

## Supplemental Information

### STATISTICAL METHOD FOR CALCULATING LOCAL AGE-NORMED MEASURES OF GLOBAL DC AND BEHAVIORAL DISINHIBITION

First, we calculated least-squares means and variances for each MDAT and KABC-II subscale for different age groups using data from the serial assessments of the entire sample of control participants. In the statistical model, we used the subscale's raw score as the dependent variable and age group as the independent variable, with the dependence of scores within the same subject being modeled using a heterogeneous, autoregressive covariance structure, which allowed

for different variances across age groups. Age groups were defined in half-year increments for the MDAT and KABC-II up to age 6 years and annually thereafter for the KABC-II. ISCI age groups were defined annually from the age of 2 years. For each subscale, the total number of patients in the control group, the mean number of assessments per patient in the control group, and the mean number of assessments per age group were as follows: MDAT 82, 3.5, and 32; KABC-II 75, 3.3, and 35; and ISCI 105, 2.4, and 44. There were <7 control participants per group in the groups aged <1 or >9 years, so norm-based analyses were

limited to children 1 to 9 years old.

Next, each participant's raw score on each subscale and at each time point was converted to a z score by using the age-appropriate mean and SD, as derived from the process described above. To calculate the global DC score, z scores for the subscales of the DC measure (4 for MDAT and 3 for KABC) were summed and divided by the estimated SD of the sum, for which we incorporated information from the pairwise correlations among the subscales at each time point.<sup>26</sup> This method is used to place the global DC on a scale with a mean of ~0 and an SD of ~1.

**SUPPLEMENTAL TABLE 2** Comparison of Demographic and Clinical Characteristics Between Patients Who Were Included in the Primary Analyses and Those Who Were Excluded and Between Case Patients and Patients in the Control Group in the Primary Analyses

	Included in Analysis of 12-Month Outcomes					
	Lost to Follow-up or Excluded, <i>n</i> = 36	Total Patients, <i>N</i> = 185	Difference in Mean (95% CI)	Case Patients, <i>n</i> = 85	Control Group, <i>n</i> = 100	OR (95% CI)
Baseline demographics, health history, and anthropometrics						
Control group, %	47.2	54.1	1.3 (0.6 to 2.7)	—	—	—
Age, mo	57.3	48.6	−8.6 (−18.8 to 1.3)	49.6	47.7	−1.9 (−9.3 to 5.4)
Male sex, %	50	51	1.0 (0.5 to 2.1)	47.1	54	1.3 (0.7 to 2.4)
HIV-positive, %	6.3	11.6	0.5 (0.1 to 2.3)	18.8 <sup>a</sup>	5.2 <sup>a</sup>	4.2 (1.5 to 12.1) <sup>a</sup>
Seizures, %	5.6	7.1	0.8 (0.2 to 3.6)	9.5	5	2.0 (0.6 to 6.4)
Malaria episode, %	26.7	21.1	1.4 (0.6 to 3.3)	29.6 <sup>a</sup>	13.8 <sup>a</sup>	2.6 (1.2 to 5.6) <sup>a</sup>
Other serious illness, %	40	40	1.0 (0.5 to 2.2)	46.9	34.0	1.7 (0.9 to 3.1)
Developmental problems, %	8.8	12.9	0.7 (0.2 to 2.3)	13.4	12.4	1.1 (0.5 to 2.6)
Height, cm	110.1	105	5.1 (−13.8 to 3.6)	105.5	104.6	−0.09 (−7.5 to 5.7)
Weight, kg	17.6 <sup>a</sup>	15 <sup>a</sup>	−2.6 (−4.8 to −0.32) <sup>a</sup>	14.6	15.3	0.7 (−0.7 to 2.1)
Mid- to upper-arm circumference, cm	15.5	15.2	−0.3 (−0.9 to 0.4)	15.1	15.3	0.1 (−0.3 to 0.6)
Family resources, %						
Mother with less than standard 5 education	35.3	33	1.1 (0.5 to 2.4)	46.2 <sup>a</sup>	21.5 <sup>a</sup>	3.1 (1.6 to 6.1) <sup>a</sup>
Father with less than standard 5 education	16.7	20.9	0.8 (0.3 to 2.1)	32.4 <sup>a</sup>	11.2 <sup>a</sup>	3.8 (1.7 to 8.6) <sup>a</sup>
One or both parents work as farmers	34.5	32.5	1.1 (0.5 to 2.5)	43.0 <sup>a</sup>	23.3 <sup>a</sup>	5 (1.2 to 4.8) <sup>a</sup>
No electricity	77.8	73	1.3 (0.5 to 3.0)	87.1 <sup>a</sup>	61.0 <sup>a</sup>	4.3 (2.0 to 9.1) <sup>a</sup>
Surface or well water	44.1	41.3	1.1 (0.5 to 2.3)	52.9 <sup>a</sup>	31.3 <sup>a</sup>	2.5 (1.3 to 4.5) <sup>a</sup>
Unfinished floor	71.6	75.5	0.8 (0.4 to 1.8)	82.3 <sup>a</sup>	67.7 <sup>a</sup>	2.2 (1.1 to 4.5) <sup>a</sup>
Natural roof	75	61.5	0.5 (0.2 to 1.1)	52.9 <sup>a</sup>	28.0 <sup>a</sup>	2.9 (1.6 to 5.3) <sup>a</sup>
Pit and/or field latrine	93.9	95	0.8 (0.2 to 3.9)	98.8	91.8	7.4 (0.9 to 60.2)
Outcomes at 1 mo						
Abnormal clinical reading of MRI, %	20.8	27.1	0.7 (0.2 to 2.0)	36.7 <sup>a</sup>	17.8 <sup>a</sup>	2.7 (1.2 to 5.8) <sup>a</sup>
Global DC, z score	−0.39	−0.29	0.1 (−0.3 to 0.5)	−0.68 <sup>a</sup>	0.05 <sup>a</sup>	0.7 (0.4 to 1.0) <sup>a</sup>
BRIEF ISCI, z score	0.19	0.37	0.2 (−0.5 to 0.8)	0.56	0.19	−0.4 (−0.8 to 0.1)
Caregiver has new behavior concerns, %	19.4 <sup>a</sup>	5 <sup>a</sup>	4.6 (1.6 to 13.3) <sup>a</sup>	10.8 <sup>a</sup>	0 <sup>a</sup>	Undefined <sup>a</sup>

—, not applicable.

<sup>a</sup> Difference at *P* < .05.