Randomized controlled trial of caregiver training for HIV-infected child neurodevelopment and caregiver well-being

Judith BASS, PhD[a], **Robert OPOKA, MMed[b]**, **Itziar FAMILIAR, PhD[c]**, **Noeline NAKASUJJA, PhD[b]**, **Alla SIKORSKII, PhD[c]**, **Jorem AWADU, MSRC[c]**, **Deborah GIVON, MS[d]**, **Cilly SHOHET, PhD[d]**, **Sarah M MURRAY, PhD[a]**, **Jura AUGUSTINAVICIUS, MHS[a]**, **Tamar MENDELSON, PhD[a]**, **Michael BOIVIN, PhD[c]**

[a]Johns Hopkins University Bloomberg School of Public Health

[b]Makerere University

[c]Michigan State University

[d]Bar Ilan University

Abstract

Objectives: HIV infection places children at neurodevelopmental risk; for young children in poverty, risk is compounded by compromised caregiving quality. The Mediational Intervention for Sensitizing Caregivers (MISC) program trained caregivers on fostering daily interactions with young children. We hypothesized that MISC could (1) enhance neurodevelopment of rural Ugandan HIV-infected children and (2) improve mental health outcomes of their caregivers, which might mediate improved caregiving quality.

Design: A randomized trial of HIV-infected young children (ages 2–5 years) and their female caregivers; cluster randomization was to MISC or a nutrition curriculum.

Setting: 18 geographic clusters in rural Uganda.

Subjects: Children and caregivers were evaluated at baseline, 6 months, 1 year, and 1-year post-training

Main outcome measures: Mullen Scales of Early Learning, the Color-Object Association Test for memory, the Early Childhood Vigilance Test of attention, and the Behavior Rating Inventory of Executive Function for the children. Caregivers completed measures of depression and anxiety symptoms and daily functioning.

Results: MISC had a significant impact on post intervention receptive language (adjusted mean difference=3.13, 95% CI 0.08, 6.18) that persisted at 1-year follow-up. MISC caregivers reported significantly less functional impairment post-program (adjusted mean difference=−0.15, 95% CI −0.28, −0.01). Other outcomes were not significant.

Conclusions: Both intervention conditions resulted in improvements in the study children over time. MISC showed additional impacts on child language and caregiver well-being. Future directions include assessing the extent enhanced language development resulting from improved caregiving may better prepare impoverished children for school.

Keywords

INTRODUCTION

Exposure to poverty-related cumulative risk in early childhood can negatively affects cognitive developmental trajectories through limited cognitive stimulation and nutrition [1,2]. HIV-infected children are at a particular disadvantage if their care depends on impoverished HIV-infected caregivers, themselves at risk for impaired functioning.

There is increasing evidence that parent-directed interventions can improve child cognitive development [3–5], including in Uganda [6]. Following earlier Ugandan feasibility and efficacy research [7,8], the present trial of caregiver training benefits for HIV-affected families was initiated in Tororo District, with 24% of the population living under the poverty line [9] and 5.8% HIV prevalence [10]. This cluster randomized controlled trial (RCT) evaluated whether a year-long biweekly caregiver training intervention could improve caregiver mental health, quality of caregiving, and child neurodevelopmental outcomes in HIV-infected children.

METHODS

Procedures and Participants

After IRB approval by Michigan State University and Makerere University School of Medicine, 18 sub-counties (unit of randomization) in Tororo and Busia districts were randomly assigned to treatment arms. Staff conducting child assessments (blind to cluster allocation) and the study coordinator (not blind to cluster allocations) enrolled study participants.

Women and child dyads (n=120) were identified over a 12-month period from AIDS support (TASO) clinics. A female caregiver provided written consent for her and her child. Child eligibility was based on confirmed perinatally-acquired HIV infection, being between 2 to 5 years of age, and no history of neurological insult, with a female caregiver able to participate.

Participants in both study arms received a bi-weekly nutritional supplement. The interventions were provided in one-hour sessions with each caregiver alternating bi-weekly between home and the project office at Tororo District Hospital. All intervention providers were Ugandan Makerere University Psychology or Social-Work graduates who received a two-week training in their respective intervention and participated in weekly supervision and a week-long refresher training.

Caregiver Training Interventions

Mediational Intervention for Sensitizing Caregivers (MISC).—MISC is a model for training caregivers to enhance their children's development [11] based on Feuerstein's theory of cognitive modifiability [12,13].

Uganda Community Based Association for Child Welfare program (UCOBAC). —The comparison condition was a manualized nutrition and hygiene information program designed for impoverished households by UCOBAC (http://ucobac.org/).

Measures

Study data were collected at baseline, at 6 months (midway through training), at 1 year (completion of training), and at a 12-month follow-up (24 months after baseline). Measures of caregiver mental health and all child outcomes were previously used in Uganda [7,8].

Demographics: child demographics included age, sex, and current use of highly active anti-retroviral treatment (HAART; yes/no). Caregiver demographics included marital status (married/unmarried), education (any/none), and relationship to study child (mother/other).

Mullen Scales of Early Learning (MSEL) [14] assesses visual reception, gross motor skills, fine motor skills, receptive, and expressive language. A composite score provides a measure of g, the general measure of fluid intelligence thought to underlie general cognitive ability.

Color Object Association Test [15] (COAT) evaluates object placement memory with principal outcomes of immediate memory (assessed by number of recalled items) and overall total recall (assessed by number of correctly placed items).

Early Childhood Vigilance Test (ECVT) [16,17] assesses sustained attention, with the principal outcome the proportion of time looking at an animation video as scored from a computer-mounted webcam video.

Behavior Rating Inventory of Executive Function–Preschool version (BRIEF-P) [18] evaluates behavior, attention and cognitive problems related to disruption of executive

functions as reported in a series of questions to the principal caregiver; a combined Global Executive Composite (GEC) score is generated [18].

Caldwell Home Observation for the Measurement of the Environment (HOME) [19] assesses quality of child-caregiver interactions in the home using 45 yes/no items. More 'yes' answers indicate higher quality interactions.

Observing Mediational Interactions (OMI). Intervention trainers collected 5-minute videos every 6 months of caregivers bathing, feeding and working with their child. Videos were scored by an independent observer using a standard rubric [20,21] to count specific occurrences of focusing, exciting, expanding, encouraging, and regulating interactions. Total number of interactions was used as a mediation indicator of caregiving quality.

Hopkins Symptoms Checklist-25 (HSCL) [22,23] contains subscales for anxiety (10 symptoms) and depression (15 symptoms). Caregivers indicated frequency of each symptom in the last two weeks on a scale of 0 (not at all) to 3 (a lot). Subscale scores were calculated using mean item responses.

Caregiver functioning indicated how much difficulty caregivers had completing 12 tasks of daily living identified during a brief qualitative study, with responses from 0 (no difficulty at all) to 4 (cannot complete it). An impairment scale was calculated using mean item responses.

Analysis

Sample size was calculated based on the magnitude of effects seen in a prior study [7]; with 54 (MISC) and 58 (UCOBAC) children, an unadjusted effect size of 0.53 was detectable with 0.80 power in two-sided tests at p=0.05. Baseline intervention arm comparisons were calculated using t-, chi-square or Fisher's exact tests. Linear mixed effects (LME) models were employed. Correlations arising from repeated measures were accounted for by specifying an autoregressive covariance structure. Inclusion of a random effect for clusters (unit of randomization) was explored, but the resulting intraclass correlation coefficients were virtually zero across outcomes.

Each outcome was analyzed separately using LME with common covariates. Time was entered as a categorical variable with levels corresponding to 6, 12, and 24 months. Time-by-intervention interactions were included to capture potential changes in differences by intervention arm over time. The least squares (adjusted) means for each time point and trial arm were output from the LME models, and differences between them by trial arm were tested to assess immediate and sustained intervention effects.

Variation in caregiver quality assessed via the HOME and OMI was explored post-hoc as a potential mediator of intervention effect on child outcomes. Caregiver mental health and functioning at baseline were explored as potential moderators of intervention effects on child outcomes. For analysis of MSEL subscale scores, Benjamini-Hochberg procedure for the control of false discovery rate was applied [24]. SAS 9.4 was used for all analyses.

RESULTS

Of the 118 child-caregiver dyads who began the interventions, 112 children (95%) and 109 caregivers (92%) completed the mid-program assessment (6-months after baseline); 107 children and caregivers (91%) completed the post-program assessment (12-months after baseline); and 106 children (90%) and 100 caregivers (85%) completed the follow-up assessment (24-months after baseline) (Supplement 1).

MISC and UCOBAC child-caregiver dyads are demographically similar and comparable in outcome scale scores at baseline (Table 1); only for the BRIEF scale of Inhibitory Self-control did MISC children score worse than UCOBAC children. At baseline, caregivers reported moderate mental health problems and low functional impairment.

Child Outcomes—Children in both interventions experienced positive neurological and cognitive development changes (Table 2). MSEL scores are presented age-standardized, so a decrease is interpreted as study children on average not making development gains on a similar trajectory as children from high-income countries, on which standardized scores are based. Of the five MSEL subscales, MISC had a significant impact on receptive language score post intervention (adjusted mean difference=3.13, 95% CI 0.08, 6.18); this effect did not remain significant after Benjamini-Hochberg adjustment and was attenuated at the maintenance follow-up (adjusted mean difference=2.56, 95% CI −0.50, 5.63). At post-program assessment, MISC children had significantly worse (higher) BRIEF metacognition and inhibitory self-control subscales and global executive function scores than UCOBAC. None of these differences were maintained at the maintenance follow-up. There were no other statistically significant effects of MISC on child outcomes.

Caregiver Outcomes—Caregivers in both intervention arms experienced improvements in mental health and functionality over time (Table 2). MISC caregivers reported near significant fewer depression symptoms at the maintenance assessment (adjusted mean difference=−0.17, 95% CI −0.34, −0.02), as well as significantly less functional impairment post-program (adjusted mean difference=−0.15, 95% CI −0.28, −0.01).

Mediation and Moderation—For the exploratory mediation analysis, MISC participants showed greater increases over time in average HOME scores (mid-program: 22.45; post-program: 23.60; 12 month follow up: 24.00) than UCOBAC participants (mid-program: 20.36; post-program: 20.38; 12 month follow up: 19.89), with significant differences by arm at all time points (p<.001). HOME and MSEL receptive language scores were significantly associated across the full sample, irrespective of intervention arm. Controlling for HOME score in the LME with the MSEL receptive language outcome resulted in the trial arm variable losing significance, indicating probable mediation. Similar results were obtained with the OMI score as a potential mediator.

In the exploratory moderation analysis, no significant interactions were found between baseline caregiver mental health and trial arm for any of the MSEL outcomes. For caregiver functionality, better baseline caregiver functionality was associated with smaller gains in receptive language.

DISCUSSION

Participation in both intervention conditions resulted in improved outcomes for children and caregivers. MISC led to additional small improvements in child receptive language acquisition and caregiver mental health. The lack of effects for other developmental domains may be a result of UCOBAC being an active control condition, which enhanced the caregiver's attention to their child's nutrition and health.

MISC caregivers showing greater improvement over time in mental health compared to controls is in line with prior findings [7]. With the MISC program encouraging caregivers to value their own ideas about childrearing, a possible mechanism by which MISC may impact caregiver mental health is through an increase in parenting-related self-efficacy and empowerment.

Baseline MSEL scores were indicative of an at-risk sample. Compared with similarly aged populations in the US, our sample had significantly lower MSEL scores [25,26], but similar to other HIV-infected samples in Uganda [7]. While children in our study showed gains in cognitive development over time, their measured rate of improvement is less than that seen in the US, which is why the standardized scores appear to decline over time.

In exploratory analyses, quality and quantity of caregiver-child interactions were identified as potential mediators of MISC's impact on receptive language; having confirmation of the hypothesized mediation model strengthens the study findings. We also found that MISC appears to be more effective in improving language outcomes of children whose caregivers reported better functionality in tasks of daily living at the beginning of program participation.

Several limitations should be noted. The MSEL and COAT have been previously used in Uganda [7,27]; however, standardized local norms were not available. We used scores standardized based on non-LMIC samples rather than raw scores to account for developmental growth. We were not able to formally test for spillover effects of the MISC intervention into the control condition, but through fidelity monitoring we think this was minimal. There is a chance through multiple testing for identifying significant differences by chance.

With more than 200 million children not reaching their developmental potential due to poverty, illness, and lack of social and educational resources, improved early caregiving is important [28]. Both interventions resulted in improvements for HIV-infected children, providing additional support for the importance of early childhood programming.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS

REFERENCES

1. Britto PR, Engle PL. Handbook of Early Childhood Development Research and Its Impact on Global Policy. Oxford University Press; 2013.

2. Walker SP, Wachs TD, Grantham-McGregor S, Black MM, Nelson CA, Huffman SL, et al. Inequality in early childhood: risk and protective factors for early child development. The Lancet 8; 378:1325–1338.

3. Landry SH, Smith KE, Swank PR. Responsive parenting: establishing early foundations for social, communication, and independent problem-solving skills. Dev Psychol 2006; 42:627–642. [PubMed: 16802896]

4. Olds DL, Robinson J, Pettitt L, Luckey DW, Holmberg J, Ng RK, et al. Effects of home visits by paraprofessionals and by nurses: age 4 follow-up results of a randomized trial. Pediatrics 2004; 114:1560–1568. [PubMed: 15574615]

5. Engle PL, Black MM, Behrman JR, Cabral de Mello M, Gertler PJ, Kapiriri L, et al. Strategies to avoid the loss of developmental potential in more than 200 million children in the developing world. The Lancet 2007; 369:229–242.

6. Singla DR, Kumbakumba E, Aboud FE. Effects of a parenting intervention to address maternal psychological wellbeing and child development and growth in rural Uganda: a community-based, cluster randomised trial. Lancet Glob Health 2015; 3:e458–469. [PubMed: 26144389]

7. Boivin MJ, Bangirana P, Nakasujja N, Page CF, Shohet C, Givon D, et al. A year-long caregiver training program improves cognition in preschool Ugandan children with human immunodeficiency virus. J Pediatr 2013; 163:1409-1416–5. [PubMed: 24160658]

8. Boivin MJ, Bangirana P, Nakasujja N, Page CF, Shohet C, Givon D, et al. A year-long caregiver training program to improve neurocognition in preschool Ugandan HIV-exposed children. J Dev Behav Pediatr JDBP 2013; 34:269–278. [PubMed: 23535340]

9. Uganda Bureau of Statistics and ICF International Inc. Uganda Demographic and Health Survey 2011. Kampala, Uganda: UBOS and Calverton, Maryland: ICF International Inc. 2012.

10. HIV and AIDS Uganda country progress report. Kampala, Uganda: Uganda AIDS Comission; 2014. http://www.unaids.org/sites/default/files/country/documents/UGA_narrative_report_2014.pdf (accessed 3 Aug2015).

11. Klein PS, Hundeide K. Early Intervention: Cross-cultural Experiences with a Mediational Approach. Taylor & Francis; 1996.

12. Feuerstein R The dynamic assessment of retarded performers. New York: University Park Press; 1979.

13. Feuerstein R Instrumental enrichment: Redevelopment of cognitive functions of retarded performers. New York: University Park Press; 1980.

14. Mullen EM. Mullen Scales of Early Learning (AGS ed.). Circle Pines, MN:; 1995.

15. Jordan CM, Johnson AL, Hughes SJ, Shapiro EG. The Color Object Association Test (COAT): the development of a new measure of declarative memory for 18- to 36-month-old toddlers. Child Neuropsychol J Norm Abnorm Dev Child Adolesc 2008; 14:21–41.

16. Zelinsky D, Hughes S, Rumsey R, Jordan C, Shaprio E. The Early Childhood Vigilance Task: A new technique for the measurement of sustained attention in very young children. J Int Neuropsychol Soc 1996; 2.

17. Goldman DZ, Shapiro EG, Nelson CA. Measurement of Vigilance in 2-Year-Old Children. Dev Neuropsychol 2004; 25:227–250. [PubMed: 15147998]

18. Gioia GA, Isquith PK, Guy SC, Kenworthy L. Behavior Rating Inventory of Executive Function. Child Neuropsychol 2000; 6:235–238. [PubMed: 11419452]

19. Caldwell BM, Bradley RH. Home Observation for Measurement of the Environment. Little Rock, AR: University of Arkansas Press; 1979.

20. Klein PS, Hundeide K. Early Intervention: Cross-cultural Experiences with a Mediational Approach. Taylor & Francis; 1996.

21. Klein P, Rye H. Interaction-oriented early intervention in Ethiopa - The MISC approach. Infants Young Child 2004; 17:340–354.

22. Hesbacher PT, Rickels K, Morris RJ, Newman H, Rosenfeld H. Psychiatric illness in family practice. J Clin Psychiatry 1980; 41:6–10.

23. Winokur A, Winokur DF, Rickels K, Cox DS. Symptoms of emotional distress in a family planning service: stability over a four-week period. Br J Psychiatry J Ment Sci 1984; 144:395–399.

24. Benjamini Y, Hochberg Y. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. J R Stat Soc Ser B Methodol 1995; 57:289–300.

25. Akshoomoff N Use of the Mullen Scales of Early Learning for the assessment of young children with Autism Spectrum Disorders. Child Neuropsychol J Norm Abnorm Dev Child Adolesc 2006; 12:269–277.

26. Swineford LB, Guthrie W, Thurm A. Convergent and divergent validity of the Mullen Scales of Early Learning in young children with and without autism spectrum disorder. Psychol Assess 2015; 27:1364–1378. [PubMed: 25894712]

27. Busman RA, Page CF, Oka E, Giordani B, Boivin MJ. Factors contributing to the psychosocial adjustment of Ugandan preschool children with HIV/AIDS. In: *Neuropsychology of children in Africa: Perspectives on risk and resilience*. Boivin MJ, Giordani B (editors).. New York: Springer; 2013.

28. Grantham-McGregor S, Cheung YB, Cueto S, Glewwe P, Richter L, Strupp B. Developmental potential in the first 5 years for children in developing countries. Lancet 2007; 369:60–70. [PubMed: 17208643]

Table 1.

Child and caregiver characteristics at baseline

	MISC N=58[*]	UCOBAC N=60[*]	P-value for difference by study arm
Child			
Age in years, Mean (SD)	3.11 (0.94)	3.34 (0.91)	0.18
Male sex, N (%)	29 (50%)	23 (38%)	0.20
On HAART, N (%)	39 (67.24%)	35 (58.33%)	0.32
Mullen Composite, Mean (SD)	70.33 (18.69)	72.62 (21.67)	0.54
Visual Reception, Mean (SD)	30.74 (11.02)	32.12 (12.60)	0.53
Gross Motor skills, Mean (SD)	26.40 (5.69)	27.75 (5.38)	0.19
Fine Motor skills, Mean (SD)	32.52 (14.31)	34.83 (15.43)	0.35
Receptive Language, Mean (SD)	35.86 (10.90)	37.67 (13.03)	0.42
Expressive Language, Mean (SD)	33.51 (11.68)	34.87 (13.70)	0.57
COAT Immediate Recall, Mean (SD)	3.63 (3.21)	3.72 (3.38)	0.89
COAT Total Recall, Mean (SD)	6.67 (7.94)	8.68 (11.99)	0.29
BRIEF Global Executive Function, Mean (SD)	63.65 (14.54)	62.86 (14.72)	0.08
BRIEF Emergent Metacognition, Mean (SD)	62.42 (13.10)	59.02 (13.45)	0.23
BRIEF Inhibitory Self-Control, Mean (SD)	68.50 (15.06)	66.20 (15.28)	0.04
BRIEF Flexibility, Mean (SD)	67.48 (13.25)	62.88 (15.02)	0.15
Early Childhood Vigilance Test, Mean (SD) Proportion of Time Looking, Mean (SD)	0.57 (0.14)	0.66 (0.11)	<0.01
Caregiver			
Age in years, Mean (SD)	36.27 (8.24)	35.30 (8.50)	0.54
Biological mother, N (%)	42 (72.41)	46 (76.67)	0.83
Married, N (%)	38 (65.52)	39 (65.00)	0.74
Any education, N (%)	43 (74.14)	48 (80.00)	0.64
Depression severity, Mean (SD)	0.98 (0.51)	0.91 (0.40)	0.46
Anxiety severity, Mean (SD)	0.88 (0.61)	0.72 (0.46)	0.09
Functional impairment, Mean (SD)	0.34 (0.41)	0.46 (0.35)	0.09

[*] results presented for non-imputed data, some missing on baseline demographics (<0.5%)

MISC=Mediational Intervention for Sensitizing Caregivers, UCOBAC= Uganda Community Based Association for Child Welfare program, COAT=Color Object Association Test, BRIEF= Behavior Rating Inventory of Executive Function, HAART=Highly Active Anti-Retroviral Therapy

Table 2.

Child and caregiver unadjusted and adjusted[1] outcomes

	MISC, N=58N Unadjusted Mean (SE)	UCOBAC, N=60 Unadjusted Mean (SE)	Unadjusted Mean Difference by Arm (95% CI)	P-value for Unadjusted Mean Difference	MISC, N=58 Adjusted Mean (SE)	UCOBAC, N=60 Adjusted Mean (SE)	Adjusted Mean Difference by Arm (95% CI)	P-value for Adjusted Mean Difference
Mullen composite								
Mid-program[2]	70.02 (1.94)	72.54 (2.80)	−2.52 (−9.28, 4.25)	0.46	70.22 (1.63)	73.22 (1.58)	−3.00 (−7.28, 1.29)	0.17
Immediate Post-program	68.56 (2.06)	69.29 (2.54)	−0.73 (−7.22, 5.76)	0.22	69.17 (1.66)	69.01 (1.56)	0.16 (−4.14, 4.47)	0.94
12 month Follow-up	67.94 (2.05)	65.85 (1.82)	2.09 (−3.35, 7.53)	0.44	68.25 (1.67)	65.52 (1.57)	2.73 (−1.59, 7.06)	0.21
Mullen gross motor								
Mid-program	29.17 (0.57)	30.00 (0.52)	−0.83 (−2.26, 0.69)	0.28	29.43 (0.52)	29.81 (0.53)	−0.38 (1.79, 0.89)	0.59
Immediate Post-program	29.44 (0.60)	30.62 (0.46)	−1.18 (−2.68, 0.33)	0.12	30.02 (0.53)	30.39 (0.52)	−0.37 (−1.90, 0.78)	0.60
12 month Follow-up	33.06 (0.44)	33.06 (0.56)	0 (−1.41, 1.42)	0.99	33.29 (0.53)	32.98 (0.52)	0.31 (−0.84, 1.84)	0.66
Mullen fine motor								
Mid-program	33.04 (1.74)	34.81 (2.00)	−1.78 (−7.03, 3.48)	0.50	34.28 (1.41)	34.33 (1.42)	−0.05 (−4.35, 3.02)	0.98
Immediate Post-program	31.42 (1.58)	34.84 (2.01)	−3.42 (−8.48, 1.65)	0.18	33.64 (1.43)	34.11 (1.40)	−0.47 (−4.19, 3.20)	0.80
12 month Follow-up	31.83 (1.63)	32.74 (1.30)	−0.91 (−5.05, 3.22)	0.66	33.88 (1.43)	32.59 (1.39)	1.29 (−1.88, 5.54)	0.50
Mid-program	28.76 (1.22)	30.61 (1.61)	−1.85 (−5.89, 2.16)	0.36	27.95 (1.17)	29.49 (1.17)	−1.54 (−5.06, 1.34)	0.33
Immediate Post-program	27.92 (1.33)	29.40 (1.56)	−1.48 (−5.54, 2.58)	0.72	27.37 (1.19)	28.03 (1.15)	−0.66 (−4.10, 2.23)	0.67
12 month Follow-up	29.58 (1.32)	27.06 (1.17)	2.52 (−0.97, 6.02)	0.16	28.59 (1.18)	26.23 (1.15)	2.36 (−0.87, 5.59)	0.14
Mullen Receptive Language								
Mid-program	35.70 (1.45)	34.93 (1.63)	0.77 (−3.55, 5.10)	0.72	36.27 (1.16)	35.08 (1.13)	1.19 (−1.85, 4.23)	0.44
Immediate Post-program	34.71 (1.40)	33.16 (1.46)	1.55 (−2.46, 5.55)	0.45	35.57 (1.18)	32.44 (1.11)	3.13 (0.08, 6.18)	0.04
12 month Follow-up	31.62 (1.22)	30.19 (1.41)	1.43 (−2.26, 5.12)	0.45	32.44 (1.18)	29.88 (1.12)	2.56 (−0.50, 5.63)	0.10
Mullen Expressive Language								

	MISC, N=58N Unadjusted Mean (SE)	UCOBAC, N=60 Unadjusted Mean (SE)	Unadjusted Mean Difference by Arm (95% CI)	P-value for Unadjusted Mean Difference	MISC, N=58 Adjusted Mean (SE)	UCOBAC, N=60 Adjusted Mean (SE)	Adjusted Mean Difference by Arm (95% CI)	P-value for Adjusted Mean Difference
Mid-program	35.06 (1.40)	35.91 (1.77)	−0.85 (−5.33, 3.63)	0.71	34.23 (1.48)	35.27 (1.48)	−1.04 (−4.98, 2.64)	0.60
Immediate Post-program	36.62 (1.53)	34.25 (1.63)	2.37 (−2.09, 6.81)	0.30	36.22 (1.49)	33.50 (1.45)	2.72 (−1.67, 5.99)	0.18
12 month Follow-up	36.04 (1.58)	34.17 (1.27)	1.87 (−2.16, 5.90)	0.36	35.42 (1.49)	33.69 (1.45)	1.73 (−1.68, 6.01)	0.38
COAT immediate recall								
Mid-program	4.26 (0.49)	5.17 (0.58)	−0.91 (−2.42, 0.61)	0.24	5.13 (0.91)	4.78 (0.90)	0.35 (−2.09, 2.78)	0.86
Immediate Post-program	5.00 (0.58)	6.45 (0.62)	−1.45 (−3.14, 0.23)	0.09	5.72 (0.93)	6.03 (0.89)	−0.31 (−2.76, 2.13)	0.99
12 month follow-up	8.25 (1.07)	9.94 (1.42)	−1.69 (−5.22, 1.83)	0.34	9.17 (0.93)	9.87 (0.89)	−0.70 (−3.16, 1.76)	0.71
COAT total recall								
Mid-program	11.07 (1.82)	13.09 (2.19)	−2.02 (−7.66, 3.62)	0.48	14.03 (2.03)	11.28 (2.00)	2.75 (−2.68, 8.18)	0.32
Immediate Post-program	13.60 (1.99)	17.98 (2.41)	−4.38 (−10.58, 1.82)	0.17	16.24 (2.07)	16.04 (1.98)	0.20 (−5.25, 5.65)	0.94
12 month follow-up	17.19 (2.02)	18.20 (2.41)	−1.01 (−7.26, 5.24)	0.75	20.40 (2.07)	16.29 (1.98)	4.11 (−1.36, 9.59)	0.14
BRIEF Emergent Metacognition Index								
Mid-program	63.46 (1.83)	62.00 (2.13)	1.46 (−4.11, 7.04)	0.60	63.48 (1.87)	61.75 (1.88)	1.73 (−2.76, 7.18)	0.49
Immediate Post-program	62.42 (2.09)	56.74 (1.98)	5.66 (−0.02, 11.40)	0.05	62.75 (1.89)	57.57 (1.89)	5.18 (−0.71, 9.34)	0.05
12 month follow-up	58.40 (2.00)	58.54 (1.90)	−0.14 (−5.60, 5.34)	0.96	58.67 (1.88)	58.99 (1.85)	−0.32 (−5.63, 4.40)	0.90
BRIEF Inhibitory Self-Control Index								
Mid-program	63.54 (1.71)	63.33 (1.77)	0.21 (−4.69, 5.09)	0.93	63.73 (1.68)	61.78 (1.70)	1.95 (−1.87, 7.02)	0.39
Immediate Post-program	62.65 (1.95)	60.11 (1.82)	2.54 (−2.74, 7.83)	0.34	63.11 (1.70)	58.63 (1.70)	4.48 (−0.22, 8.75)	0.05
12 month follow-up	58.23 (1.66)	59.22 (1.86)	−0.99 (−5.93, 3.95)	0.69	58.69 (1.70)	57.97 (1.68)	0.72 (−3.80, 5.16)	0.75
BRIEF Flexibility Index								
Mid-program	56.61 (1.70)	58.63 (1.83)	−2.02 (−6.97, 2.93)	0.42	56.11 (1.76)	57.84 (1.76)	−1.73 (−5.18, 4.17)	0.47
Immediate Post-program	55.90 (2.04)	55.02 (1.81)	0.89 (−4.51, 6.28)	0.75	55.58 (1.78)	54.09 (1.77)	1.49 (−3.35, 6.08)	0.53
12 month follow-up	52.33 (1.52)	55.57 (1.95)	−3.25 (−8.16, 1.67)	0.19	52.30 (1.77)	54.29 (1.74)	−1.99 (−7.39, 2.03)	0.40
BRIEF Global Executive Composite								
Mid-program	63.74 (1.88)	63.28 (1.98)	0.46 (−4.95, 5.87)	0.87	63.73 (1.79)	62.41 (1.82)	1.32 (−2.73, 6.91)	0.59

	MISC, N=58 Unadjusted Mean (SE)	UCOBAC, N=60 Unadjusted Mean (SE)	Unadjusted Mean Difference by Arm (95% CI)	P-value for Unadjusted Mean Difference	MISC, N=58 Adjusted Mean (SE)	UCOBAC, N=60 Adjusted Mean (SE)	Adjusted Mean Difference by Arm (95% CI)	P-value for Adjusted Mean Difference
Immediate Post-program[2]	62.29 (2.22)	58.91 (1.89)	3.38 (−1.39, 10.16)	0.13	63.64 (1.82)	58.59 (1.82)	5.05 (−0.34, 9.39)	0.04
12 month follow-up	57.96 (1.81)	58.89 (2.00)	−0.93 (−6.28, 4.43)	0.73	58.29 (1.81)	58.42 (1.79)	−0.13 (−5.28, 4.44)	0.96
Caregiver Depression symptoms								
Mid-program[2]	0.94 (0.07)	0.84 (0.06)	0.10 (−0.08, 0.27)	0.28	0.96 (0.06)	0.86 (0.06)	0.10 (−0.11, 0.25)	0.26
Immediate Post-program	0.76 (0.06)	0.77 (0.06)	−0.01 (−0.17, 0.15)	0.89	0.73 (0.06)	0.77 (0.06)	−0.04 (−0.21, 0.15)	0.68
12 month follow-up	0.72 (0.07)	0.93 (0.07)	−0.21 (−0.42, −0.01)	0.04	0.75 (0.06)	0.92 (0.06)	−0.17 (−0.34, 0.02)	0.06
Caregiver Anxiety symptoms								
Mid-program	0.83 (0.08)	0.70 (0.07)	0.13 (−0.08, 0.33)	0.23	0.82 (0.07)	0.72 (0.07)	0.10 (−0.12, 0.30)	0.34
Immediate Post-program	0.68 (0.07)	0.72 (0.07)	−0.04 (−0.24, 0.15)	0.64	0.60 (0.08)	0.73 (0.08)	−0.13 (−0.32, 0.10)	0.27
12 month follow-up	0.74 (0.07)	0.82 (0.09)	−0.08 (−0.33, 0.15)	0.47	0.70 (0.08)	0.79 (0.08)	−0.09 (−0.28, 0.15)	0.40
Caregiver Impaired function								
Mid-program	0.28 (0.04)	0.48 (0.05)	−0.20 (−0.34, −0.07)	<0.01	0.32 (0.05)	0.49 (0.05)	−0.17 (−0.31, −0.04)	0.02
Immediate Post-program	0.20 (0.04)	0.39 (0.06)	−0.19 (−0.34, −0.04)	0.01	0.24 (0.05)	0.39 (0.05)	−0.15 (−0.28, −0.01)	0.04
12 month follow-up	0.19 (0.04)	0.37 (0.05)	−0.18 (−0.31, −0.06)	<0.01	0.22 (0.05)	0.34 (0.05)	−0.12 (−0.26, 0.01)	0.08

[1] adjusted for child age, sex, child highly active anti-retroviral (HAART) status during the trial, outcome score at baseline, caregiver functionality at baseline, Behavior Rating Inventory of Executive Function (BRIEF) inhibitory self-control index, BRIEF global executive composite, and child attention measured via the Early Childhood Vigilance Test (ECVT) at baseline.

[2] The mid-program assessment took place 6 months after baseline, the immediate post-program assessment 12 months after baseline, and the 12 month follow-up assessment 24 months after baseline.

MISC=Mediational Intervention for Sensitizing Caregivers, UCOBAC= Uganda Community Based Association for Child Welfare program