-Aventis; and received research support from GlaxoSmithKline, Eisai Inc., Marinus Pharmaceuticals, Inc., Myriad Genetics, Inc., NeuroPace, Inc., Pfizer, SAM Technology Inc., SCHWARZ PHARMA (UCB), the NIH (NINDS 2RO1-NS38455 Meador [PI], NINDS R01-NSO31966-11A2 [consultant], NINDS N01-NS-5-2364 [consultant], NINDS R01-NSO39466 [coinvestigator], and 1RC1MD004563 [coinvestigator]), and the Epilepsy Foundation. Dr. Baker serves on a scientific advisory board for Sanofi-Aventis; serves on the editorial board of *Epilepsy and Behavior*; has received speaker honoraria from Eisai Inc., UCB, and Janssen; receives research support from UCB, Sanofi-Aventis, Pfizer Inc., Epilepsy Research UK, Medical Research Council, and Epilepsy Action UK; and has served as an expert witness in litigation related to neurodevelopment effects of antiepileptic drugs. Dr. Browning receives research support from the NIH (NINDS R01 NS050659 [Statistician, Data Center PI]) and holds stock in Human Genome Sciences, Inc. Dr. Clayton-Smith is journal editor for *Clinical Dysmorphology* and has served as an expert witness in litigation related to neurodevelopment effects of antiepileptic drugs. Dr. Combs-Cantrell has received speaker honoraria from GlaxoSmithKline. Dr. Cohen serves on the editorial board of *Developmental Neuropsychology* and receives royalties from the publication of *Children's Memory Scale* (The Psychological Corp., 1997). Dr. Kalayjian has received speaker honoraria from GlaxoSmithKline and Ortho-McNeil-Janssen Pharmaceuticals, Inc. and receives research support from Marinus Pharmaceuticals, Inc. Dr. Kanner has served on scientific advisory boards for GlaxoSmithKline, Ortho-McNeil-Janssen Pharmaceuticals, Inc., UCB, Valeant Pharmaceuticals International, and Pfizer Inc.; has received speaker honoraria from GlaxoSmithKline, Ortho-McNeil-Janssen Pharmaceuticals, Inc., UCB, and Pfizer Inc.; serves on the editorial boards of *Epilepsy & Behavior*, *Epilepsia*, and *CNS Spectrums*; receives royalties from the publication of *Psychiatric Issues in Epilepsy, Second Edition: A Practical Guide to Diagnosis and Treatment* (Lippincott Williams & Wilkins, 2006) and *Controversial Issues in Psychiatric Aspects of Epilepsy* (Elsevier, 2008); has served on speakers' bureaus for GlaxoSmithKline, UCB, and Pfizer Inc.; and receives research support from GlaxoSmithKline and Novartis. Dr. Liporace receives royalties from the publication of *Crash Course Neurology* (Elsevier, 2006) and has served on speakers' bureaus for and received speaker honoraria from UCB and GlaxoSmithKline. Dr. Pennell has served on a scientific advisory board for and received funding for travel from UCB and the Epifellows Foundation; serves as a contributing editor for *Epilepsy Currents* and on the editorial board of *Epilepsia*; and has received research support from UCB, GlaxoSmithKline, Marinus Pharmaceuticals, Inc., the NIH (1P50 MH68036-01 [Project 1 PI], NINDS RO3 NS063233 [PI], NINDS RO1 NS 39466 [Site PI], and NINDS RO1NS38455 [PI, Codirector of Administrative Core]), the Centers for Disease Control and Prevention, and the Emory University Research Council. Dr. Privitera has served on scientific advisory boards or as a consult for Ortho-McNeil-Janssen Pharmaceuticals, Inc., UCB, Johnson & Johnson, and the Epifellows Foundation; has received funding for travel and speaker honoraria from Ortho-McNeil-Janssen Pharmaceuticals, Inc., Pfizer Inc., GlaxoSmithKline, Janssen, and UCB; has served on speakers' bureaus for UCB, Pfizer Inc., GlaxoSmithKline, and Ortho-McNeil-Janssen Pharmaceuticals, Inc.; and has received research support from UCB, Ortho-McNeil-Janssen Pharmaceuticals, Inc., the NIH (K01-DA020485 [co-I], K23 NS052468 [co-Mentor], 1K23NS02170-01 [co-I], 2R01-NS38455 [site PI]), the American Epilepsy Society, and the Shor Foundation for Epilepsy Research. Dr. Loring serves on scientific advisory boards for the Epilepsy Foundation and Sanofi-Aventis; serves as a consulting editor for the *Journal of Clinical and Experimental Neuropsychology*, as contributing editor for *Epilepsy Currents*, and on the editorial board of *Neuropsychology Review*; serves as a consultant for NeuroPace, Inc., Sanofi-Aventis, and UCB; receives royalties from the publication of *Neuropsychological Assessment, 4th ed.* (Oxford University Press, 2004) and *INS Dictionary of Neuropsychology* (Oxford University Press, 1999); estimates that 50% of his clinical effort involves neuropsychological testing; and receives research support from NeuroPace, Inc., SAM Technology Inc., Myriad Pharmaceuticals, Inc., Novartis, the NIH (NINDS R01038455 [co-I] and NINDS R01NS031966 [consultant)], and the Epilepsy Foundation.

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