

# Executive Function in Children with Mild to Moderate CKD

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## Introduction

Neurocognitive dysfunction, with selective defects in executive function (EF), complicates advanced CKD and ESRD. In children, performance improves with renal transplantation. It is unknown whether EF is also impaired by moderate CKD; this would impact educational interventions during rapid neurocognitive development in childhood.

## Methods

Tests of EF were incorporated into the prospective, observational NIH-sponsored CKiD cohort study of children with mild to moderate CKD. Tasks included: Conner's Continuous Performance Test (CPT), a computer-based test of sustained visual attention, vigilance and inhibitory control/impulsivity; Delis-Kaplan Executive Function System Tower Subtest (D-KEFS Tower) Total Achievement Score, used to measure planning and reasoning (normalized for  $\geq 8$  yrs); Wechsler Intelligence Scale for Children Fourth Edition (WISC-IV) and Wechsler Adult Intelligence Scale Fourth Edition (WAIS IV) Reverse Digit Span Subtest, in which a sequence of verbally-presented numbers is repeated in reverse order to assess working memory.

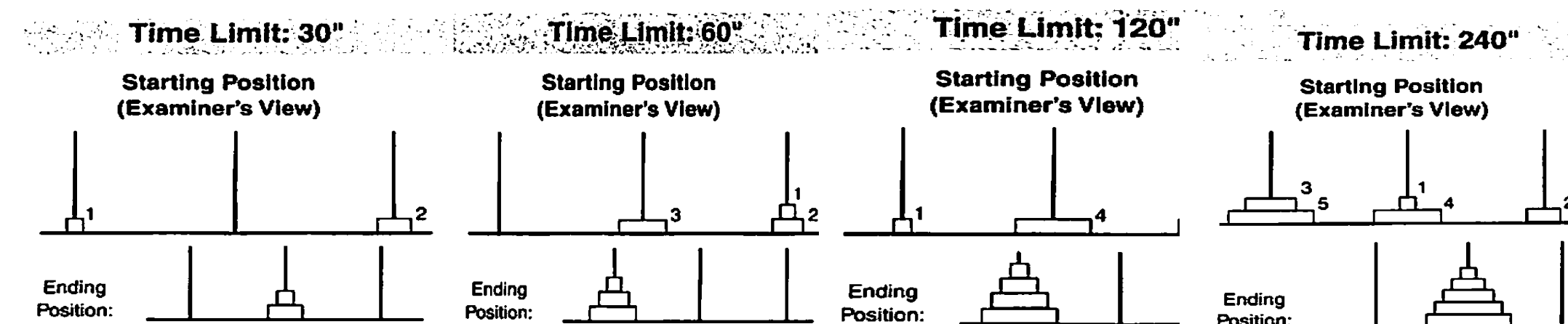
All outcomes were normalized scores; linear regression was used to assess effects of covariates listed in Table 1. Simultaneous estimated GFR (by validated CKiD formula) was used in initial analysis since measured GFR by iohexol disappearance preceded EF testing by 6-12 mos (results later confirmed with iGFR). EF outcomes were dichotomized at 1 SD from the mean in the direction of poorer performance ( $\leq 7$  vs.  $> 7$  for D-KEFS and WISC/WAIS scaled scores;  $\geq 60$  vs.  $< 60$  for CPT scaled scores) and logistic regression used to assess predictors of poor performance.

## Results

Table 1, N=340

Characteristic	% (n) or Median [IQR]	Characteristic	% (n) or Median [IQR]
Age, yrs	13 [10, 17]	Glomerular Dis	18 (62)
Duration CKD	10 [6, 13]	Urine Pro:Cr $\geq 2$	12 (38)
Male	61 (206)	Elevated BP	26 (78)
African-American	17 (57)	Preterm Birth	12 (37)
Maternal Ed $\leq$ HS	41 (136)	eGFR: $< 30$	22 (76)
Some college	28 (91)	30 to $< 40$	22 (75)
College or more	31 (103)	40 to $< 50$	25 (85)
		$\geq 50$	30 (103)

### D-KEFS, selected tasks



### Delis-Kaplan Tower Test

Planning and problem solving by DKEFS was not affected by disease-related variables. While, **22%** of the study group performed  $> 1$  SD below the mean on this task, only preterm birth approached significance as predictor of poor performance.

Table 2 Logistic regression for poor performance on DKEFS

Predictor	Odds Ratio	p-value
Duration CKD	0.983	0.69
A-A	2.487	0.06
Maternal Educ		
Some college	0.504	0.14
College or more	0.721	0.42
eGFR (per 10)	1.244	0.10
Glomerular Dis	0.600	0.29
Elevated BP	0.770	0.58
Urine Pro:Cr $\geq 2$	1.416	0.55
Preterm Birth	2.760	0.05



Connor's CPT

Inhibitory control (**Errors of Commission**) was not affected by disease-related variables. A-A subjects performed better. **28%** of subjects scored  $> 1$  SD above the mean (worse inhibitory control); subjects with longer duration of CKD may be more likely to perform poorly.

Table 3a. Linear regression of performance on CPT Errors of Commission

Covariate	Estimate	Std. Err.	p-value
Duration CKD	0.26	0.18	0.16
A-A	-4.48	2.31	0.05
Maternal Educ			
Some college	-1.21	1.86	0.52
College or more	-3.20	1.73	0.06
eGFR (per 10)	0.03	0.54	0.95
Glomerular Dis	-0.40	1.98	0.84
Elevated BP	1.54	1.87	0.41
Urine Pro:Cr $\geq 2$	-0.43	2.45	0.86
Preterm Birth	-0.78	2.49	0.76

Table 3b Logistic regression for poor performance on CPT Errors of Commission

Predictor	Odds Ratio	p-value
Duration CKD	1.074	0.06
A-A	0.580	0.31
Maternal Educ		
Some college	0.667	0.29
College or more	0.538	0.09
eGFR (per 10)	1.101	0.39
Glomerular Dis	0.896	0.79
Elevated BP	1.145	0.73
Urine Pro:Cr $\geq 2$	0.519	0.24
Preterm Birth	0.602	0.38

Sustained vigilance, as assessed by **variability in CPT**, was not affected by disease-related or demographic variables. Performance was  $> 1$  SD below mean in **24%** of the study group.

Table 4a. Linear regression of performance on reverse digit span

Covariate	Estimate	Std. Err.	p-value
Duration CKD	0.04	0.05	0.44
A-A	-0.70	0.61	0.25
Maternal Educ			
Some college	-0.08	0.47	0.87
College or more	1.57	0.46	0.001
eGFR (per 10)	0.06	0.14	0.68
Glomerular Dis	-0.44	0.53	0.41
Elevated BP	0.58	0.49	0.23
Urine Pro:Cr $\geq 2$	-0.82	0.63	0.19
Preterm Birth	-0.86	0.64	0.18

Table 4b Logistic regression for poor performance on reverse digit span

Predictor	Odds Ratio	p-value
Duration CKD	0.960	0.30
A-A	2.523	0.04
Maternal Educ		
Some college	0.963	0.92
College or more	0.275	0.003
eGFR (per 10)	0.908	0.41
Glomerular Dis	1.113	0.80
Elevated BP	0.412	0.04
Urine Pro:Cr $\geq 2$	2.019	0.16
Preterm Birth	1.901	0.19

### Reverse Digit Span

Highest maternal educational level predicted better performance on reverse digit span, a test of working memory. **28%** of group scored  $> 1$  SD below mean; subjects with elevated casual BP were less likely and A-A subjects were more likely to fall in poor performance group.

## Conclusion

In this baseline study, an unexpectedly high percentage of children with mild-moderate CKD performed poorly on standardized tests of executive function which measure planning and problem solving, inhibitory control and working memory. A direct effect of eGFR (or iohexol GFR) could not be determined in cross-sectional analysis. Longitudinal studies are ongoing.



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