

Association of caregiver quality of care with neurocognitive outcomes in HIV-affected children aged 2–5 years in Uganda

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ABSTRACT

Children affected by HIV are at increased risk of developmental and neuropsychological disturbances due to direct effects of HIV on the brain and direct effects associated with living in poverty. Caregivers can play an important role, through quality caregiving, in mitigating the negative effect of these stressors. This study used baseline data from an ongoing caregiver training intervention trial to evaluate the association between quality of caregiver–child interactions and neurocognitive outcomes in rural HIV-infected and HIV-exposed but uninfected children in Uganda. We also assessed the extent to which caregiver distress moderated this relationship. Data on 329 caregiver–child dyads were collected between March 2012 and July 2014, when the children were between 2 and 5 years of age. Child outcomes include the Mullen Scales of Early Learning to assess general cognitive ability and the Color Object Association Test to assess immediate memory and total recall. Caregiving quality was assessed using the Home Observation for the Measurement of the Environment (HOME) total and subscale scores. Caregiver distress was assessed using the Hopkins Symptom Checklist. General linear regression models assessed the association between the HOME total and subscale scores and child outcomes, with interaction terms used to test moderation by caregiver distress. Total HOME scores were positively and significantly associated with Mullen scores of cognitive ability; HOME acceptance subscale scores were positively and significantly associated with immediate recall scores. No other associations were statistically significant. As hypothesized, there is a strong association between the HOME and Mullen scores of cognitive ability in our study population, such that children who were assessed as living in environments with more stimulation also presented with a higher level of general neurocognitive development. Our results support the view of program guidance for HIV-affected children that suggest family-oriented care with emphasis on parent–child relationships for optimal child development.

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Background

Over 2 million children aged 0–14 years in sub-Saharan Africa are living with HIV including 650,000 orphans due to AIDS and 150,000 children living with HIV in Uganda (UNAIDS, 2015). Uganda is typical of low-income countries in that it does not have a social service infrastructure to provide for the developmental, social and educational needs of preschool-aged children, leaving a critical gap in care for HIV-affected children.

Children infected with HIV are at increased risk of developmental and neuropsychological disturbances due to direct effects of the HIV virus on brain structures involved in the regulation of emotion, behavior, and cognition, and direct effects associated with living in

poverty, including increased social stressors, poverty, illness and trauma (Benton, 2010; Scharko, 2006; Sherr, Croome, Castaneda, Bradshaw, & Romero, 2014). HIV-infected school-aged children frequently exhibit behavioral problems associated with attention-deficit/hyperactivity disorder (i.e., such as impulsivity, hyperactivity and difficulties concentrating) (Mellins et al., 2012) and affective disorders (i.e., depression and anxiety) (Musisi & Kinyanda, 2009). Compromised executive function and slowed information processing have also been reported (Wachsler-Felder & Golden, 2002).

With the availability of programs to prevent vertical transmission of HIV from mother to child, children are living as HIV-exposed but uninfected throughout

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the region (Franklin, 2002; Wilfert, 2002). These children are also at increased risk of developmental delay due to poverty-related stressors. Most of these children live in rural areas and in areas of great social and economic instability. Longitudinal studies in low-income countries demonstrate that children born into poverty are more likely to experience impairments in cognitive development (Grantham-McGregor et al., 2007; Walker et al., 2011), particularly in sub-Saharan Africa (Escueta, Whetten, Ostermann, O'Donnell, & Positive Outcomes for Orphans Research, 2014; Sigman, Neumann, Jansen, & Bwibo, 1989). These disadvantages can undermine academic and social achievement.

Caregivers can play an important role, through quality caregiving, in mitigating the negative effect of these stressors. In a US study, the quality of caregiving was found to moderate the association between poverty and school readiness and language development in children, suggesting that caregiving practices can serve as a buffer (McCartney, Dearing, Taylor, & Bub, 2007). Findings from the USA also suggest that improvements in caregiver quality can lead to positive cognitive development outcomes in young children who are already experiencing early signs of cognitive delay (Jaffee, 2007). While evidence from low-income countries is limited, a study of rural children aged 1–3 years in India found that children of mothers who were more involved and provided more stimulation exhibited more positive cognitive development than their counterparts receiving less responsive care (Agarwal et al., 1992).

Research has shown association between the ability of a caregiver to provide high quality care to their children and the caregiver's own mental health. Stein, Malmberg, Sylva, Barnes, and Leach (2008) found in a UK study that maternal depression was associated with poorer caregiving of children through age 36 months and that poorer caregiving was subsequently associated poorer language development. A study from South Africa found that maternal depression was related to poorer quality interactions between the mother and her infant compared with non-depressed mothers (Cooper et al., 1999).

Maternal depression and anxiety are common in low-income countries (Fisher et al., 2012; Sawyer, Ayers, & Smith, 2010). For HIV-infected individuals, the prevalence of depression and anxiety has been demonstrated to be significantly greater than the general public (Nakasujja et al., 2010; Rabkin, 2008; Tostes, Chalub, & Botega, 2004) and among those with symptomatic as compared to asymptomatic HIV infection (Collins, Holman, Freeman, & Patel, 2006). Prevalence estimates of depression among HIV-infected adults in low-income countries range from 30% to 40% (Chandra, Ravi, Desai, & Subbakrishna, 1998; Tostes et al., 2004). A study of

depression among HIV/AIDS patients in eastern Uganda, which included the districts included in this study, estimated a 47% depression prevalence using the Center for Epidemiological Studies Depression scale.

The primary aim of this study is to evaluate the cross-sectional relationship between the quality of caregiver–child interactions (as assessed by the Home Observation for the Measurement of the Environment (HOME)) and neurocognitive outcomes (as assessed by the Mullen and COAT measures) in rural HIV-infected and HIV-exposed but uninfected children (children born to positive mothers who were not themselves infected) in Uganda. We also examine the extent to which child HIV status and caregiver distress moderate the relationship between interaction quality and child outcomes, as well as assess caregiver distress as a possible mechanism of the relationship. We also assess whether the associations vary by HOME subscales, which assess different domains of caregiver–child interactions.

Methods

Study data come from baseline assessments of a randomized controlled trial entitled “Enhancing Ugandan HIV-Affected Child Development with Caregiver Training Study”. This trial tests the Meditational Intervention for Sensitizing Caregivers, a one-year structured training focused on enhancing a caregiver's sensitivity and attentiveness to her child in order to improve child cognitive and social development. Children were recruited into the trial based on HIV status; a first cohort of HIV-infected (Infected) children was recruited with a corresponding female caregiver followed by a second cohort of HIV-exposed but uninfected children (Uninfected) children with a corresponding female caregiver. HIV children and their caregivers were identified from clinic and NGO referral lists in Tororo and Busia districts in eastern Uganda; infected and uninfected children were also enrolled from rosters of concluding trials of HIV- and anti-malarial treatment among HIV-infected pregnant women.

Of 417 children (147 infected; 270 uninfected) assessed for eligibility, 78 children were not enrolled due to severe malnutrition ($n=6$), out of age range ($n=10$), out of catchment area ($n=15$), participating in another study ($n=7$), active tuberculosis ($n=1$), uncontrolled epilepsy ($n=2$), deaths prior to enrollment ($n=10$) and 6 households that could not be located. Among the infected children assessed, six were identified as non-infected after baseline and were subsequently excluded and among the uninfected children assessed, nine caregivers refused to participate in the study (e.g., were too busy or not interested) and one husband did not allow his wife to participate, resulting in a total of

339 child–caregiver dyads (118 infected and 221 uninfected children) participating in the study.

Study eligibility included that the child was between 2 and 5 years of age at enrollment with no history of illness or injury that could have caused a central nervous system insult. Caregiver eligibility included being willing and able to participate in the intervention and not having a severe mental illness or disability that would have prevented active engagement in the study. Caregiver–child dyads were enrolled and caregivers provided written informed consent between March 2012 and July 2014. Caregiver and child-specific measures were administered in the home (caregiver demographics and well-being, and assessment of the quality and quantity of child and caregiver interactions) or in the study office (all child outcomes) in one of three languages spoken in Eastern Uganda (Japhadola, Ateso or Luganda). The Institutional Review Boards of Michigan State University, the School of Medicine Research Ethics Committee at Makerere University and the Ugandan National Council for Science and Technology approved this study.

Measures

Caregiver demographic information included marital status (married vs. unmarried), education (any vs. none), sub-county of residence, relationship to study child (mother vs. other), HIV status and socioeconomic status (SES) as assessed by a wealth index. Child demographics included age, sex, HIV status and current use of highly active anti-retroviral treatment (HAART; yes/no). An economic wealth index was constructed from a checklist of eight material possessions (shoes, radio, mattress, blanket, bicycle, motorcycle, cows and goats) and six housing quality items (type of roof, availability of water supply, type of fuel used, frequency of meat in diet and food security). For the wealth index, top 20th, middle 60th, and bottom 20th percentiles were defined based on factor scores derived from exploratory factor analysis. Age, sex and wealth index were controlled for in the study models.

Quality and quantity of child–caregiver interactions were assessed using the HOME (Caldwell & Bradley, 2003). This measure has been validated previously in Uganda (Bangirana et al., 2009). For this analysis we use the Infant Toddler version which includes 45 yes/no items clustered into six subscales: (1) parental responsiveness, (2) acceptance of child, (3) organization of the environment, (4) learning materials, (5) parental involvement and (6) variety in experience. A total HOME score and subscale specific scores are generated by summing the number of “yes” responses to each item, with higher scores indicating higher quality.

The Mullen Scales of Early Learning (Mullen, 1995) was used to assess the domains of (1) visual reception, (2) fine motor skills, (3) receptive and (4) expressive language. The early learning composite score provides a measure of *g*, the general measure of fluid intelligence thought to underlie general cognitive ability. This composite measure is derived from standardized *t*-scores of the four domains.

The Color Object Association Test (COAT) (Jordan, Johnson, Hughes, & Shapiro, 2008) was used to assess childhood memory capability. This is an experimental test that evaluates declarative (explicit) memory in children during the toddler and preschool years. This memory test uses 4-inch square wooden boxes with pictures and a set of small, colorful familiar toys (e.g., ball, doll, book). Children are asked to do a variety of tasks related to identifying what is in the boxes as items are moved around. Boxes are rotated throughout the assessment and the number of pictures and boxes increases over time to increase the difficulty of the test. The principal outcomes are the number of recalled items for assessing immediate memory and an overall total recall or learning score of correctly placed items over the course of a test.

Caregiver distress was measured using the Hopkins Symptoms Checklist-25 (HSCL; Hesbacher, Rickels, Morris, Newman, & Rosenfeld, 1980; Winokur, Winokur, Rickels, & Cox, 1984). The HSCL-25 contains 10 symptoms that measure anxiety and 15 symptoms that measure depression. Participants used a Likert scale of 0 (not at all) to 3 (a lot) to rate how often they experienced each symptom within the last two weeks. This measure has been used among communities affected by HIV (Gupta et al., 2010; Kagee & Martin, 2010). The depression subscale was adapted to the Ugandan context in prior studies (Bolton, Wilk, & Ndogoni, 2004). The total caregiver distress score was measured continuously as a mean 25-item score that could range from 0 to 3, with higher scores indicating more severe symptoms.

Analysis

Sociodemographic characteristics, Mullen cognitive ability, COAT memory scales, HOME and distress scores were summarized and compared by child HIV status using *t*- or chi-square tests. General linear regression models were used to assess associations between caregiver–child interaction quality and child cognitive development operationalized as three different outcomes: general Mullen cognitive ability, COAT immediate recall and COAT total recall. The total HOME score was included as the primary predictor of these outcomes in three separate models that all controlled for child age, sex, HIV status and family SES. Interaction terms were added to these models to assess the extent to which

child HIV status and caregiver distress moderated the association between caregiver–child interaction and child cognitive development. This process was then repeated for the HOME subscales. To determine whether caregiver distress mediated the effect of caregiver–child interactions on child cognitive developments, we compared the magnitude and significance of the coefficients for the HOME scores in models with and without maternal distress score. All statistical tests were two-sided. Since outcomes were identified and research questions were stated a priori, p -values $< .05$ indicated statistical significance. The analyses were performed in SAS 9.4.

Results

Demographic characteristics are presented for the total sample and separately by child HIV status in Table 1. Caregivers were on average 35 years of age. There were differences in across infected and uninfected cohorts with uninfected children being slightly older on average (3.2 years compared with 2.9 years), more likely to be female (56% vs. 43%) and more likely to be cared for by their biological mother (77% vs. 90%). There were

no significant differences across the cohorts in caregiver marital status, education attainment, family SES average caregiver distress scores (as assessed with the caregiver distress measure) and child neurodevelopment outcomes (Table 1). Higher responsivity, involvement and variety scores, as measured by the HOME, were reported among uninfected as compared with infected dyads.

The regression models revealed significant associations between quality of caregiver–child interactions and fluid intelligence (Table 2). Specifically, a one-unit increase in total HOME score was associated with a 0.56 (95% CI) unit increase in Mullen general cognitive ability. Additionally, a one-unit increase in HOME acceptance subscale score was associated with a 0.57 unit increase in COAT immediate recall score. The associations between the HOME Learning and Variety subscales and the Mullen general cognitive ability score were large, though not statistically significant. Significance did not change when child HIV status was removed from the models nor were associations modified by child HIV status. Caregiver distress score was not significantly associated with child outcomes (Table 2), and did not attenuate the associations between the HOME scores and child outcomes (Table 3), as seen

Table 1. Child and caregiver characteristics.

	Total sample <i>N</i> = 339	Uninfected <i>N</i> = 221	Infected <i>N</i> = 118	<i>p</i> -Value ^a
Child				
Age, mean (SD)	3.00 (0.67)	2.87 (0.42)	3.23 (0.93)	<0.01
Male sex, <i>N</i> (%)	177 (52.21%)	125 (56.56%)	52 (44.07%)	0.03
On HAART, <i>N</i> (%)	74 (21.83%)	0	74 (62.71%)	N/A
Mullen composite, mean (SD)	71.06 (14.93)	70.82 (11.18)	71.50 (20.22)	0.69
COAT immediate recall, mean (SD)	2.76 (9.19)	2.28 (11.11)	3.68 (3.28)	0.19
COAT total recall, mean (SD)	6.56 (12.64)	5.95 (13.74)	7.70(10.23)	0.23
Caregiver				
Age, mean (SD)	35.31 (8.25)	35.07 (8.20)	35.77(8.35)	0.45
Biological mother, <i>N</i> (%)	283 (85.50%)	197 (90.07%)	88 (75.86%)	<0.01
Married, <i>N</i> (%)	229 (69.18%)	152 (70.70%)	77 (66.38%)	0.64
Any education, <i>N</i> (%)	261 (78.85%)	170 (79.07%)	91 (78.45%)	0.45
Socio-economic status				
Wealth group				
Lowest 20%	66 (20%)	46 (21.4%)	20 (17.24%)	0.45
Middle 60%	199 (60%)	124 (57.68%)	75 (64.67%)	
Top 20%	66 (20%)	45 (20.93%)	21 (18.1%)	
Distress score, mean (SD) (range 0–2.44)	0.93 (0.51)	0.96 (0.54)	0.89 (0.45)	0.22
Caregiver quality measure (HOME)				
Total, mean (SD) (range 7–28)	20.18 (3.15)	20.56 (3.18)	19.48 (2.98)	<0.01
Responsivity subscale, mean (SD) (range 0–10)	6.87 (1.40)	7 (1.40)	6.62 (1.38)	0.02
Acceptance subscale, mean (SD) (range 0–7)	3.71 (1.72)	3.75 (1.80)	3.65 (1.57)	0.61
Organization subscale, mean (SD) (range 0–4)	3.22 (1.72)	3.19 (0.71)	3.28 (0.76)	0.24
Learning subscale, mean (SD) (range 0–5)	1.44 (1.28)	1.48 (1.37)	1.37 (1.09)	0.44
Involvement subscale, mean (SD) (range 0–4)	3.00 (0.73)	3.10 (0.66)	2.82 (0.81)	<0.01
Variety subscale, mean (SD) (range 0–4)	1.94 (1.14)	2.05 (1.10)	1.74 (1.19)	0.02

^a p -Value for Infected vs. Uninfected sample comparison.

Table 2. Summary of the associations of HOME scores and caregiver distress with child cognitive outcomes.^a

HOME scales	Mullen composite		COAT immediate recall		COAT total recall	
	Coefficient (SE)	p-Value	Coefficient (SE)	p-Value	Coefficient (SE)	p-Value
Total	0.56 (0.27)	0.04	0.08 (0.17)	0.62	0.14 (0.23)	0.53
Responsivity	-0.11 (0.59)	0.86	0.06 (0.37)	0.87	0.23 (0.50)	0.65
Acceptance	0.60 (0.48)	0.21	0.59 (0.29)	0.05	0.70 (0.40)	0.08
Organization	0.49 (1.14)	0.67	-0.81 (0.70)	0.25	-0.39 (0.95)	0.69
Learning	1.08 (0.65)	0.10	-0.43 (0.40)	0.28	-0.75 (0.54)	0.16
Involvement	0.38 (1.16)	0.75	-0.05 (0.71)	0.94	0.45 (0.96)	0.64
Variety	1.17 (0.44)	0.12	0.06 (0.46)	0.89	0.01 (0.62)	0.99
Caregiver distress	2.30 (4.33)	0.60	-0.23 (1.02)	0.82	0.02 (1.38)	0.99

^aAdjusted for child age, sex, HIV status and family SES.

Table 3. Summary of the associations of HOME scores with child cognitive outcomes, adjusting for caregiver distress to test attenuation.^a

HOME scales	Mullen composite		COAT immediate recall		COAT total recall	
	Coefficient (SE)	p-Value	Coefficient (SE)	p-Value	Coefficient (SE)	p-Value
Total	0.64 (0.28)	0.02	0.08 (0.17)	0.64	0.15 (0.23)	0.52
Responsivity	-0.03 (0.60)	0.97	0.05 (0.37)	0.89	0.23 (0.50)	0.64
Acceptance	0.64 (0.48)	0.19	0.59 (0.29)	0.05	0.70 (0.40)	0.08
Organization	0.59 (1.15)	0.66	-0.81 (0.70)	0.25	-0.39 (0.95)	0.68
Learning	1.18 (0.65)	0.07	-0.45 (0.40)	0.26	-0.76 (0.54)	0.16
Involvement	0.52 (1.17)	0.65	-0.07 (0.72)	0.91	0.46 (0.97)	0.63
Variety	1.20 (0.74)	0.11	0.06 (0.46)	0.90	0.01 (0.61)	0.99

^aAdjusted for child age, sex, HIV status and family SES.

from the lack of differences in coefficients for the HOME scores and their standard errors presented in Tables 2 (without controlling for caregiver distress) and 3 (controlling for caregiver distress).

Discussion

The HOME total score was statistically and clinically associated with the Mullen early learning composite score. The HOME measure was designed to assess the quality and quantity of stimulation that the child is exposed to in their home environment. As hypothesized, there is a strong association between these two constructs in our study population, such that children who were assessed as living in environments with more stimulation also presented with a higher level of general neurocognitive development. We had also expected that certain HOME subscales, particularly those related to Learning (i.e., provision of appropriate play and learning materials) and Variety (i.e., a measure of observed daily stimulation) would be more highly associated with the Mullen general cognitive ability score compared with the other HOME subscales. We found that the associations for both of these subscales with the Mullen general cognitive ability scores were strong (i.e., a one-unit increase in either subscale was associated with a greater than one-unit increase in Mullen general cognitive ability score), however neither was statistically significant.

The COAT assessment is specifically focused on memory skills, one particular domain of neurocognitive

development. While the HOME composite score was not associated with either of the memory skills subscales, the HOME subscale measuring the caregiver's acceptance of the child with general avoidance of restriction and punishment was associated with the COAT subscale on immediate recall. It is not clear what mechanism underlies this association if it is indeed a true effect, but one hypothesis is that exposure to aggression or violence in the home could negatively impact child's capacity for short-term memory. A meta-analysis by Masson, Bussieres, East-Richard, R-Mercier, and Cellard (2015) showed that working memory was significantly affected by experiencing maltreatment, and the effect was greater in young children as compared to adults. Similarly, a US study found that familial trauma exposure was associated with poorer executive functioning in children (including working memory) (DePrince, Weinzierl, & Combs, 2009). While we cannot specifically equate a lower HOME acceptance score with child trauma exposure, this finding warrants further exploration to understand if a higher (i.e., better) HOME acceptance score manifests as a caregiver using non-violent or less aggressive forms of child discipline.

Our finding of similar neurodevelopmental outcomes across children despite HIV status is consistent with other studies among HIV-exposed but uninfected children versus HIV-unexposed children (Kerr et al., 2014). Taken as a group, a larger proportion of HIV-infected and HIV-exposed but uninfected children in low-resource settings have neurodevelopmental scores

that are 1–2SDs below the population mean, as compared to HIV-infected and HIV-exposed children from higher resource settings (Le Doare, Bland, & Newell, 2012). Within the context of poverty, the home environment may be even more important to child neurodevelopment among children affected by HIV as compared to other settings.

We hypothesized that increased levels of caregiver distress would attenuate the association between a cognitively richer home environment (represented by higher HOME scores) and child neurocognitive outcomes; however, we did not observe this effect in our sample. It may be that the challenges of poverty and the effects of living in an HIV-affected home outweigh the impact caregiver distress may have on these child outcomes (Fernald, Weber, Galasso, & Ratsifandrihamana, 2011). This is supported by results from the UK Millennium Cohort Study, which found that economic deprivation had a stronger impact on child cognitive development while maternal mental state is a stronger predictor of children's behavioral adjustment (Kiernan & Huerta, 2008).

It may be that caregivers provide less stimulating and learning opportunities to their children because of their own HIV status. Over 50% of HIV-infected adults, mostly females, in Uganda seeking health care have symptoms of depression (Nakasujja et al., 2010), which is likely to affect their socialization and interaction with the children, thus resulting in low HOME scores. Worrying in HIV-infected mothers is associated with having an HIV-infected child (Bennetts et al., 1999). This may explain why HIV-infected children and their caregivers had lower HOME scores; caregivers of HIV-infected children may exhibit interactions with their children that are “laced” with worrying and impact their HOME scores.

Our results support the view of program guidance for HIV-affected children that suggest family-oriented, home-based care with emphasis on parent-child relationships and strengthening of caregivers' abilities to provide for the child as tenants for optimal child development. Home visiting and parenting training are promising caregiver-centered programs addressing the multiple needs of HIV-infected women; bringing services and support to socially isolated and disadvantaged HIV-affected families across sub-Saharan Africa. Parenting programs directed at improving both caregiver well-being and child development represent an opportunity in low-resource settings. However, self-efficacy and inability to perform caregiver duties due to poverty, functional impairment and isolation should be assessed further as mediators of the relationship between child development and quality of caregiving.

Limitations

There are some limitations that should be noted. First, the cross-sectional nature of the data does not allow for causal interpretations of any associations. Results presented here constitute the baseline data from participants, and future analyses will include the longitudinal (follow-up) assessments. To limit the number of statistical comparisons, we relied on the composite neurocognitive measures, particularly for the Mullen general cognitive ability assessment. In doing so, we may have missed specific associations between different home environment domains and different aspects of neurocognitive development. We felt that if we looked at all possible associations we would risk finding associations by chance. With the increased power that comes with longitudinal data, we will be able to explore more of these associations in the future. We also recognize that the sample size may not have been adequate to fully assess interactions of child outcomes by caregiver distress, though the very poor p -values (greater than $p = .65$ for all outcomes) do not provide much support for trends that were missed due to sample size limitations.

Conclusions

Our primary results are supported by previous observations indicating that the child's early home environment is associated with general cognitive development. Research has shown that a negative environment during the child's first three years is linked with developmental problems including poor language development, behavior problems and deficits in school readiness (Vernon-Feagans, Garrett-Peters, Willoughby, Mills-Koonce, & The Family Life Project Key, 2012). Using measures of caregiving quality add to the understanding of the specific influences within complex home environments in the context of poverty and HIV that might impact a child's cognitive and neurodevelopment.

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