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ORIGINAL PAPER

Longitudinal Dyadic Interdependence in Depression Symptoms of Caregivers Living with HIV in Uganda and Their Dependent Children's Neurodevelopment and Executive Behavior Outcomes

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Abstract
We tested a model of dyadic interdependence in depression symptoms experienced by female caregivers living with HIV in Uganda (n = 288) and behavioral problems of their HIV-infected (n = 92) and perinatally HIV-exposed uninfected (HEU) children (n = 196). Three repeated measures of caregiver depression symptoms and child neurodevelopment and behavioral outcomes were related to their own outcomes at a previous time point (actor effects), and the outcomes of the other member of the dyad (partner effects). Caregiver depression and child behavioral problem were interdependent over the 24 months of observation. Caregiver depression at T_n predicted child's behavioral problems at T_{n+1} (coefficient = 0.1220, $SE = 0.0313$, $p < 0.01$); child behavioral problems at T_n predicted maternal depression at T_{n+1} (coefficient = 0.0984, $SE = 0.0253$, $p < 0.01$). Results suggest the importance of services addressing behavioral needs of affected children and mental health of their mothers.

Keywords HIV · Maternal depression · Interdependence · Child behavior · Dyads · Mixed modeling

Resumen
Evaluamos la interdependencia en relaciones diádicas entre síntomas de depresión en mujeres viviendo con VIH en Uganda (n = 288) y medidas de neurodesarollo y comportamiento en sus hijos no infectados pero expuestos a VIH (HEU) (n = 196). Tres mediciones repetidas de síntomas de depresión en mujeres y de neurodesarollo y comportamiento en niños estuvieron relacionadas con sus propios resultados en mediciones anteriores (efecto de actor), y con los resultados del otro miembro de la pareja (efecto de pareja). Síntomas depresivos y problemas conductuales fueron interdependientes durante los 24 meses de observación. Síntomas depresivos en mujeres en T_n predijeron problemas conductuales en el niño en T_{n+1} (coeficiente = 0.1220, SE = 0.0313, p < 0.01); problemas conductuales en el niño en T_n predijeron depresión en mujeres en

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T_{n+1} (coeficiente = 0.0984 , SE = 0.0253, $p < 0.01$). Los resultados sugieren la importancia de servicios que se enfoquen en atender problemas conductuales y de salud mental materna.

Palabras clave VIH · Depresión materna · Interdependencia · Comportamiento infantil · Modelaje mixto

Introduction

Globally, HIV+ women are more likely to experience depressive symptoms than their uninfected peers (19.4 vs. 4.8%) [1–4]. Stigma/discrimination, social isolation [5], and long-term physical discomfort, among others, have been attributed to this increase [6]. Observational and longitudinal studies in low- and middle-income countries (LMIC) suggest that depression in mothers or primary caregivers can contribute to multiple early child growth and developmental problems including poor nutritional status, health and compromised socio-emotional behaviour [7–10]. In high-income countries, longitudinal studies show that persistent and severe depression symptoms in caregivers are associated with behavioural problems [11–13], and lower school performance in young children [14].

A limitation of the current literature is the assumption of a linear and unidirectional association between maternal depression and child outcomes. However, from a systems perspective, actions of individuals within a family system are interrelated [15], and patterns in families, including between mothers and children, are reciprocal as opposed to linear [16]. Empirically, longitudinal associations among mothers' and children's outcomes are unclear. On one hand, mothers' outcomes at a given time point may contribute to children's later outcomes. For example, conduct problems can contribute to maternal depressive symptoms, by placing a considerable burden on mothers and challenging parental self-efficacy [17]. More specifically, mothers may feel they have little control over their child's behavior [18] or that they are to blame for their child's disruptive behavior [19]. On the other hand, children with behavioral problems or delayed development may be more stressful to parents, which may lead to the onset or exacerbation of depression in mothers according to the stress generation hypothesis [20]. For example, one study found that children's impaired functioning was associated with more maternal stress, which was associated with additional maternal distress and caregiving burden [21]. Thus, children's outcomes may also influence mother–child relationship quality and maternal mental health over time. Understanding the relationship between maternal distress and child behavior in the context of HIV is critical because children with HIV and HEU are at particular risk for poor development [22].

The actor-partner interdependence model (APIM) is used to analyze the influence that members of a dyad have on each other, identifying and comparing different types of dyadic patterns that characterize interpersonal influences of actors and partners [23]. Hence, analysis of dyadic data within the APIM can be characterized, to a large extent, as studying of non-independence or inter-dependence [24]. Cross-sectional versions of APIM have been used in many populations [25, 26] but not with people living with HIV, while analyses using longitudinal APIM are a new recent addition to the dyadic literature [27–30].

Based on past research, we hypothesized the presence of (a) Actor effects for child and caregiver (i.e., child's or caregiver's outcomes at a previous time point would be predictive of that person's outcome at the next time point). (b) Partner effects of caregiver's depression symptoms on child outcome (i.e. caregiver's depressive symptoms at a previous time point would be predictive of child outcome at the next time point). (c) Partner effects of child's cognition/behavior on caregiver's depression (i.e. child's cognition/behavior at a previous time point would be predictive of caregiver's distress at the next time point).

Methods

This is a secondary analysis of longitudinal data collected from caregiver-child dyads enrolled between March 2012 and April 2014 in a randomized controlled trial (RCT) of a parenting training intervention (mediational intervention for sensitizing caregivers, MISC) [31, 32], in Tororo, Uganda. The MISC RCT included caregivers with a child living with HIV (n = 118) or HIV-exposed uninfected (HEU) child (n = 164). Eligibility criteria included that a caregiver was female, aged 18 or older, and be willing and able to participate in a year of MISC training. Women were excluded if they had a severe mental illness or disability that would prevent engagement in training. Caregiver was not defined as the biological mother of the child, but rather as the adult predominantly taking care of the child. The child had to be between 2 and 5 years old without having experienced a prior illness or injury that could have caused a central nervous system insult (including a serious birth complication or an episode of severe malnutrition, cerebral malaria, bacterial meningitis or encephalitis).

Child neurodevelopment was assessed with the Mullen Scales of Early Learning (MSEL), a comprehensive, performance-based test with 124 items measuring specific domains of gross motor, fine motor, visual reception, receptive language, and expressive language. Four scales (visual

reception, fine motor, receptive language, and expressive language) are combined to yield the early learning composite score (MELC). The MELC serves as a general measure of fluid intelligence thought to underlie cognitive ability in general [33]. Age-normed scores (T-scores) were obtained from normative tables in the MSEL administration manual. The MSEL has previously been adapted for use with young children in rural Uganda and has proven to be a sensitive and useful measure in this population [34]. Cronbach's alpha for the MSEL was 0.84.

Each child's caregiver was interviewed with the Behavior Rating Inventory of Executive Function (BRIEF) for preschool children (1.5–5 years). The BRIEF evaluates executive function behaviors in children through 86-items that cover 6 primary scales (inhibit, self-control, shift, emotional control, working memory and plan/organize) that can be combined into 3 broad indices (inhibitory-self-control, flexibility and emergent metacognition) and a global executive composite score [35]. BRIEF T-scores provide information about the child's individual scores relative to the scores of other respondents from a standardized sample, by age. High scores on the BRIEF suggest a higher level of dysfunction in a specific domain of executive functions. Publisher copyright permission was obtained for the BRIEF and was translated into the three local languages (forward and backward translation) as specified by the publisher (PAR, Inc.), and the final version was approved by one of the test authors (Peter Isquith). Cronbach's alpha for the BRIEF was 0.89.

Caregivers' depressive symptoms were assessed with the Hopkins Symptom Checklist-25 (HSCL-25) [36, 37], which has 15 items assessing depression. The HSCL-25 depression scale has been adapted and validated among adults in HIV-affected Ugandan communities [38]. Caregivers were asked to report how frequently they experienced 15 specific depressive symptoms in the prior 2 weeks using a Likert scale ranging from 0 (not at all) to 3 (all the time). All 15 items were averaged to generate a depression symptom score. Cronbach's alpha for the HSCL-25 depression subscale was 0.73.

Child-caregiver dyads living in Tororo District or nearby areas of Busia District in Eastern Uganda were recruited from: (1) health centers in these districts with participating PEPFAR-sponsored prevention of mother to child transmission programs (AIDS support organizations or TASO), and (2) from a concluding RTC of anti-retroviral treatment (PROMOTE Study 1) at the infectious disease research collaboration (IDRC) in Tororo. After administering informed consent, child testing and caregiver questionnaires were done in one of three languages spoken in Eastern Uganda (Dophadola, Ateso, or Luganda) in a private, quiet setting in the project's office or/and at their homes at four time-points: baseline (pre-intervention), 6-months (mid-intervention), 12-months (immediate post-intervention) and 24 months after enrollment. 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.

Descriptive statistics were obtained for between- and within-dyad variables at baseline. All scores for the outcome measures (caregiver depression symptoms, BRIEF composite, MSEL composite) were converted to z-scores using baseline means and standard deviations for the respective variables.

The longitudinal analysis of dyadic interdependence was conducted using the APIM [24, 39]. Actor effects reflected the association of scores of the same person at two time points, e.g., caregiver depression at time 1 predicting caregiver depression at time 2, and child BRIEF at time 1 predicting child BRIEF at time 2. Partner effects reflected the associations of one person's score at one point with the other person's score at the next time point, e.g., caregiver depression at time 1 predicting child BRIEF at time 2 and child BRIEF at time 1 predicting caregiver depression at time 2. In estimation of these effects, nesting of individuals within dyads and repeated measurements for each dyad were accounted for by specifying the corresponding random effects in the linear mixed effects (LME) models. The LME models used three repeated measures of each outcome (6, 12, and 24 months) for both members of the dyad. The LME models generalize classical analysis of repeated measures and allow for data missing at random, structured covariance, and time-varying covariates. Analyses were conducted in the MIXED procedure in SAS 9.4 [40] specifying a heterogeneous autoregressive (order 1) covariance structure that assumes unequal covariances between observations on the same dyad, decreasing toward zero with increasing lag. We fit two separate models, one for caregiver's depression symptoms and child's BRIEF score, and one for caregiver depression and child' MSEL score. To reflect the design of the studies that produced data for this analysis, we controlled for the interventions received by dyads (MISC or treatment as usual, TAU). The other between-dyad variables adjusted for in the analysis were child's HIV status (HIV-infected or HEU) and wealth group of the household. Within dyads effects included role (caregiver, child), the actor effects for caregiver and child, and the partner effects emanating from caregiver and child. Actor and partner effects were specified as time-varying lagged effects (e.g., T_n predicting T_{n+1}). Because of lagging, the child and caregiver outcomes at 6, 12, and 24 months were the dependent variables, whereas outcomes at baseline, 6, and 12 months were used as predictors.

For the depression-BRIEF analyses, both z-scores were in the same direction (higher is worse) and were used as such in the analysis. To ensure that within-dyad effects can be

interpreted in a meaningful way, for the analysis of depression-MSEL, maternal depression scores were reversed so that higher score indicated less depression. As a result, in the depression-MSEL analysis, higher score reflected better outcome.

Results

Socio-demographic characteristics of child-caregiver dyads at baseline are presented in Table 1. The majority of caregivers were biological mothers and were on ART. Among children, 51% were boys, and 49% were girls, with a 2–5 age range at baseline. The majority of children were perinatally HIV-exposed uninfected (HEU) (68%), while 32% were born HIV-infected. The descriptive statistics for caregiver and child outcomes at all time points are in Table 2.

In the APIM analysis of caregiver depression and child BRIEF (Table 3), the actor effects were significant: caregiver depression symptoms at Tn predicted caregiver depression symptoms at Tn + 1 (coefficient = 0.62, *SE* = 0.03, p < 0.001); child behavioral problems at Tn predicted child behavioral problems at Tn + 1 (coefficient = 0.68, *SE* = 0.03, p < 0.001). In addition, caregiver depression symptomatology and child executive functioning (EF) behavior problems as measured with the BRIEF were interdependent over the 24 months of observation. Over and above actor effects, both partner effects were significant. Caregiver depression symptoms at T_n predicted child's EF behavior problems at T_{n+1} (coefficient = 0.12, *SE* = 0.03, $p < 0.001$); child EF behavioral problems at T_n predicted caregiver depression symptoms at T_{n+1} (coefficient = 0.09, *SE* = 0.03, $p < 0.001$).

In the APIM analysis of caregiver depression symptomatology and child MSEL composite score (Table 4), the actor effects were significant: caregiver depression symptoms at Tn predicted caregiver depression at Tn + 1 (coefficient = 0.80, *SE* = 0.03, p < 0.001); child MSEL composite at Tn predicted child MSEL composite at Tn + 1 (coefficient = 0.72, *SE* = 0.03, p < 0.001). However, none of the partner effects were significant.

Table 1 Socio-demographic characteristics of caregiver-child dyads living with HIV in Tororo, Uganda (n = 288)

	Caregiver N (%) or mean (St Dev)	Child N (%) or mean (St Dev)
Between-dyad characteristics		
Marital status		
Married	199 (69%)	
Single/divorced	40 (14%)	
Widowed	49 (17%)	
Education level		
None	56 (19%)	
Primary	190 (66%)	
Secondary	39 (13%)	
Technical	3 (1%)	
Employment status		
Farmer	235 (82%)	
Trades/small business/ employee	28 (10%)	
Professional	12 (4%)	
Unemployed/house wife	13 (4%)	
Relationship to child		
Biological mother	281 (98%)	
Other	7 (2%)	
Wealth group		
Lowest 20%	41 (14%)	
Middle 60%	193 (67%)	
Top 20%	53 (18%)	
On ARV	232 (81%)	
Experimental group		
MISC	139 (48.26)	
UCOBAC	149 (51.74)	
HIV status		
Infected		92 (32%)
Exposed uninfected		196 (68%)
Within-dyad characteristics		
Age	33.5 (5.81)	2.9 (0.64)
Sex		
Male	0 (0%)	148 (51%)
Female	288 (100%)	140 (49%)

Discussion

In this study, we aimed to better understand the complex pathways through which maternal depressive symptoms and child behavior and development are interrelated. Controlling for actor effects, we found that both partner effects were significant; caregiver depression and child behavioral problems were interdependent over the 24 months of observation. These findings are supported by qualitative accounts from Ugandan caregivers of young children describing not only how their emotions and behaviors impacted their children, but also how the multifaceted effects of child behavior have a bearing on their mental health [41].

Mechanisms proposed to explain the co-occurrence of children's behavior problems and maternal depressive symptoms include genetic vulnerability and intergenerational transmission [42], family characteristics such as socio-economic disadvantage and its accompanying factors [43], and depression symptoms curtailing caregiving availability and disposition [44]. Another leading explanation of

Table 2 Descriptive statistics for maternal depression, child's BRIEF and MSEL composite at 4 time points

	Time 1, N mean (SD)	Time 2, N mean (SD)	Time 3, N mean (SD)	Time 4, N mean (SD)
Maternal depression	288 0.99 (0.50)	271 0.96 (0.55)	258 0.89 (0.54)	248 0.91 (0.58)
Child's BRIEF GEC	288 66.26 (13.96)	269 61.81 (14.62)	257 59.50 (14.35)	258 56.56 (13.47)
Child's MSEL	288 71.45 (14.90)	269 70.26 (14.71)	260 69.57 (13.19)	259 65.37 (11.80)

Table 3 Longitudinal APIM for child's BRIEF and caregiver depression: coefficients, standard errors, and tests of significance

	Coefficient (SE)	t	p
Between-dyad variables			
Intervention group: TAU	− 0.11 (0.03)	− 2.89	0.004
Intervention group: MISC (reference)	–	–	–
Child HIV+	0.01 (0.04)	0.29	0.772
Child HEU (reference)	–	–	–
Wealth lowest 20%	− 0.04 (0.05)	− 0.73	0.466
Wealth middle 60%	− 0.02 (0.04)	− 0.50	0.630
Wealth top 20% (reference)	–	–	–
Within-dyad variables			
Caregiver	0.23 (0.04)	5.79	< 0.001
Child(reference)	–	–	–
Caregiver actor effect	0.62 (0.03)	19.79	< 0.001
Child actor effect	0.68 (0.03)	26.91	< 0.001
Caregiver→child partner effect	0.12 (0.03)	3.90	< 0.001
Child→caregiver partner effect	0.09 (0.03)	3.88	< 0.001

Table 4 Longitudinal APIM for child's MSEL and caregiver depression: coefficients, standard errors, and tests of significance

	Coefficient (SE)	t	p
Between-dyad variables			
Intervention group: TAU	− 0.01 (0.03)	− 0.05	0.962
Intervention group: MISC (reference)	–	–	–
Child HIV+	0.03 (0.03)	1.01	0.351
Child HEU (reference)			
Wealth lowest 20%	− 0.08 (0.05)	− 1.64	0.102
Wealth middle 60%	− 0.06 (0.04)	− 1.45	0.149
Wealth top 20% (reference)			
Within-dyad variables			
Caregiver	0.23 (0.03)	6.63	< 0.001
Child(reference)			
Caregiver actor effect	0.70 (0.03)	25.18	< 0.001
Child actor effect	0.72 (0.02)	34.66	< 0.001
Caregiver→child partner effect	0.01 (0.03)	0.18	0.863
Child→caregiver partner effect	0.01 (0.02)	0.73	0.463

interdependence from the psychological sciences is known as emotional contagion [45–47]. Emotional contagion is theorized to result from social interactional processes whereby people match each other's nonverbal communication behaviors that play a role in generating specific emotional experiences [47, 48]. The process of emotional contagion underwrites a compelling predication that child's adverse behavioral outcomes can have a pathogenic effect on caregiver psychological distress and vice versa.

Specifically, exposure to maternal depressive symptoms in the first 3 years of life has been found to be particularly critical for executive functioning (EF) behavior development; as maternal depression symptoms increase, parenting behaviors promoting children's sustained attention and EF tend to decline [49]. Although the exact mechanism is still elusive, studies in high income countries have shown that depressed mothers frequently display hostile and unresponsive behaviors that can affect the development of basic cognitive skills in children, including EF [49–51].

The lack of actor-partner effects between caregiver's depressive symptomatology and a performance-based measure such as the MSEL suggests that neurodevelopment before the age of 5 may not be as influenced by caregivers' psychological well-being as behavioral traits. These findings are consistent with a previous study among children infected with HIV and HEU in Zimbabwe, Uganda, Malawi and South Africa [52]. Studies from India, Bangladesh [8], South Africa [53] and Brazil [54] have found that perinatal depression is associated with negative clinical and developmental outcomes in children. However, other studies have found no association [55, 56]. Important methodological differences may account for these inconsistencies and include different depression assessment instruments, varying cut-offs used to determine associations, variations in cognitive assessments employed, small samples and different age ranges.

Hastings (2002) described the factors related to the child behavior-parent stress relationship in his stress model for families of children with disabilities [57]. Understanding these maternal factors may help interventionists reduce maternal stress as part of a child-focused programs and open another avenue to enhance outcomes. As parenting stress poses an increased risk for maternal depression, considering parental appraisal variables may enhance outcomes for parents and children in intervention programs. In the context of interventions, maternal depression may be a barrier to engage in, or successfully complete, child-focused programs, thereby limiting the opportunity for children to benefit from these programs [44]. Further, maternal depression may increase or decrease depending on improvements, or lack thereof, in children's cognition and behavior.

A few limitations should be noted. Depression symptoms were collected by self-report and thus social desirability bias may have led to underreporting, or similarly worded items may have influenced women to respond consistently regardless of actual experience. However, this effect is likely to have remained consistent over time and thus provided acceptable assessment of symptom change. Use of secondary data limits the interpretation of findings since data are constrained by the original study design. Interventions received by the dyads may have affected the degree of inter-dependence. While we controlled for interventions received in the analysis, there was no control group. The findings from APIM reflect associations and not necessarily causal relationships. However, within longitudinal APIM we controlled for within-dyad and within-person associations over time, and estimated both longitudinal actor and partner effects using rigorous methods.

Despite limitations, the actor and partner effects among caregivers and children presented here highlight the value of integrating interventions for at-risk families. Programs that simultaneously provide services to mothers and their young children by combining strategies that address maternal symptoms of depression and child behavior have proven effective and may be able to produce positive outcomes over time [31, 58]. In this sense, understanding the reciprocal connections between mother's behavioral health and that of her child may be crucial inputs in the design and implementation of strategies addressing maternal and infant morbidity.

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