

Executive Functioning, Barriers to Adherence, and Nonadherence in Adolescent and Young Adult Transplant Recipients

Ana M. Gutiérrez-Colina,¹ MS, Cyd K. Eaton,¹ MS, Jennifer L. Lee,² PhD, Bonney Reed-Knight,² PhD, Kristin Loiselle,³ PhD, Laura L. Mee,⁴ PhD, Julia LaMotte,¹ BS, Rochelle Liverman,⁵ PHARM D, and Ronald L. Blount,¹ PhD

¹Department of Psychology, University of Georgia, ²Department of Pediatrics, Emory University School of Medicine, ³Cincinnati Children's Hospital Medical Center, ⁴Department of Psychiatry and Behavioral Science, Emory School of Medicine, and ⁵Children's Healthcare of Atlanta

All correspondence concerning this article should be addressed to Ana M. Gutiérrez-Colina, MS, Department of Psychology, University of Georgia, 125 Baldwin St. Athens, GA 30602, USA. E-mail: acolina@uga.edu

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Abstract

Objective To evaluate levels of executive functioning in a sample of adolescent and young adult (AYA) transplant recipients, and to examine executive functioning in association with barriers to adherence and medication nonadherence. **Method** In all, 41 caregivers and 39 AYAs were administered self- and proxy-report measures. **Results** AYA transplant recipients have significant impairments in executive functioning abilities. Greater dysfunction in specific domains of executive functioning was significantly associated with more barriers to adherence and greater medication nonadherence. **Conclusion** AYA transplant recipients are at increased risk for executive dysfunction. The assessment of executive functioning abilities may guide intervention efforts designed to decrease barriers to adherence and promote developmentally appropriate levels of treatment responsibility.

Key words: adherence; adolescents and young adults; barriers; executive functioning; transplant.

Pediatric transplantation has become the treatment of choice for an increasingly large number of chronically ill patients with organ failure and end-stage disease. In 2014, a total of 1,795 pediatric patients received an organ transplant in the United States (OPTN, 2014). The Organ Procurement and Transplantation Network has documented a growing number of pediatric transplant candidates over the past several years. Unfortunately, there continues to be a significant imbalance between the supply of available organs and the number of patients wait-listed for transplantation (OPTN, 2012 annual report). This shortage of organs creates challenges and dilemmas regarding fair organ allocation and highlights the tremendous

responsibility that transplant centers, recipients, and their families undertake. Caring for a transplanted organ involves lifelong adherence to complex medical regimens. Failing to follow medical advice as prescribed can have serious consequences for the health of the transplanted organ and the life of the recipient (Falkenstein, Flynn, Kirkpatrick, Casa-Melley, & Dunn, 2004; Fredericks, Lopez, Magee, Shieck, & Oipari-Arrigan, 2007).

Many patients with solid organ transplants struggle to follow medical regimens as prescribed (Dew et al., 2009). Among adolescents, rates of nonadherence have been documented to average 43%, compared with 22% in younger children (Dobbels et al.,

2010). Nonadherence has been linked to various negative medical outcomes including graft loss, hospitalizations, need for additional biopsies, and death (Falkenstein et al., 2004; Fredericks et al., 2007). In addition to higher rates of morbidity and mortality, nonadherence has been associated with decreased health-related quality of life, higher health care utilization, and higher health expenditures (Fredericks et al., 2007; Pinsky et al., 2009).

Given the high rates of nonadherence and associated consequences, researchers have increasingly worked to identify factors related to nonadherence, especially factors that can be reliably and validly assessed. Significant progress has been made in the identification of demographic (Dew et al., 2009), medical (Tucker et al., 2002), and psychosocial (Rapoff, 2010) factors related to nonadherence, though no research to date has examined how cognitive and neuropsychological factors relate to medication nonadherence in pediatric transplant recipients. Executive functioning (EF) is a neuropsychological factor encompassing many of the higher-level cognitive skills (e.g., organization, planning, self-monitoring, problem solving) required to manage complex tasks, such as following a medical regimen. In youth with Type 1 diabetes, caregiver-report of children's EF has been shown to be associated with children's adherence to their medical regimen (Bagner, Williams, Geffken, Silverstein, & Storch, 2007) and to play a larger role in self-management than other cognitive abilities (Alioto & Janusz, 2004). In children with spina bifida, higher levels of caregiver-reported EF abilities have also been associated with greater adherence even after controlling for the effects of age, intelligence quotient (IQ), and level of other cognitive abilities (O'Hara & Holmbeck, 2013).

Deficits in EF skills have the potential to impact adherence in adolescents and young adults (AYAs) by making barriers more difficult to overcome. Barriers have been previously associated with lower levels of treatment adherence in child and adolescent populations (Modi & Quittner, 2006). Barriers have also emerged as one of the proximal factors associated with nonadherence among pediatric solid organ transplant recipients (Simons, McCormick, Devine, & Blount, 2010). Adherence barriers related to regimen adaptation issues in particular, including running out of pills, forgetting to pick up a prescription before medicines run out, or having a hard time sticking to a fixed medication schedule, are especially likely to be associated with metacognitive domains of EF given that these barriers are related to self-monitoring, planning, and organizational skills. Similarly, AYAs with overall EF difficulties may be more likely to experience greater barriers related to parent reminders, as those patients struggling with executive deficits will also be the ones needing more reminders to take medications as prescribed.

The role of EF may be particularly critical during adolescence and young adulthood. During this developmental period, the brain and cognition are still developing, EF skills are underdeveloped in comparison with adults, and youth begin to assume increasing responsibility for self-managing their medical condition (Reed-Knight, Blount, & Gilleland, 2014). Decreased caregiver involvement and increased AYA responsibility for medical management is appropriate for typically developing patients as they get older. However, premature granting of autonomy can negatively impact adherence (Psihogios, Kolbuck, & Holmbeck, 2015). Overall, the literature suggests that a patient's journey through adolescence and into adulthood may be a particularly difficult period for overcoming barriers to adherence and that developmentally appropriate levels of caregiver involvement and patient responsibility are critical for optimal adherence (Reed-Knight et al., 2014). Thus far, no formal guidelines exist to direct developmentally appropriate allocation of treatment responsibility.

Understanding the role of EF in pediatric transplant recipients is particularly important owing to their vulnerability for cognitive insults resulting from neurocognitive side effects of prescribed pharmacotherapies. Anti-rejection medications, such as tacrolimus, have been associated with lower cognitive functioning compared with controls (Martinez-Sanchis et al., 2011), and high doses of steroids have been associated with poorer short-term memory and more problems with EF (Mrakotsky et al., 2005). EF may also be affected as a result of a patient's underlying medical condition. End-stage renal failure, for example, is one of the underlying chronic illnesses leading to kidney transplantation and has been associated with neurocognitive developmental deficits (Brouhard et al., 2000).

The current study sought to investigate EF abilities among AYA transplant recipients and to examine EF, as it relates to barriers to adherence and medication nonadherence. The following hypotheses were examined: (1) AYA transplant recipients will exhibit significantly more deficits in EF skills compared with norm-referenced scores, (2) greater executive dysfunction will be significantly associated with more barriers to adherence as reported by caregivers and AYAs, and (3) greater executive dysfunction will be significantly associated with greater medication nonadherence as reported by caregivers and AYAs.

Method

Participants

In all, 41 caregivers and 39 AYAs with a solid organ transplant participated in this study. Inclusion criteria specified that AYAs (1) received a heart, liver, or kidney transplant at least 1 year before enrollment in the

study, (2) were between the ages of 12 and 21 years, and (3) spoke English fluently. AYAs with developmental delay, as reported by the caregiver or as indicated in the medical record, were excluded from the study. Six families declined to participate owing to lack of interest.

Procedure

This study is part of the baseline data from a larger longitudinal investigation examining predictors of medication nonadherence. All study procedures were in full compliance with the Health Insurance Portability and Accountability Act (HIPAA) and approved by the institutional review boards of the participating institutions. Eligible families were identified before their follow-up medical visit by a trained research assistant. Families were approached by a study investigator during their medical appointment. Interested families were provided with information about the study and any questions were answered before enrollment. Informed consent, assent, and HIPAA release were obtained. Participating dyads completed paper-and-pencil measures independently. A trained interviewer administered adherence semi-structured interviews during or after the medical visit. All participants received a \$10 gift card as compensation for their time.

Measures

Participants completed a brief sociodemographic questionnaire. Medical data (e.g., time since transplant) were collected via retrospective medical chart review.

Behavior Rating Inventory of Executive Function

Caregiver-report of EF was included in this study (Gioia, Isquith, Guy, & Kenworthy, 2000b). Proxy-report assessment of EF has been shown to be valid and reliable (Gioia et al., 2000b). The Behavior Rating Inventory of Executive Function (BRIEF) is a caregiver-report, 86-item measure for children 8–18 years used to assess different domains of EF. Caregivers are asked to endorse on a 3-point scale ranging from *never* to *often* the extent to which their child engaged in a certain behavior over the previous 6 months. A total of eight different subscales comprise the BRIEF, including plan/organize, monitor, emotional control, inhibit, shift, initiate, working memory and organization of materials. These subscales are organized into two broad indices: the Metacognition Index (MCI) and the Behavioral Regulation Index (BRI), both of which constitute a total score for EF abilities called the Global Executive Composite (GEC) score. Age- and gender-based T-scores were used. Higher scores on the BRIEF subscales and indices indicate greater executive dysfunction. Convergent

validity for this measure has been demonstrated to be good (Gioia et al., 2000b). In the current study, Cronbach's alphas for the GEC, MCI, and BRI scores were $\alpha = .97$, $\alpha = .97$, and $\alpha = .93$, respectively.

Medication Adherence Measure

The Medication Adherence Measure (MAM) is a semi-structured interview used to assess patient adherence to their medication regimen over the previous 7 days (Zelikovsky & Schast, 2008). AYAs and caregivers are independently interviewed and report on the names and dosages of prescribed medications for the patient, as well as the number of prescribed medications that were missed or taken late. Medication nonadherence is calculated by dividing the number of missed/late doses by the total number of prescribed doses that week, and then calculating a percentage. The MAM has been shown to have adequate predictive (Simons et al., 2010) and convergent (Dobbels et al., 2010) validity. In this study, nonadherence was calculated as the average percent across all missed or late prescription medications.

Adolescent Medication Barriers Scale

The Adolescent Medication Barriers Scale (AMBS) is a 17-item measure used to assess AYAs' self-report of their own barriers to medication adherence (Simons & Blount, 2007). AYAs responded to a 5-point Likert scale ranging from *strongly disagree* to *strongly agree*, and endorsed the extent to which different barriers got in the way of medication-taking. Barriers are classified into three subscales including: (1) regimen adaptation/cognitive issues, (2) disease frustration/adolescent issues, and (3) ingestion issues. The psychometric properties of the AMBS have been well-established. Criterion-related validity of the AMBS has been demonstrated to be strong (Simons & Blount, 2007). In the current study, Cronbach's alphas for the Total Barriers score and the three AMBS subscales were $\alpha = .90$ (total), $\alpha = .84$ (disease frustration/adolescent issues), $\alpha = .72$ (ingestion issues), and $\alpha = .61$ (regimen adaptation/cognitive issues).

Parent Medication Barriers Scale

The Parent Medication Barriers Scale (PMBS) is a 16-item measure used to assess caregivers' report of their children's barriers to adherence (Simons & Blount, 2007). Caregivers responded to a 5-point Likert scale ranging from *strongly disagree* to *strongly agree*, and endorsed the extent to which different barriers get in the way of their children's adhering to their medication regimen. Barriers are classified into four different factors including: (1) regimen adaptation/cognitive issues, (2) disease frustration/adolescent issues, (3) ingestion issues, and (4) parent reminder, which is a single item (i.e., "My child relies on me to remind him

Table I. Demographic Information

Variable	AYAs		Caregivers	
	N = 39		N = 41	
	M	SD	M	SD
Age (years)	16.21	1.63	45.03	8.10
	Frequency	%	Frequency	%
Sex				
Male	22	56.40	3	7.30
Female	17	43.60	36	87.80
Ethnicity				
Caucasian	22	56.40	23	56.10
African American	11	28.20	9	22.00
Asian	3	7.70	3	7.30
Hispanic	0	0	1	2.40
Biracial	3	7.70	2	4.90
Type of health insurance				
Private	12	30.80	–	–
Medicare/Medicaid	17	43.60	–	–
Multiple types	8	20.50	–	–
Other	1	2.60	–	–
Family income				
<\$10,000	–	–	3	7.30
\$10,000–24,999	–	–	5	12.20
\$25,000–49,999	–	–	14	34.10
\$50,000–74,999	–	–	5	12.20
\$75,000–99,999	–	–	4	9.8
\$100,000+	–	–	8	19.50
Prefer not to report	–	–	2	4.90
Caregiver education level				
High school/GED	–	–	8	17.90
Some college	–	–	9	22.00
Associate's degree	–	–	5	12.20
Bachelor's degree	–	–	7	17.1
Advanced degree	–	–	9	22.00
Caregiver marital status				
Married	–	–	24	58.50
Single	–	–	5	12.20
Divorced	–	–	9	22.20
Partnered	–	–	1	2.40

Note. AYA = adolescent and young adult; GED = General Educational Development.

or her to take his/her medication"). Criterion-related validity for this measure is strong (Simons & Blount, 2007). In the current study, Cronbach's alphas for the Total Barriers score and the PMBS subscales were $\alpha = .84$ (total), $\alpha = .67$ (disease frustration/adolescent issues), $\alpha = .65$ (regimen adaptation/cognitive issues), $\alpha = .29$ (ingestion issues). Because of low reliability, the ingestion issues subscale was excluded from data analyses.

Data Analytic Plan

All data analyses were conducted using IBM SPSS Statistics, Version 21. Descriptive statistics were calculated for all study variables. Independent sample *t* tests, Wilcoxon–Mann Whitney tests, or Chi-Square tests were used depending on the nature of the variable (e.g., continuous, ordinal, dichotomous) to test for significant

differences between the demographics of those who enrolled in the study and those who declined to participate. One-way analysis of variance was used to examine whether significant differences existed between organ groups on measures of EF and nonadherence.

Spearman rank-order, point-biserial or Pearson product-moment correlations were used depending on the nature of the variables (e.g., ordinal, dichotomous, continuous) to examine associations between the primary construct of interest (i.e., EF) and demographic variables (i.e., age, race, gender, family income, caregiver education level). Significant covariates with EF were used in subsequent correlational analyses. Because the BRIEF is a norm-referenced test, one-sample *t*-test analyses were conducted to compare T-scores in the current sample with 50, which is the mean score of the normative sample used to derive T-scores for the BRIEF.

Partial correlational analyses were conducted to examine associations between the BRIEF and barriers to adherence. Owing to the positive skewness of the nonadherence data and the overrepresentation of zeros, a square root transformation was used. This is a preferable approach to log transformation because a log value of zero cannot be obtained. Given that the nonadherence data violated the normality assumption of parametric tests even after square root transformation, the nonparametric Spearman's rho coefficient was used to measure associations between the BRIEF and the original nonadherence data. Only complete caregiver-dyads were used to conduct correlational analyses between caregiver- and AYA-reported data. To limit the number of total comparisons and reduce the probability of Type I error, only the BRIEF GEC, BRI, and MCI scores were examined in planned analyses.

Results

Participant Characteristics

A total of 41 caregivers and 39 AYAs participated in this study. AYAs included 17 females and 22 males, who ranged in age from 12 to 19 years ($M = 16.21$; $SD = 1.63$). Of the AYAs enrolled in the study, 16 received a heart transplant, 12 received a liver transplant, and 11 received a kidney transplant. The medical profile of these AYAs was heterogeneous and included a wide range of prescribed medications, as well as time since transplantation ($M = 9.08$ years ago; $SD = 5.87$; range = 1.44–18.44 years). Participating caregivers were 45.03 years of age on average ($SD = 8.10$; range = 34–64 years). A detailed description of participant demographics is presented in Table I. No significant differences were found between organ groups or between those who agreed to participate and those who declined with regards to measured participant characteristics.

Table II. Executive Functioning in AYA Transplant Recipients

BRIEF domain	Mean <i>T</i> -score (<i>SD</i>)	<i>T</i> -score range	% clinical ^a	Mean difference (95% CI)	<i>t</i>	<i>p</i>	Cohen's <i>d</i> ^b
Global Executive Composite	56.49 (12.49)	36–87	24.40	6.49 (2.51 to 10.46)	3.30	.002	0.57
Behavioral Regulation Index	53.66 (12.15)	37–81	24.40	3.66 (–0.18 to 7.49)	1.93	.061	0.33
Inhibit	52.46 (13.18)	35–88	17.07	2.46 (–1.70 to 6.62)	1.20	.238	0.21
Shift	55.12 (12.58)	38–88	29.27	5.12 (1.15 to 9.09)	2.60	.013	0.45
Emotional control	52.59 (11.11)	37–80	19.51	2.59 (–0.92 to 6.09)	1.49	.144	0.25
Metacognition Index	56.83 (12.59)	37–88	31.71	6.83 (2.85 to 10.80)	3.48	.001	0.60
Initiate	57.88 (12.98)	36–83	34.15	7.88 (3.78 to 11.97)	3.88	.000	0.68
Working memory	59.17 (12.61)	40–87	34.15	9.17 (5.19 to 13.15)	4.66	.000	0.81
Plan/organize	56.02 (11.24)	38–77	29.27	6.02 (2.48 to 9.57)	3.43	.001	0.57
Organization materials	53.95 (11.22)	34–72	21.95	3.95 (0.64 to 8.10)	2.26	.030	0.37
Monitor	53.73 (14.71)	24–91	19.51	3.73 (–0.64 to 8.10)	1.73	.092	0.30

Note. BRIEF = Behavior Rating Inventory of Executive Function; AYA = adolescent and young adult.

^a*T*-score ≥ 65 .

^bSmall effect size: $d = 0.20$, medium effect size: $d = 0.50$, large effect size: $d = 0.80$.

Preliminary Analyses

Preliminary correlational analyses revealed that only age was significantly associated with GEC and BRI scores (GEC: $r = -.37$, $p = .02$; BRI: $r = -.35$, $p = .02$), with younger youth demonstrating more executive dysfunction. Because age was the only demographic variable significantly associated with BRIEF scores, this variable was used as a covariate in subsequent correlational analyses to statistically account for its effect on the primary construct of interest. Caregiver-reported nonadherence ranged from 0 to 42.86% ($M = 7.41\%$; $SD = 12.63\%$). AYA-reported nonadherence ranged from 0 to 57.14% ($M = 8.03\%$; $SD = 13.22\%$). No significant differences were found between organ groups on measures of executive dysfunction (BRIEF GEC: $F(2,38) = 0.83$, $p = .45$; BRIEF MCI: $F(2,38) = 1.57$, $p = .22$; BRIEF BRI: $F(2,38) = 0.15$, $p = .86$) or nonadherence (caregiver-reported nonadherence: $F(2,38) = 1.08$, $p = .35$; AYA-reported nonadherence: $F(2,36) = 1.21$, $p = .31$).

Executive Dysfunction in AYA Transplant Recipients

T-test analyses revealed that compared with norm-referenced scores of healthy peers, AYAs with an organ transplant experience, on average, significantly greater caregiver-reported dysfunction across a number of BRIEF domains (Table II), including GEC, MCI, shift, initiate, working memory, plan/organize, and organization of materials. In addition, approximately 25% of the sample exhibited clinically significant levels of executive dysfunction (BRIEF GEC). In terms of composite scores, results indicated clinically significant levels of dysfunction in metacognition (31.71%) and behavioral regulation (24.40%) domains. Examination of Cohen's d revealed effect sizes ranging from small to large. Small and medium effect sizes were found for the BRI and MCI composite scores, respectively. A medium effect size was found for the GEC score. Mean scores on the BRIEF Total

and Index scores were not significantly different between kidney (GEC $M = 53.91$; BRI $M = 51.91$; MCI $M = 54.18$), liver (GEC $M = 54.93$; BRI $M = 54.29$; MCI $M = 54$), and heart (GEC $M = 59.63$; BRI $M = 54.31$; MCI $M = 61.13$) transplant recipients.

Correlates of Executive Dysfunction in AYA Transplant Recipients

Is Executive Dysfunction Correlated With Caregiver-reported Barriers to Adherence?

As shown in Table III, partial correlations controlling for age revealed that caregiver-reported BRIEF GEC and MCI scores were significantly and positively correlated with caregiver-reported barriers including the parent reminder and regimen adaptation/cognitive issues subscales, and total barriers, with greater executive dysfunction related to more barriers to adherence. The composite score for the behavioral regulation domain was also significantly and positively associated with the PMBS parent reminder and regimen adaptation/cognitive issues subscales. Effect sizes ranged from small to medium. There were no significant correlations between any of the BRIEF domains and the PMBS disease frustration/adolescent issues subscale.

Is Executive Dysfunction Correlated With AYA-Reported Barriers to Adherence?

Partial correlations controlling for age revealed that caregiver-reported BRIEF GEC and MCI scores were significantly and positively correlated with the Total AMBS score and several of its subscales, including regimen adaptation/cognitive issues and ingestion issues. The BRI composite score was also significantly and positively correlated with the AMBS regimen adaptation/cognitive issues and the AMBS total barriers scores. As shown in Table III, effect sizes ranged from small to medium. There were no significant correlations between any of the BRIEF domains and the AMBS disease frustration/adolescent issues subscale.

Table III. Partial Correlations Between Caregiver-Reported ED and Barriers to Adherence

Caregiver variables	PMBS DF	PMBS RA	PMBS PR	PMBS T
Global Executive Composite	.21	.47**	.45**	.36*
Behavioral Regulation Index	.12	.39**	.40**	.27
Metacognition Index	.20	.47**	.39**	.35*
AYA variables	AMBS DF	AMBS RA	AMBS II	AMBS T
Global Executive Composite	.30	.36*	.37*	.38*
Behavioral Regulation Index	.30	.41**	.23	.34*
Metacognition Index	.30	.37*	.41**	.40*

Note. ED = executive dysfunction; AMBS = Adolescent Medication Barriers Scale; PMBS = Parent medication Barriers Scale; DF = disease frustration/adolescent issues; RA = regimen adaptation/cognitive issues; II = ingestion issues; PR = parent reminder; T = total; partial correlations controlled for the effect of age on barriers to adherence.

* $p < .05$, ** $p < .01$.

Is Executive Dysfunction Correlated With AYA- and Caregiver-Reported Nonadherence?

Analyses revealed significant and positive correlations between AYA-reported nonadherence and caregiver-reported BRIEF MCI scores ($r_s = .37$, $p = .02$). Associations between AYA-reported nonadherence and the BRIEF GEC and BRI scores approached significance (GEC: $r_s = .30$, $p = .07$; BRI: $r_s = .31$, $p = .06$). No significant associations emerged between caregiver-reported nonadherence and BRIEF scores.

Discussion

The current study aimed to evaluate levels of executive dysfunction in AYA transplant recipients and to examine its association with barriers to adherence and medication nonadherence. Consistent with our hypotheses, results indicated that AYA solid organ transplant recipients have significant levels of executive dysfunction. Specifically, the BRIEF GEC score and the MCI composite score were both significantly higher in the current sample compared with norm-referenced scores, suggesting that AYA transplant recipients experience dysfunction in overall levels of EF and metacognitive skills. The MCI composite encompasses skills related to the ability to plan, organize, initiate, and maintain future-oriented problem solving. These findings are in partial contrast with other pediatric populations in which EF difficulties were also found in behavioral regulation domains (O'Hara & Holmbeck, 2013).

Given that caring for a transplanted organ often involves following complex medical regimens that require organization and future-oriented planning, deficits in metacognition and overall EF skills can pose significant challenges for AYAs. For example, as AYAs get older, they are typically expected to assume increasing levels of responsibility for the management of their health and eventually transition from pediatric to adult medical facilities. Health care providers may gain valuable information about AYAs' neurocognitive and developmental status from assessing EF,

which can inform the guidance given to families about appropriate levels of patient responsibility and independence. This information can be useful for identifying areas of relative weakness and strength in EF. It might also direct health care professionals and caregivers to gradually provide AYAs with developmentally appropriate opportunities to engage in tasks that they can manage independently (e.g., filling the pillbox once a week under caregiver supervision) and, depending on their EF skills, provide scaffolding or support for tasks that may be more challenging (e.g., remember to take medications daily).

In addition to having significantly higher levels of executive dysfunction as a group, clinically significant deficits were found in a quarter of AYAs, based on their overall GEC. Clinically significant deficits in metacognitive abilities were found in 32% of the sample, and deficits in behavioral regulation were found in 24% of participating AYAs. These numbers represent high levels of impairment among transplant recipients, which can significantly impact an AYA's ability to successfully engage in behaviors required for following a complex medical regimen. Even though it is not possible to determine the etiology of these significant cognitive deficits, these difficulties are likely the result of a number of cumulative risk factors including decreased opportunities to master developmentally appropriate tasks, the negative effects of an underlying medical condition (Brouhard et al., 2000), and the potential neurocognitive side-effects of pharmacological treatments (Martinez-Sanchis et al., 2011).

As expected, caregiver-reported executive dysfunction was significantly correlated with a number of caregiver- and AYA-reported barriers to adherence. The AMBS and PMBS regimen adaptation/cognitive issues subscales, in particular, were associated with the BRIEF GEC score and both Index scores, suggesting that greater executive dysfunction may place AYAs at particular risk for experiencing barriers that are related to tasks with high cognitive demand (e.g., remembering to pick up a prescription before medicines run out, sticking to a fixed medication schedule).

Health care professionals are encouraged to pay special attention to these types of barriers among AYAs with executive deficits, as this information may help guide treatment planning by identifying EF domains that are particularly challenging for AYAs. Furthermore, in busy and fast-paced clinical settings where routine assessment of EF skills is not feasible for every patient, cognitive barriers may provide clues of potential underlying executive dysfunction in AYAs. In these cases, a follow-up assessment of cognitive functioning may be advisable. Referrals for neuropsychological testing may also be warranted if EF difficulties are deemed to be significant or appear to be interfering with AYAs' ability to engage in health-promoting behaviors (e.g., following their medical regimen), school tasks, or activities of daily living (e.g., adaptive skills). Interestingly, the BRIEF GEC and Index scores were all significantly associated with the PMBS Parent Reminder scale, indicating that when parents report greater executive dysfunction, they also endorse a greater need to remind their children to take their medications as prescribed.

Analyses examining the association between the BRIEF and medication nonadherence revealed that only AYA-reported nonadherence emerged as a significant correlate of caregiver-reported BRIEF MCI scores. These results indicate that metacognitive skills, including AYAs' ability to initiate problem solving, sustain working memory, plan future-oriented tasks, organize, and monitor one's own behavior are key skills that may facilitate successful adherence to the medical regimen. These results build on previous literature in other pediatric populations showing that higher metacognitive skills are related to better adherence (Bagner et al., 2007). Overall, these findings are consistent with previous studies demonstrating that higher levels of executive dysfunction are associated with worse adherence even after controlling for the effects of age, IQ, and level of cognitive abilities (Alioto & Janusz, 2004; O'Hara & Holmbeck, 2013). The lack of significant correlations between executive dysfunction and caregiver-reported nonadherence suggests that caregivers may not be as aware as their children about the frequency with which AYAs miss prescribed doses. In fact, descriptive statistics in this sample indicate that the rate of caregiver-reported nonadherence is lower than the rate of AYA-reported nonadherence.

Taken together, these findings emphasize the need for further research examining the role of executive dysfunction and metacognitive skills in particular in the context of nonadherence. Furthermore, these findings suggest that early identification of pre- or post-transplant executive deficits should be explored as a potential complementary way to identify pediatric patients at risk for experiencing higher barriers to

adherence and greater nonadherence. Patients identified as having greater executive dysfunction may benefit from engaging in cognitive remediation intervention programs (Luton, Reed-Knight, Loiselle, O'Toole, & Blount, 2011) to teach skills that support areas of cognitive vulnerability, target barriers to adherence, and help carry out tasks associated with the medical regimen. Information about executive dysfunction may also allow medical staff to advise developmentally appropriate allocation of responsibility for medical care, and inform caregiver education programs focused on supporting children while simultaneously granting responsibility in a way that optimizes both disease management and appropriate independence.

Unexpectedly, age was significantly correlated with executive dysfunction in preliminary analyses despite the use of age- and gender-based T-scores. Although these results were unexpected, it is possible that younger AYA transplant recipients are granted less than average responsibility for activities that they would be capable of performing on their own. This potential lack of opportunities to master developmentally appropriate tasks could delay the development of EF abilities. As adolescents grow up, the reality of transitioning to adult care becomes increasingly salient for caregivers. On this realization, caregivers may begin to provide older adolescents with significantly more opportunities to develop the EF skills that will be critical for self-management. The change in expectations and opportunities could result in a trajectory of EF skills acquisition that deviates from that of healthy children.

The current results are novel but must be interpreted in light of several considerations. There was a disproportionately small number of kidney recipients compared with the proportion of this organ group among the greater population of transplant recipients. Future research should determine whether results from this sample are representative of the larger pediatric transplant population. Although the BRIEF has been validated for children 8–18 years, our sample included a 19-year-old. Executive dysfunction was also not assessed using objective neuropsychological tests, and all analyses were based on caregiver report of perceived ability. Further, due to clinic flow restrictions, we were unable to obtain AYA-report of EF abilities. Future research should investigate whether self-report and direct neurocognitive assessments produce similar results. Lastly, given the susceptibility to reporter bias and the use of subjective measures of nonadherence in this study, future research should include objective measures of nonadherence (e.g., electronic monitoring, lab results, daily diaries) to determine whether the results reported in this study can be replicated with other types of nonadherence measurement.

Despite these limitations, this study is novel in a number of ways. This study is the first to examine the neurocognitive construct of EF and its relationship to barriers to adherence and medication nonadherence among pediatric solid organ transplant recipients. Overall, findings from the current study indicate that pediatric transplant recipients are at increased risk for executive dysfunction, which may affect their ability to manage their medical regimen and assume increasing levels of health care responsibility as they grow into adulthood. These results also stress the importance of monitoring executive dysfunction in this vulnerable population and its potential role in granting developmentally appropriate levels of autonomy to decrease barriers and improve adherence. This study highlights the need for additional research on the role of neurocognitive difficulties among pediatric transplant recipients and how this construct can be assessed and used to promote positive outcomes. Future researchers should examine more complex models to identify potential mechanisms underlying the association between executive dysfunction and barriers to adherence, as well as nonadherence.

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