Cognitive Performance Scores for the Pediatric Automated Neuropsychological Assessment Metrics in Childhood-Onset Systemic Lupus Erythematosus

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Background: Patients with childhood-onset SLE (cSLE) may experience neuropsychiatric SLE (NPSLE) manifested as neurocognitive dysfunction (NCD). Formal neurocognitive testing (FNCT) is the most accepted method for diagnosing NCD. However, access is limited and it is costly and time-consuming. The Pediatric Automated Neuropsychological Assessment Metrics (PedANAM) is a computerized test battery that assesses multiple domains of cognitive performance. However, it is unclear how PedANAM-generated variables can be interpreted in a clinical setting as measures of NCD.

Our purpose was to explore and initially test approaches to the calculation of a summary score (PedANAM Cognitive Performance Score (PedANAM-CPS)) to screen NCD in cSLE with high sensitivity.

Methods: Two cohorts were analyzed. The development cohort included cSLE patients (pts) and controls that completed the PedANAM and FNCT at two research study visits 18 months apart. The validation cohort consisted of cSLE pts and controls recruited in a clinical setting who completed the PedANAM and Pediatric Perceived Cognitive Function-43 questionnaire (PCF-43). Candidate PedANAM-CPSs were generated based upon the development cohort's first visit using 3 statistical methods: 1) *Simple-summary score:* Mean accuracy score of all PedANAM's subtests; 2) *Logit-based score* developed by logistic regression modeling; 3) *PCA-based score* derived from Principal Component Analysis (PCA) . The latter 2 methods assigned in a different way a statistical weight to each subtest accuracy score. Receiver operating characteristic curve analysis was used to assess the accuracy of candidate scores as predictors of NCD in the study cohorts.

Results: A total of 166 pts were studied, including 108 cSLE pts (Table 1). As shown in Table 2 the candidate PedANAM-CPSs significantly differentiated between NCD and non-NCD groups. The Logit-based and PCA-based scores performed well and were able to detect NCD on the second visit of the development and validation cohorts. The usefulness of the 3 PedANAM-CPS scores and their cut-off scores to define NCD was confirmed when using visit 2 data of the development cohort and the validation cohort.

Conclusion: Candidate PedANAM-CPS showed good construct and criterion validity, with a Logit-based score performing somewhat better for discriminating cSLE pts based on the presence or absence of NCD. The PedANAM-CPS may be a useful tool to summarize cognitive performance in assessing for NCD in cSLE. Confirmation studies are required to confirm its overall accuracy and clinical usefulness in cSLE.

Table 1. Demographics of Development and Validation Dataset at Enrollment *

Variable	Category	Development Dataset			Validation Dataset		
		cSLE (n=40)	Controls (n=40)	p-value	cSLE (n=68)	Controls (n=18)	p-value
Age (years)		14.8 ± 2.3	13.9 ± 3.2	0.03	15.3 ± 3.3	14.0 ± 2.5	0.131
Age (years) in median (range)		14 (9, 17)	14 (9, 17)	0.767	15 (10, 20)	14 (11,18)	0.239
Female		85	85	1.0	91.2	72.2	0.032
Ethnicity							
	White	30	32.5	0.98	30.9	94.4	<0.001
	Black	45	47.5		30.9	5.6	
	Hispanic	17.5	15		11.8	0	
	Asian and other	7.5	5		26.5	0	
On Prednisone therapy		77.5			76.5		
Prednisone dose (mg/day)		19.8 ± 17.4			17.1 ± 16.1		
Disease activity(mean ± SD)‡		4.9 ± 4.4			4.3 ± 4.7		
PCF-43† T-score (mean ± SD)					60.5 ± 7.9	63.2 ± 5.8	0.167
Neurocognitive dysfunction¥		22.5	7.5		8.8	11.1	0.766

*Except where indicated otherwise, values are percentages; cSLE = childhood-onset systemic lupus erythematosus

‡ Systemic Lupus Disease Activity Index 2k version, SLEDAI; range 0 – 104; 0 = inactive SLE

† PCF-43 questionnaire: Perceived Cognition Functioning -43 questionnaire.

¥ Neurocognitive dysfunction categories are defined based on z-scores of the standardized tests completed for the formal neuropsychological testing (FNCT) on the research cohort, and on T-scores of the pediatric perceived cognitive function questionnaire-43 (PedsPCF-43) on the clinical cohort. FNCT measures following cognitive domains: working memory, psychomotor speed, attention and executive functioning, visuoconstructional ability.

Table 2. PedANAM-CPS performance to identify neurocognitive deficit^ in the development cohort, visit 1

Candidate PedANAM- CPS	Non-NCD (N=68)*	NCD (N=12)*	p-value†	AUC ¥	Sensitivity	Specificity
Simple Summary Score	0.08 ± 0.07	-0.39 ± 0.18	0.036	0.60	83.3 %	37.3%
PCA-based Score	0.09 ± 0.08	-0.42 ± 0.19	0.027	0.60	83.3 %	41.8 %
Logit-based Score	-2.26 ± 0.16	-0.60 ± 0.37	0.001	0.77	91.7 %	31.3 %

PedANAM-CPS = Pediatric Automated Neuropsychological Assessment Metrics – Cognitive Performance Score. ^ Neurocognitive deficit as measured by formal neuropsychological assessment; NCD = neurocognitive deficit; AUC = area under the curve; PCA = Principal Component Analysis; Logit = logistic regression model

* Values are mean ± SD

† *P* values are adjusted for age

¥ Interpretation of AUC values: 1.0–0.91: outstanding, 0.81–0.90: excellent, 0.71–0.8: good, 0.61–0.7: fair, and <0.6: poor