EXECUTIVE FUNCTIONING, ADHERENCE, AND TRASITION READINESS IN ADOLESCENT TRANSPLANT RECIPIENTS

by

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(Under the Direction of Ronald L. Blount)

ABSTRACT

Objective: This study aimed to evaluate executive functioning in a sample of adolescent transplant recipients and to examine its associations with adherence and readiness to transition from pediatric to adult care. *Method*: Thirty-six adolescents (*M* = 16.64; *SD* = 1.53) with a solid organ transplant and their caregivers were administered self- and proxy-report measures. *Results*: T-test analyses revealed clinically significant elevations in executive functioning abilities in adolescent transplant recipients compared to normally developing youth. Better executive functioning abilities were a significant predictor of better medication adherence, fewer barriers to adherence, and greater transition readiness. *Discussion*: Adolescent transplant recipients are at risk for deficits in executive functioning. The assessment of executive functioning abilities may guide adherence and transition readiness intervention efforts designed to promote positive outcomes.

INDEX WORDS: Executive functioning, Adherence, Transition Readiness, Barriers, Transplant, Adolescent

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CHAPTER 1

INTRODUCTION

Pediatric transplantation has become the treatment of choice for an increasingly large number of chronically ill children and adolescents with organ failure and end-stage disease. In 2013, a total of 1,818 pediatric patients received a transplanted organ in the United States (OPTN, 2013). Medical progress and technological innovations in the field of transplantation have led to higher survival rates among chronically ill children, and today, many of the children who receive a transplant are able to reach adulthood. In addition to higher rates of survival, the Organ Procurement and Transplantation Network (OPTN) has documented an increasingly large number of pediatric transplant candidates over the last several years. Despite this increase in the number of eligible patients who could benefit from transplantation, there continues to be a significant imbalance between the supply of available organs and the number of children wait-listed to receive a transplant (OPTN, 2011 annual report). This shortage of organs creates significant challenges and dilemmas regarding fair allocation, and highlights the tremendous responsibility that pediatric recipients and their families undertake in caring for a transplanted organ.

In addition to the lifelong responsibility that comes with a transplant, the tasks associated with caring for an organ can be onerous and frequently present important challenges for children and their families. Postoperative management of a transplanted organ, for example, often includes lifelong adherence to complex medical regimens that include following strict pharmacotherapy schedules, frequent labs, and periodic clinic visits to different health care providers. Thus, even though transplantation can positively impact the lives of chronically ill children by increasing their life expectancy and giving them the opportunity to follow more normative developmental trajectories, the responsibility that comes with a transplanted organ can burden families with therapies that need to be closely monitored to sustain the health of the child and avoid organ allograft rejection.

Failing to follow medical advice as prescribed can have serious consequences for the health of the transplanted organ and the life of the recipient. In pediatric populations, adherence is defined by the World Health Organization as “the extent to which a person’s behavior - taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed [upon] recommendations from a health care provider” (Sabate, 2003, p. 3). Poor adherence has been linked to various negative medical outcomes including organ loss, hospitalizations, need for biopsies and, in severe cases, death (Fredericks, et al., 2007; Falkenstein et al., 2004). In addition to higher rates of morbidity and mortality, nonadherence has also been associated to decreased health-related quality of life (HRQOL), higher healthcare utilization and higher financial costs (Butler et al., 2004; Fredericks et al., 2008; Fredericks et al., 2007; Pinsky et al., 2009). Furthermore, nonadherence has been identified as one of the key factors that may negatively affect a child’s ability to successfully transition from pediatric to adult care (Fredericks et al., 2013). Thus, given that the consequences of nonadherence affect not only the well-being of pediatric patients but also the healthcare system and society as a whole, understanding individual and contextual factors that predict poor adherence is critically important to identify children at risk for nonadherence.

Despite the well-established evidence that adherence is of vital importance, many children and families struggle to follow prescribed medical regimens (Dew et al., 2009). Among pediatric transplant recipients, rates of nonadherence have been documented to average 43% (Dobbels et al., 2010). Among adolescents, rates of nonadherence have been found to be even higher than those documented in younger patients. In a study of pediatric renal transplant recipients, for example, the rate of nonadherence among adolescents was 64% compared to 17% in younger children (Ettenger et al., 1991). Adolescence is a transitional developmental period characterized by emotional, cognitive, behavioral, and brain maturation changes. It is a time when children start to seek greater independence as they begin to develop a more autonomous sense of self. During this period, adolescents may also have difficulty predicting the future consequences of their actions, which may result in perceived invulnerability (Nevins, 2002). Given these developmental characteristics, it is not surprising that adolescents may engage in risky behaviors such as medication nonadherence (Griffin, 2001).

In addition to this vulnerable stage for nonadherence, the transition from pediatric to adult medical care has also been identified as a period of particular vulnerability for medication nonadherence among pediatric transplant recipients (Annunziato, 2007). Parallel to the developmental transition that occurs from childhood to adulthood, the transition from pediatric to adult health care is characterized by significant changes and challenges that may lead to reduced levels of adherence among chronically ill children. Adult-oriented medical facilities, for example, often expect recently transitioned youth to be independent and fully responsible for the management of their medical care. These facilities also tend to engage less with families (Viner, 2001), potentially leading parents to feel excluded from the management of their child's illness. This may result in the removal of a critical support system for adolescents, who may not be ready to assume full responsibility for their medical care. In addition, adult medical settings often adopt a less developmentally sensitive and more hands-off approach to treatment and care. This approach typically provides less guidance to recently transitioned adolescents, who may not receive the assistance they need in coordinating supportive services (e.g., psychosocial services) or resolving health coverage issues (Tuchman, Schwartz, Sawicki, & Britto, 2010). While these practices and expectations are typically reasonable for adult patients, they may be unrealistic for recently transitioned youth who may struggle to manage their health independently as they learn how to navigate a completely different, and often less friendly, healthcare system. In this regard, some authors have argued that the transition process should not only be individualized according to adolescents' neuro-cognitive and developmental status, but that in some cases, transition of responsibilities from parents to youth may need to occur after the adolescent has been transferred to adult care, once he or she is ready to assume full responsibility for his or her medical care (Bell, 2008).

This may be particularly important among adolescent transplant recipients given that pediatric populations often experience delays in maturation due to diminished opportunities to master developmentally appropriate tasks as a result of their medical condition. Unfortunately, caregivers and medical staff who are unaware of these issues may continue to rely on age as the primary indicator of how much responsibility adolescents are ready to assume (Nevins, 2002). Thus, while decreased parental involvement and increased adolescent responsibility is developmentally appropriate as children get older and prepare to transition to adult care, premature granting of autonomy can negatively impact both adherence and successful transition to adult care. In children and adolescents with a liver transplant, the age at which transition of responsibility occurs has been reported to start relatively early, with children as young as 9 assuming medication-taking responsibilities (Shemesh et al., 2004). Overall, the literature on transition readiness suggests that a child's journey through adolescence and into adulthood may be a particularly vulnerable period for medication nonadherence, and that developmentally appropriate levels of parental involvement and adolescent responsibility are critical for optimal adherence, successful transfer to adult care, and positive health outcomes.

To help understand the factors related to children's health behaviors, expectations and intentions, the Children's Health Belief Model (CHBM; Bush & Iannotti, 1999) was developed to reflect developmental theories not originally considered in the original adult-oriented Health Belief Model (Rosenstock, 1966). The CHBM integrates elements of Social Learning Theory, Cognitive Developmental Theory and Behavioral Intention Theory (Bush & Iannotti, 1999). According to the CHBM, there are three different types of factors related to children's health-related beliefs and behaviors, including 1) modifying factors (e.g., cognitive/affective, environmental), 2) readiness factors (e.g., motivations), and 3) behavior factors (e.g., expected medication use, actual medication use). This model places particular emphasis on readiness and cognitive factors related to children's ability to perceive risks and benefits, and highlights the importance of malleable factors (e.g., cognitive, psychosocial, or family factors), as opposed to fixed factors (e.g., age, sex, ethnicity, SES), in the prediction of health-related behaviors such as adherence.

Significant progress has been made in the identification of factors related to adherence. Fixed factors such as older age and minority ethnicity, for example, have been associated with poorer adherence in pediatric populations (Dew et al., 2009; Tucker et al., 2001). Medical-related factors such as complexity of the medical regimen or unpleasant pill taste have also been shown to affect adherence negatively (Tucker et al., 2002). Potentially modifiable factors including disturbed emotional functioning, anger, psychiatric illness, and barriers to adherence have also been associated with lower levels of treatment adherence in child and adolescent populations

(Penkower et al., 2003; Lurie et al., 2000; Shaw et al., 2003; Marhefka et al., 2008; Modi & Quittner, 2006; Rapoff, 2010). Cognitive barriers in particular have emerged as one of the proximal causes that are negatively associated with adherence to prescribed medical regimens (Simons et al., 2010). Cognitive barriers have also been shown to mediate the relationship between several patient internalizing factors (anxiety, depression, post-traumatic stress symptoms) and adherence in adolescent transplant recipients (King, Mee, Gutiérrez-Colina, Eaton, Lee, & Blount, 2013). Further, in patients with IBD, cognitive barriers have been found to mediate the relationship between adolescents' externalizing factors and adherence (Reed-Knight, Lewis, & Blount, 2013). In a recent meta-analysis (Dew et al., 2009), other contextual malleable factors such as parental distress and lower family cohesion were also documented to correlate significantly with lower levels of adherence. Modifiable factors such as hope and illness-related uncertainty have started to receive greater attention in the literature and appear to be indirectly related to adherence via depressive symptoms (Maikranz et al., 2006).

The transition literature has also identified a number of fixed and modifiable factors that are related to transition readiness. Older age and fewer years of medical treatment, for example, have been identified as fixed factors typically associated with greater readiness to transition from pediatric to adult care (Fredericks, 2010; Wiener, Battles, Ryder, & Zobel, 2007). Potentially malleable factors such as higher levels of state anxiety, less adolescent responsibility, lack of confidence in the medical provider, less medication knowledge, worse teen-parent relationship quality, greater parental involvement, lack of continuity of care, developmental readiness, logistical difficulties, and lack of communication between patients, family, and healthcare providers have all been associated with less transition readiness in chronically ill children (Wiener et al., 2007; Gilleland et al., 2012; Wiener et al., 2011). Other factors such as lack of health insurance, lack of funds to pay for out-of-pocket expenses and lack of knowledge about the medical condition, have also been described by Winer and colleagues (2007) and conceptualized as barriers that may hinder successful transition to adult care among pediatric patients.

Thus far, limited attention has been directed towards modifiable cognitive and neuropsychological factors related to nonadherence and transition readiness. This is despite extant evidence indicating that children with a solid organ transplant have significantly lower scores on cognitive functioning compared to healthy peers (Adeback et al., 2007). Furthermore, research comparing pediatric liver transplant recipients and children with other chronic conditions matched for age, SES, age at diagnosis, and physical growth, has demonstrated that transplant recipients experience greater deficits in several areas of intellectual and academic functioning (e.g., nonverbal intelligence, academic achievement, visual-spatial function, motor function) (Stewart et al., 1991). While not yet examined in pediatric transplant recipients, higher cognitive functioning has been reported to be positively associated with medication adherence in other pediatric populations (Mitchell et al., 2000). No research to date has examined the role of cognitive factors in the transition literature.

Even though intellectual functioning, verbal abilities and academic skills have received some attention in the literature, the cognitive construct of executive functioning (EF), in particular, has been largely ignored despite its critical role in successful medical management and adherence. Executive functioning encompasses many of the higher-level cognitive skills (e.g., organization, planning abilities, self-monitoring, working memory, task initiation, problem solving, attention, emotion regulation, inhibitory control) required to manage complex tasks, such as following a medical regimen or navigating the adult healthcare system. Consequently, children with EF difficulties may be at particular risk for nonadherence following transplantation as they may struggle to plan for medication-taking, foresee the consequences of nonadherence, or execute medical recommendations as prescribed. These children may also be at increased risk of transitioning to adult care before they are developmentally ready to do so.

The role of EF may be particularly critical during adolescence and young adulthood, a developmental period when the brain is still developing, and youth begin to assume increased responsibility for self-managing their illness (Bagner, 2007). Even though no investigation to date has explicitly addressed this question, it is possible that an adolescent's EF abilities may serve as a more accurate and developmentally sensitive marker of responsibility and transition readiness than chronological age. This may be particularly true for children with chronic medical conditions, who have been shown to be at risk for delayed developmental trajectories (Wayman et al., 1997; Alonso, 2008). Furthermore, even though we know that adherence decreases as children get older, very little is known about the potential mechanisms that link chronological age and lower rates of adherence (La Greca, 1990). It is possible that EF abilities and degree of adolescent responsibility are one of the potential mechanisms that might help explain the well-established connection between developmental status and nonadherence. To date, no empirical data exists to inform recommendations and guidelines for developmentally appropriate autonomy and independence for adolescents' medical self-management (Wysocki, 1996).

Understanding the role of EF in pediatric transplant recipients may also be particularly important given their vulnerability for cognitive insults resulting from underlying medical conditions. End stage renal failure, for example, is one of the underlying chronic illnesses leading to kidney transplantation that has been associated with neurocognitive developmental delays (Brouhard et al., 2000). Renal failure may also result in uremic encephalopathy, an organic brain disorder partially caused by the accumulation of neurotoxic substances in the body sometimes resulting from failure to receive hemodialysis (DiMartini et al., 2008). Cerebral atrophy and central nervous system infarcts have also been documented in patients with end stage renal failure (Schnaper et al., 1983; Qvist et al., 2002). In children with chronic liver disease, another chronic condition leading to transplantation, medical complications can lead to a different type of encephalopathy termed hepatic encephalopathy, a type of delirium that has been associated with increased risk for cerebral edema, increased intracranial pressure, and seizures in adult populations (DiMartini et al., 2008). In addition to these risks for neurocognitive deficits, children who have received a liver transplant have also been reported to demonstrate lower scores on intelligence measures compared to a normative population (Adeback et al., 2007). In children with congenital and acquired heart disease waiting for a transplant, cardiac arrest episodes may result in low cardiac output, hypoxia or reduced central nervous system oxygenation, all of which could potentially lead to cognitive deficits (Olbrisch et al., 2002).

Executive functions may also be affected in pediatric transplant recipients as a result of neurocognitive side effects of prescribed pharmacotherapies. Steroids, for example, have been implicated in cognitive deterioration (Wolkowitz et al., 1990) and hippocampal degeneration (Sapolsky, 2000). In pediatric patients with IBD, high doses of steroids have been associated with poorer short-term memory, slower speed, and more problems with executive functioning abilities and sleep (Mrakotsky et al., 2005). Immunosuppressants such as tacroliums, a commonly used anti-rejection medication in pediatric populations, have also been associated with lower cognitive functioning compared to controls and patients on cyclosporine, another immunosuppressant medication (Martinez et al., 2011).

Even though EF has not been investigated as a predictor of adherence or transition readiness in pediatric transplant recipients, several studies have examined the relationship between EF and medication adherence in other patient populations. In youth with type 1 diabetes, parent report of children's executive functioning has been shown to predict children's adherence to their medical regimen (Bagner et al., 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 parent- and teacher-reported executive functioning abilities have also been associated with greater adherence even after controlling for the effects of age, IQ and level of cognitive abilities (O'Hara et al., 2013). These findings emphasize the importance of executive functioning for optimal medical self-management in chronically ill children. Furthermore, if EF is found to be predictive of nonadherence, early identification of pre- or post-transplant deficits in EF abilities may be a way to identify children at high risk for poor clinical outcomes and to optimize adherence and transition readiness through early intervention efforts that guide developmentally appropriate granting of responsibility.

Proposed Study

Based on the existing body of literature and guided by the Children's Health Belief model, the current study sought to document executive functioning abilities among adolescent transplant recipients and to examine executive functioning and its associations with variables related to medication adherence and transition readiness in a sample of adolescent transplant recipients. More specifically, the following hypotheses were explored: 1) pediatric transplant recipients will exhibit significantly lower levels of executive functioning skills compared to a normative sample of matched-age peers across all index and total scores, 2) better executive functioning will be significantly associated with higher levels of medication adherence and fewer barriers to adherence as reported by the caregiver and the adolescent, 3) better executive functioning will be significantly associated with higher levels of transition readiness and adolescent responsibility, and lower levels of parent involvement as reported by the caregiver and the adolescent, 4) lower executive functioning will be a significant predictor of medication nonadherence above and beyond the effects of variables previously identified as important correlates of adherence (e.g., age, barriers to adherence), and 5) executive functioning will be a significant predictor of transition readiness above and beyond variables previously identified as important correlates of transition readiness (e.g., age, adolescent responsibility).

CHAPTER 2

METHOD

Participants

Participants included 36 adolescents who had received a solid organ transplant and their parent or guardian. Inclusion criteria specified that adolescents 1) had received a heart, liver or kidney transplant at least 4 months prior to enrollment in the study, 2) were between the ages of 12 and 21 years, 3) spoke English fluently, and 4) were accompanied by a parent or caregiver to the follow-up medical visit. Developmentally delayed adolescents, as reported by the parent or as indicated in the medical record, were excluded from the study. A detailed recruitment flow chart for this study is presented in Figure 1.

All adolescent-caregiver dyads were recruited at a large tertiary-care pediatric hospital during one of their follow-up medical appointments. There were 17 females (47.2%) and 19 males (52.8%), who ranged in age from 14 to 19 years (*M* = 16.64; *SD* = 1.53). Almost half of the adolescents enrolled in the study received a heart transplant (*n* = 17; 47.2%), 12 (33.3%) received a liver transplant, and 7 (19.4%) received a kidney transplant. The medical profile of these adolescents was quite heterogeneous and included a wide range of prescribed medications, as well as significant variability in time since transplantation. On average, adolescents were on 7 prescribed medications (*SD* = 3.2; range = 1 – 16) and received their transplanted organ 9.43 years ago (*SD* = 5.82; range = 1.42-18.31 years). The majority of participants were Caucasian (*n* = 21; 58.3%), followed by African American (*n* = 10; 27.8%), Asian (*n* = 3; 8.3%), and biracial (*n* = 2; 5.6%). Participating parents/caregivers included 32 (88.9%) females and 4 (11.1%) males. On average, they were 45.64 years of age (*SD* = 8.11; range = 34-67 years). The majority of caregivers were biological parents (*n* = 30; 83.3%), 11.1% were legal guardians (*n* = 4), 2.8 were step-parents (*n* = 1), and 2.8% were grandparents (*n* = 1). A detailed description of adolescent and caregiver demographics is presented in Table 1.

Procedure

This study is part of a larger investigation. 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 prior to their follow-up medical visit by a trained research assistant using the hospital patient scheduling system. Families were approached by a graduate student or other investigator during their scheduled medical appointments. Interested families were provided information about the study and were invited to participate. Informed consent, assent and HIPAA release were obtained prior to participation in the study, and any questions about the study were answered prior to enrollment.

Participating dyads completed paper and pencil self-report measures independently. In addition, a trained interviewer administered self- and proxy-report adherence semi-structured interviews during or after the adolescent’s medical visit. Adolescents and their caregivers who completed all study measures received a $10 gift card each as compensation for their time. Families who declined to participate in the study were asked to complete a brief anonymous demographic questionnaire to test for significant differences between families who agreed to participate and those who declined.

Measures

Parents completed a brief sociodemographic questionnaire about participants' age, sex, ethnicity, family income, and type of transplant. Adolescents and their caregivers independently completed self- and parent-report measures, as well as adherence interviews. Medical data (e.g., prescribed medications, time since transplant) were collected via retrospective electronic medical chart review.

Executive Functioning

The Behavior Rating Inventory of Executive Functions (BRIEF; Gioia, Isquith, Guy, & Kenworthy, 2000). The BRIEF is a parent-report 86-item measure used to assess different domains of executive functioning in children and adolescents. Parents 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 8 different subscales comprise the BRIEF, including Plan/Organize, Monitor, Emotional Control (EC), Inhibit, Shift, Initiate, Working Memory (WM) and Organization of Materials. These subscales are additionally organized into two broad indices, the Metacognition Index (MCI; Plan/Organize, Organization of Materials, Working Memory, Initiate, and Monitor subscales) and the Behavioral Regulation Index (BRI; Inhibit, Shift, and Emotional Control subscales), both of which constitute a total score for executive functioning abilities called the Global Executive Composite score. Higher numbers on the total and subscale scores indicate lower levels of executive functioning abilities. Convergent validity for this measure has been demonstrated to be good (Gioia et al., 2000), and internal consistency reliability has been shown to range from excellent to good, with alphas ranging from .98 to .84 (Gioia et al., 2000). In the current study, Cronbach's alphas for the Global Executive

Composite score, and the two Indices scores (MCI and BRI) were α = .98, α = .98 and α = .93 respectively. Cronbach's alphas for the 8 BRIEF subscales ranged from α = .72 to α = .92.

Transition Readiness

The Readiness for Transition Questionnaire (RTQ; Gilleland, Amaral, Mee, & Blount, 2012). The RTQ is a 22-item measure designed to assess overall transition readiness, degree of parental involvement and degree of adolescent responsibility in healthcare behaviors. A total of 3 subscales comprise the RTQ, including the RTQ-Overall subscale, the RTQ-Adolescent Responsibility (RTQ-AR) subscale and the RTQ-Parental Involvement (RTQ-PI) subscale. Parallel adolescent and parent-proxy report forms are available. For the RTQ-Overall subscale, adolescents and parents are asked about how ready they think they are (or their teen is) to assume complete responsibility for their healthcare, and also how ready they think they are (or their teen is) to transition to adult care. The degree of transition readiness is rated on a 4-point Likert scale ranging from *not at all ready* (1) to *completely ready* (4). The total Teen and Parent RTQ-Overall scores are calculated by adding the 2 item scores. Total scores can range from 2 to 8, with higher scores indicating greater perceived readiness for healthcare responsibility and transition to adult care. For the RTQ-Parental Involvement and RTQ-Adolescent Responsibility subscales, parents and adolescents are asked to report on the frequency of parental involvement and adolescent responsibility for 10 different healthcare behaviors (e.g., taking medication daily, getting monthly labs, calling in refills) that have been identified in the literature as being critically important for transition readiness (Wiener et al., 2007; Bell et al., 2008). The frequency of parental involvement and adolescent responsibility in each health behavior is also rated on a 4-point Likert scale ranging from *not at all responsible/not at all involved* (1) to *responsible almost all the time/ involved almost all the time* (4). The total Teen and Parent RTQ-Parental

Involvement and RTQ-Adolescent Responsibility scores are calculated by adding the 10 item scores. Total scores can range from 10 to 40, with higher scores indicating greater degree of parental involvement and greater degree of adolescent responsibility in healthcare behaviors. Preliminary psychometric properties of the 3 subscales that comprise this measure indicate that internal consistency reliability is strong with Cronbach's alphas ranging from .79 (Teen RTP-Overall) to .94 (Teen RTQ-Parental Involvement). Construct and criterion validity for the RTQ have also been supported (Gilleland et al., 2012). In the current study, Cronbach's alphas for the parent-reported subscales ranged from .91 to .93, and from .90 to .89 for adolescent-reported subscales.

Medication Adherence

The Medication Adherence Measure (MAM; Zelikovsky & Schast, 2008; Zelikovsky, Schast, Palmer, & Meyers, 2008). The MAM is a semi-structured interview used to assess adolescent adherence to their medication regimen over the previous 7 days. Adolescents and caregivers are independently interviewed and report on the names and dosages of prescribed medications that the adolescent is taking, as well as the number of prescribed medications that the adolescent missed, took late, or took on time. Once the interview is completed, medication nonadherence is calculated by dividing the number of missed/late doses by the total number of prescribed doses that week. Those values are then multiplied by 100 to calculate the percentage of medications taken late and missed over the last 7 days. The MAM has been shown to have adequate predictive validity as indicated by empirical data documenting significant associations between MAM-reported nonadherence, clinical outcomes and barriers to adherence (Simons et al., 2010; Zelikovsky, Schast, Palmer, & Meyers, 2008). The MAM has also been shown to have adequate convergent validity (Dobbels et al., 2010).

Barriers to Adherence

The Adolescent Medication Barriers Scale (AMBS; Simons & Blount, 2007). The AMBS is a multidimensional factor analytically derived 17-item measure used to assess adolescents' self-report of their own barriers to medication adherence. Adolescents respond to a 5-point Likert scale ranging from *strongly disagree* (1) to *strongly agree* (5), and endorse the extent to which different barriers get in the way of medication-taking. Barriers are classified into 3 factor-analytically derived 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 in the literature. Criterion-related validity of the AMBS has been demonstrated to be strong with nonadherent adolescents reporting significantly more barriers than adherent adolescents (Simons & Blount, 2007). Internal consistency reliability has also been demonstrated to be good, with an alpha of .86 for the total score (Simons & Blount, 2007). In the current study, Cronbach's alphas for the Total Barriers score and each of the 3 AMBS subscales were $\alpha = .90$ (Total), $\alpha = .84$ (Disease Frustration/Adolescent issues), $\alpha = .72$ (Ingestion Issues), and $\alpha = .65$ (Regimen Adaptation/Cognitive Issues).

The Parent Medication Barriers Scale (PMBS; Simons & Blount, 2007). The PMBS is a factor analytically derived 16-item measure used to assess parents' report of their adolescents' barriers to medication adherence. Parents respond to a 5-point Likert scale ranging from *strongly disagree* (1) to *strongly agree* (5), and endorse the extent to which different barriers get in the way of their adolescents' adhering to their medication regimen. Barriers are classified into 4 different factors including (1) Regimen Adaptation/Cognitive Issues, (2) Disease Frustration/Adolescent Issues, (3) Ingestion Issues, and (4) Parent Reminder. The psychometric properties of the PMBS have been documented in the literature. Criterion-related validity for this measure has been demonstrated to be strong with the parents of nonadherent adolescents reporting significantly more barriers than the parents of adherent adolescents (Simons & Blount, 2007). Internal consistency reliability has also been demonstrated to be good, with an alpha of .87 for the total score (Simons & Blount, 2007). In the current study, Cronbach's alphas for the Total Barriers score and the PMBS subscales were $\alpha = .78$ (Total), $\alpha = .61$ (Disease Frustration/Adolescent Issues), $\alpha = .60$ (Regimen Adaptation/Cognitive Issues), $\alpha = .31$ (Ingestion Issues). Because of low alpha, the Ingestion Issues subscale was not included for data analyses.

Data Analytic Plan

All data analyses were conducted using IBM SPSS Statistics, Version 21. Descriptive statistics for all study variables were examined to characterize the sample. To assess external validity, demographic characteristics of families who declined participation in the study were compared to those families who agreed to participate. Pearson product moment correlations were used to examine the associations between study variables. Correlational analyses were also used to examine potential associations between demographic factors and variables of interest. T-test analyses were conducted to compare executive functioning scores in the current sample to normative data.

Hierarchical regression analyses were conducted to examine the amount of variance accounted for by EF abilities on medication nonadherence and transition readiness. Specifically, regression analyses examined parent-reported levels of executive functioning as a predictor of medication nonadherence and transition readiness, after controlling for the effects of pertinent variables.

Power Analyses

Using G*Power (Faul et al., 2007) to calculate sample size for multiple regression analyses with power = .80, α = .05, a medium effect size = .15, and 3 predictor variables, the sample size necessary to detect effects was determined to be 55 participants. The sample size necessary to detect effects for *t*-test analyses between groups with power = .80, α = .05, and medium effect size = .50, was determined to be 51. Fifty-five participants would provide adequate power for all planned analyses.

CHAPTER 3

RESULTS

Preliminary Analyses

Descriptive statistics including means, standard deviations (*SD*) and ranges for all study variables are shown in Table 2. Bivariate correlations revealed significant differences on the following study variables based on medical and demographic factors: Age was significantly associated with all BRIEF composite and subscale scores (GEC: $r = -.48$, $p < .01$; BRI: $r = -.39$, $p <. 05$; MCI: $r = -.47$, $p < .01$; Shift: $r = -.47$, $p < .01$; EC: $r = -.37$, $p < .05$; Initiate: $r = -.39$, $p < .05$; WM: $r = -.41$, $p < .05$; Plan/Organization: $r = -.44$, $p < .01$; Monitor: $r = -.56$, $p < .01$), except the Inhibit and Organization of Materials subscales. Age was also significantly associated with all RTQ subscales as reported by the adolescent (Overall: $r = .50$, $p < .01$; TR: $r = .50$, $p < .01$; PI: $r = -.41$, $p < .05$) and the caregiver (Overall: $r = .59$, $p < .01$; TR: $r = .44$, $p < .01$), except caregiver-reported RTQ-Parent Responsibility. Gender was significantly associated with the Inhibit ($r = .42$; $p < .05$) and Initiate ($r = .33$; $p < .05$) subscales of the BRIEF, such that males exhibited more deficits in these domains than females. Time since transplantation was significantly associated with the AMBS Ingestion Issues ($r = -.46$; $p < .01$) and Total ($r = -.38$; $p < .05$) subscales, and the PMBS Disease Frustration/Adolescent Issues subscale ($r = -.37$; $p < .05$). Parent race was significantly associated with the AMBS Ingestion Issues ($r = .36$; $p < .05$) and Total scores ($r = .43$; $p < .05$), such that adolescents whose parents were Caucasian reported fewer barriers related to ingestion issues. Significant demographic and medical variables were used as covariates in all subsequent analyses (e.g., partial correlations, hierarchical regression) to statistically control for their effects on the study variables of interest.

Primary Analyses

Executive Functioning in Adolescent Transplant Recipients

T-test analyses were conducted to compare executive functioning scores in the current sample to those of a normative sample of matched-age peers. T-test analyses revealed that adolescents with a solid organ transplant have, on average, significantly lower levels of executive functioning ability across a number of executive functioning domains compared to healthy peers (Table 3). Specifically, adolescents' executive functioning abilities were significantly lower than normative data in the following BRIEF domains: Global Executive Composite, Metacognition Index, Initiate, Working Memory, Shift, Plan/Organize, and Organization of Materials.

In addition to overall lower levels of executive functioning ability, almost 50% of the sample exhibited clinically significant deficits in overall executive functioning. In terms of composite scores, caregivers reported clinically significant deficits in the BRIEF Metacognition Index (19.44%) and Behavioral Regulation Index (27.77%) domains.

Correlates of Executive Functioning in Adolescent Transplant Recipients

Is Executive Functioning Correlated with Medication Nonadherence?

Partial correlations indicated that the BRIEF Monitor subscale was significantly and positively correlated with adolescent- and parent-reported medication nonadherence ($r = .37$, $p < .05$; $r = .40$, $p < .05$). The BRIEF Plan/Organize subscale was also significantly and positively correlated with caregiver-reported nonadherence (Table 4). No other BRIEF subscales or composite scores were significantly associated with medication nonadherence.

Is Executive Functioning Correlated with Caregiver-reported Barriers to Adherence?

As shown in Table 4, partial correlations indicated that overall executive functioning was significantly and positively correlated with the PMBS Parent Reminder, Regimen Adaptation/Cognitive Issues, and Total scores. The BRIEF Metacognition Index, Plan/Organize, Organization of Materials, and Emotional Control domains were all significantly and positively correlated with the PMBS Parent Reminder, Regimen Adaptation/Cognitive Issues, and Total scores. The Behavioral Regulation Index domain was significantly and positively associated with the PMBS Regimen Adaptation/Cognitive Issues and Parent Reminder subscales. The BRIEF Inhibit subscale was significantly and positively associated with the PMBS Parent Reminder subscale. The BRIEF Shift subscale was significantly and positively correlated with the PMBS Parent Reminder subscale. The BRIEF Working Memory subscale was significantly and positively associated with the PMBS Parent Reminder subscale. The BRIEF Monitor subscale was significantly and positively correlated with the PMBS Parent Reminder and Regimen Adaptation/Cognitive Issues subscales. Lastly, the BRIEF Initiate subscale was significantly and positively correlated with the PMBS Total score. There were no significant correlations between any of the executive functioning domains and the PMBS Disease Frustration/Adolescent Issues subscale.

Is Executive Functioning Correlated with Adolescent-reported Barriers to Adherence?

Partial correlations indicated that the BRIEF Organization of Materials subscale was significantly and positively correlated with the AMBS Total (r = .37; p < .05) and Ingestion Issues (r = .39; p < .05) scores. The BRIEF Emotional Control subscale was significantly and positively correlated with the AMBS Total score ($r = .40$; $p < .05$), and the BRIEF Monitor subscale was significantly and positively associated with the AMBS Regimen Adaptation scores ($r = .38$; $p < .05$). There were no significant correlations between executive functioning and the AMBS Disease Frustration/Adolescent Issues subscale.

Is Executive Functioning Correlated with Overall Transition Readiness?

As shown in Table 5, partial correlations indicated that overall executive functioning deficits as measured by the GEC were significantly and negatively correlated with caregiver-reported overall transition readiness. The BRIEF Metacognition Index, and the Monitor subscale were also significantly and negatively correlated with parent report of overall transition readiness. None of the BRIEF executive functioning domains were significantly correlated with adolescents' report of their own transition readiness.

Is Executive Functioning Correlated with Adolescent Responsibility?

Partial correlations indicated that deficits in overall executive functioning ability (i.e., GEC score) were significantly and negatively correlated with adolescent responsibility as reported by the parent (Table 5). The BRIEF Metacognition Index, Initiate, and Plan/Organize scores were also significantly and negatively correlated with parent-report of adolescent responsibility. None of the BRIEF executive functioning domains were significantly correlated with adolescents' report of their own responsibility.

Is Executive Functioning Correlated with Parent Involvement?

Bivariate correlations indicated that none of the executive functioning domains were significantly correlated with parent involvement as reported by the caregiver or the adolescent.

Executive Functioning as a Predictor of Nonadherence and Transition Readiness

Is Executive Functioning a Significant Predictor of Nonadherence?

Hierarchical linear regression analyses were conducted to examine the contribution of executive functioning to the prediction of parent-reported medication nonadherence, while accounting for the effects of relevant demographic and study variables. Only those variables found to be significantly correlated with nonadherence at the bivariate level were considered for inclusion in the regression models. Age was entered in Step 1 of the first regression model, parent-reported barriers was entered in Step 2, and the BRIEF Plan/Organize subscale was entered in Step 3. Multicollinearity diagnostic analyses were performed and no multicollinearity issues were detected (VIF ≤ 2 and Tolerance $\geq .5$).

In the first model, as shown in Table 6, age was not found to be a significant predictor of medication nonadherence. Parent-perceived barriers to adherence and age did not emerge as significant predictors of parent-reported nonadherence in Step 2. Executive functioning was the only significant predictor of medication nonadherence in Step 3, as barriers and age continued to be non-significant predictors in the final model. As shown in Table 6, executive functioning accounted for an additional 12.3% of the variance in medication nonadherence in the third model. The final model accounted for a total of 22.6% of the variance in nonadherence.

Given that the BRIEF Monitor subscale was also significantly associated with parent-reported nonadherence at the bivariate level, a second set of hierarchical linear regression analyses were conducted to examine the contribution of this executive functioning domain to the prediction of parent-reported medication nonadherence. Age was entered in Step 1 of the regression model, parent-reported barriers was entered in Step 2, and the BRIEF Monitor subscale was entered in Step 3. No models were found to be significant in the prediction of parent-reported nonadherence. Similarly, given that the BRIEF Monitor subscale was correlated with adolescent-reported nonadherence at the bivariate level, a third set of hierarchical linear regression analyses were conducted with age, adolescent reported barriers, and the BRIEF Monitor subscale entered on successive steps. No models were found to be significant in the prediction of adolescent-reported nonadherence.

Is Executive Functioning a Significant Predictor of Transition Readiness?

As shown in Table 7, hierarchical linear regression analyses were conducted to examine the contribution of executive functioning to the prediction of parent-reported transition readiness, while accounting for the effects of relevant demographic and study variables. To reduce the number of potential analyses, only the Global Executive Composite (GEC) was entered from the BRIEF. Age was entered in Step 1 of the regression model, parent-report of adolescent responsibility was entered in Step 2, and the GEC was entered in Step 3. Multicollinearity diagnostic analyses were performed and no multicollinearity issues were detected (VIF < 2 and Tolerance > .7).

In the first and second steps of the regression models, age emerged as a significant predictor of transition readiness, such that older age predicted greater transition readiness. Adolescent responsibility was also a significant predictor in models 2 and 3, with higher levels of responsibility predicting greater readiness to transition. In the final model, executive functioning emerged as a significant predictor of transition readiness accounting for 7.5% of the variance in transition readiness above and beyond age and adolescent responsibility. Overall, this model accounted for 55.3% of the variance in transition readiness.

CHAPTER 4

DISCUSSION

The current study sought to evaluate executive functioning in adolescent transplant recipients and to examine its role in the prediction of medication nonadherence and transition readiness. Results revealed that consistent with the study's hypotheses, adolescent transplant recipients have significantly higher rates of parent-reported executive functioning difficulties compared to a normative sample of matched-age peers. Specifically, the BREIF Global Executive Composite score and the Metacognition Index Composite score were both significantly higher in the current sample, suggesting that adolescent transplant recipients experience particular difficulties in these domains of neurocognitive functioning. Of the subscale scores that were found to be significantly higher than those in the normative sample, all of them, with the exception of the Shift subscale, were domains that comprised the Metacognition Index - a composite score that encompasses skills such as the ability to plan, organize, initiate, and maintain future-oriented problem solving.

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 executive functioning can pose significant challenges for adolescents who are expected to assume increasing levels of responsibility for the management of their health as they prepare to transition to adult medical care. Health care providers may gain valuable information about adolescents' neurocognitive and developmental status from assessing executive functioning. This information may also be valuable in identifying areas of relative weakness and strength, rather than assuming that adolescents who struggle in one area of executive functioning are not competent in other areas. For example, an adolescent with clinical elevations on the BRIEF Initiate subscale, but not on the BRIEF Organization of Materials subscale, may be able to organize his or her pillbox and keep track of the number of medications left, but may need extensive prompts or cues to initiate the process of taking medications. This information might also direct healthcare providers and parents to provide adolescents with opportunities to both engage in tasks that they can manage independently, as well as tasks that may be more challenging and require scaffolding or the provision of additional support. This developmentally tailored approach would also have the potential to positively affect adolescents' ability to gradually gain competencies in the areas identified as important prior to transition to adult care. This gradual development of skills would simultaneously facilitate a smoother transition of responsibility from parent to adolescent and a less abrupt transfer to adult care.

In addition to having significantly lower levels of executive functioning as a group, clinically significant deficits were found in almost 50% of adolescents based on their overall Global Executive Composite. Clinically significant deficits in metacognitive abilities were also found in 28% of the sample, and about 20% of participating adolescents had deficits in executive functioning domains related to behavioral regulation. These numbers represent high levels of impairment among adolescent transplant recipients and are suggestive of difficulties that can significantly affect adolescents' ability to successfully engage in behaviors that require the use of executive functioning skills, including following a medical regimen, coping and emotion regulation (Campbell et al., 2009). 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, and the potential neurocognitive side-effects of pharmacological treatments.

Unexpected findings included the associations between age and age-adjusted executive functioning scores. Even though BRIEF scores were transformed to *t*-scores prior to conducting analyses, age still emerged as a significant correlate of age-adjusted EF scores. This significant association suggests that even after controlling for the direct and indirect effects of age on the development of executive functioning, age continues to be a significant correlate of EF ability in this population, above and beyond what would be normative in healthy developing children. These findings may be explained in a number of different ways. Firstly, as a result of these adolescents' delayed developmental trajectories and lack opportunities to master developmentally appropriate tasks (Wayman et al., 1997; Alonso, 2008), parents may be overprotective of their children or assume greater than average responsibility for activities that their children would be capable of performing on their own. Furthermore, parents may believe that their adolescents are unable to perform certain health-related tasks (e.g., organizing a pillbox), and as a result, prohibit their children from even attempting to engage in those activities, limiting opportunities for skill development.

As adolescents begin to grow into young adulthood, the reality of transition to adult care becomes increasingly salient for both parents and healthcare professionals, who might, upon this realization, begin to provide adolescents with significantly more opportunities to develop the executive functioning skills that will be critical for self-management once they transition into adult care. Thus, given the notable change in expectations and opportunities that occurs during late adolescence, the acquisition of executive functioning skills may not follow a linear trajectory but rather change exponentially as adolescents approach the transfer from pediatric to adult care.

Therefore, it is possible that even after controlling for the normative developmental effects of age, executive functioning skills among adolescent transplant recipients develop at a different rate than would be expected based on normally developing youth. The second possibility is that the significant correlation between age-adjusted executive functioning scores and age reflects the relatively wide range of ages (14-18 years) that were grouped together to obtain BRIEF normative scores for adolescents in that age range. It is possible that as a result of the rapid changes that occur in executive functioning throughout adolescence and young adulthood, there's significant variability in executive functioning scores for adolescents and young adults in that age group.

When examining relationships between executive functioning and nonadherence, only one of the metacognitive domains of executive functioning, the BRIEF Plan/Organize subscale, emerged as a significant correlate of caregiver-reported nonadherence, indicating that adolescents' ability to manage present and future-oriented tasks, along with their ability to set goals and anticipate the steps needed to accomplish those goals, is an important skill that can facilitate successful adherence to the medical regimen. The BRIEF Monitor subscale was another metacognitive domain significantly related to both caregiver- and adolescent-reported medication nonadherence, suggesting that better checking habits and personal monitoring (i.e., keeping track of one's behavior) may be particularly important aspects of executive functioning that facilitate adolescents' ability to successfully follow their medication regimen. These findings are consistent with previous literature showing that in children with diabetes, the ability to self-monitor is related to adherence to the diabetes regimen (Bagner et al., 2007).

Results also indicated that besides nonadherence, executive functioning was also significantly correlated with a number of caregiver- and adolescent-reported barriers to adherence. Specifically, lower levels of executive functioning were associated with higher scores in the PMBS Total, Parent Reminder, Regimen Adaptation/Cognitive Issues subscales, and the AMBS Total and Regimen Adaptation/Cognitive Issues subscales, suggesting that lower levels of executive functioning may place adolescents at particular risk for experiencing barriers related to cognitive issues. Health care professionals are encouraged to pay special attention to these types of barriers among adolescents with executive functioning deficits. Furthermore, in busy and fast-paced clinical settings where routine assessment of executive functioning is not feasible for every patient, cognitive barriers may provide clues of potential underlying executive functioning deficits in adolescents. In these cases, a follow up assessment of cognitive functioning may be indicated among adolescents reporting cognitive barriers. Referrals for neuropsychological testing may also be warranted if executive functioning difficulties are deemed to be significant or appear to be interfering with an adolescent's ability to engage in health promoting behaviors such as following their medical treatment, or managing some of their healthcare needs. No domains of executive functioning were associated with barriers related to disease frustration issues, which are more likely to be related to psychosocial difficulties (e.g., being tired of taking medicine, being embarrassed about taking medications in front of other children) and problems related to behavioral regulation.

Besides these correlational findings, results from hierarchical linear regression analyses revealed that the BRIEF Plan/Organize subscale of executive functioning was a significant predictor of parent-reported medication nonadherence, above and beyond the contributions of age and parent-reported barriers to adherence. These findings are consistent with previous studies showing that higher levels of executive functioning are associated with greater adherence and self-management even after controlling for the effects of age, IQ and level of cognitive abilities (Alioto & Janusz, 2004; O'Hara et al., 2013). Taken together, these findings emphasize the importance of the role of executive functioning in the prediction of adherence behavior above and beyond the influence of other factors. Furthermore, these findings suggest that early identification of pre- or post-transplant deficits in EF abilities may be an alternative way to identify both children at risk for poor adherence who could benefit from additional supports around their medical regimen, and also areas of cognitive vulnerability that may need to be addressed in cognitive remediation intervention programs. Information about executive functioning difficulties may also guide developmentally appropriate allocation of responsibility and parent education programs to teach caregivers how to support their children and how to share responsibility with them in a way that optimizes both disease management and appropriate independence in chronically ill pediatric populations.

Besides adherence, and consistent with hypothesized findings, greater overall executive functioning deficits were significantly correlated with lower transition readiness and lower adolescent responsibility. The Metacognitive Index score was also negatively related to transition readiness and adolescent responsibility. These significant findings, however, only emerged for caregiver-reported measures and not adolescents' report of their own transition readiness or responsibility. Discrepancies between caregiver and adolescent's perceptions of decision-making autonomy have been documented in the literature (Miller & Drotar, 2003), suggesting that caregivers and adolescents may have different perceptions about what it means to assume enough responsibility to be ready to transition to adult care, or what different levels of responsibility look like. It is possible that as a result of their different roles in the management of the adolescent's condition, parents and adolescents have different views about what transitioning to adult care would entail. For example, it is possible that parents have a more comprehensive and nuanced picture of the transition process and are also aware of some of the adolescent's executive functioning difficulties that may interfere with successful transition. Alternatively, teens may not fully realize that adult-oriented hospitals often expect patients be fully responsibility for medical care. They may also fail to recognize that there is more to managing their medical illness, besides the health-related tasks that they are able to perform with minimal supervision from their parents. For example, adolescents may be unaware of health-coverage issues that may become a problem following transfer, or ignore the fact that they will typically be the recipients of complex health-related information regarding their medical condition. Future research should empirically examine whether one of these perspectives reflects a more accurate representation of reality and whether different perceptions of transition readiness are associated with different clinical outcomes following transfer to adult care.

Executive functioning also emerged as a significant predictor of parent-reported transition readiness above and beyond the effects of age and degree of adolescent responsibility. Even though prior research has identified factors related to transition readiness, such less medication knowledge, less adolescent responsibility and logistical difficulties (Wiener et al., 2007; Gilleland et al., 2011; Wiener et al., 2011), no research to date has examined the role of cognitive factors in transition readiness. These findings suggest that executive functioning, along with other factors related to adolescents' readiness to transition, may influence the transition process and should be considered in preparing the adolescent for successful transition. Given that many of the tasks that adolescents will become responsible for after transfer from pediatric to adult care require the use of executive functioning abilities, assessment of this cognitive domain prior to transition may be particularly helpful to guide the development of a transfer plan that is developmentally sensitive to each individual's level of neurocognitive and developmental status.

These findings also suggest that children with deficits in executive functioning abilities may benefit from interventions that seek to optimize transition readiness.

Contrary to our hypothesis, executive functioning was not associated with parental involvement in health-related behaviors. This lack of association is likely the result of a significant ceiling effect given the restricted variability in the RTQ-Parent Involvement subscale, which indicated that parents were overall highly involved in the management of their adolescent's medical condition. Parents in this sample were highly involved and shared significant responsibilities with their teens regardless of adolescents' executive functioning abilities. Parental involvement in the medical care of a child is generally seen as positive and has been associated with better adherence (Wiebe et al., 2005); however, it is important that caregivers find the appropriate balance between parental involvement and adolescent independence, as both extremes of the continuum can negatively affect skill acquisition and become barriers to the successful transfer from pediatric to adult-oriented care. Thus, while high levels of parental involvement are appropriate and necessary among younger adolescents, the promotion of developmentally appropriate levels of independence becomes increasingly important as adolescents get older. This gradual shift in responsibility should be based on children's neurocognitive and developmental status rather than purely age. Future research should address the question of appropriate responsibility allocation between the caregiver and the adolescent, and determine how to estimate the optimal ratio that will lead to positive clinical outcomes.

Despite the novelty of these findings, these results should be interpreted in light of several considerations. One of the limitations of the current investigation was the small sample size, which reduced statistical power, and thus the likelihood of detecting significant associations among study variables of small and medium magnitude. This study also included a disproportionally small number of kidney recipients compared to the representation of this organ group among the population of transplanted patients. Future research should determine whether results from this sample are representative of the general pediatric transplant population. In addition, these results may not be generalizable to transplant recipients from diverse backgrounds, as the majority of participants in the sample were Caucasian. Further research is needed to replicate current findings in a more ethnically diverse sample. In addition, this investigation was cross-sectional and therefore, it is not possible to determine the directionality and temporal ordering of the relationships between study variables. Future longitudinal studies should determine whether executive functioning deficits lead to worse adherence or whether poor adherence might lead to poorer executive functioning via a deteriorating condition or requiring neurotoxic medications. Executive functioning abilities were not assessed directly in this study and all analyses were based on caregiver report of perceived executive functioning skills. Parents' perceptions may or may not be a fully accurate representation of teen's actual cognitive abilities. Future research should investigate whether neurocognitive assessment measures that directly test this construct produce similar results. Lastly, there were limitations regarding the assessment of medication adherence as only subjective measures of medication adherence were used. Given the susceptibility to reporter bias, future research should include objective measures of adherence such lab results to determine whether the results reported in this study can be replicated with other types of adherence measurement.

Despite these limitations, this study is novel in a number of ways. First, this study is the first to examine the neurocognitive construct of executive functioning and how it relates to medication nonadherence among pediatric transplant recipients. Further, this investigation is the first to document the role of executive functioning in the prediction of transition readiness among adolescents and young adults who have received a solid organ transplant. Overall, findings from the current study indicate that pediatric transplant recipients are at risk for executive functioning deficits, which may affect their ability to manage their medical regimen and assume increasing levels of health care responsibility as the grow into adulthood. These results also stress the importance of monitoring executive functioning problems in this vulnerable population as this information might be used to guide developmentally appropriate granting of autonomy. This study highlights the need for additional research on the role of neurocognitive difficulties among pediatric transplant recipients, and suggests that future investigations should examine the extent to which this construct may be used to inform the development of guidelines for transferring medical responsibility from parents to their children in order to ensure that adolescents are optimally equipped to make a successful transition from pediatric to adult care.

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Table 1. Demographic Information

Variable	Adolescents		Caregivers	
	N = 36		*N* = 36	
	M	*SD*	*M*	*SD*
Age (years)	16.64	1.53	45.64	8.11
	Frequency	%	Frequency	%
Sex				
Male	19	52.8	4	11.1
Female	17	47.2	32	88.9
Ethnicity				
Caucasian	21	58.3	21	58.3
African American	10	27.8	9	25.0
Asian	3	8.3	3	8.3
Hispanic	0	0	1	2.5
Biracial	2	5.6	2	5.6
Type of health insurance				
Private	14	38.9	--	--
Medicare/Medicaid	12	33.3	--	--
Multiple types	8	22.2	--	--
Other	2	5.6	--	--
Family income				
< $10,000	--	--	2	5.6
$10,000-24,999	--	--	3	8.3
$25,000-49,999	--	--	12	33.3
$50,000-74,999	--	--	5	13.9
$75,000-99,999	--	--	5	13.9
$100,000+	--	--	8	22.2
Prefer not to report	--	--	1	2.8
Caregiver education level				
High school/GED	--	--	9	25
Some college	--	--	7	19.4
Associate's Degree	--	--	4	11.1
Bachelor's Degree	--	--	5	13.9
Advanced Degree	--	--	10	27.8
Caregiver marital status	--	--		
Married	--	--	21	58.3
Single	--	--	6	16.7
Divorced	--	--	8	22.2
Partnered	--	--	1	2.8

Table 2. Descriptive Statistics of Study Variables

Variable	*M*	*SD*	Range
Readiness to Transition Questionnaire - Adolescent			
Overall Readiness	5.00	1.72	2-8
Parent Involvement	31.62	7.55	17-40
Adolescent Responsibility	28.35	7.82	15-40
Readiness to Transition Questionnaire - Parent			
Overall Readiness	4.31	1.64	2-8
Parent Involvement	35.89	6.36	15-40
Adolescent Responsibility	26.20	8.16	13-40
Adolescent Medication Barriers Scale			
Disease Frustration/Adolescent Issues	18.89	6.57	8-35
Regimen Adaptation/Cognitive Issues	8.34	3.05	4-16
Ingestion Issues	10.60	4.99	5-22
Total	38.97	15.54	17-87
Parent Medication Barriers Scale			
Disease Frustration/Adolescent Issues	13.81	5.23	7-24
Regimen Adaptation/Cognitive Issues	9.44	3.73	5-17
Parent Reminder	2.16	1.25	1-5
Total	30.31	8.96	16-46
Medication Nonadherence			
% Missed Medications – Adolescent report	4.63	11.32	0-51.43
% Missed Medications – Parent report	2.79	8.07	0-31.17

Table 3. Executive Functioning in Adolescent Solid Organ Transplant Recipients compared to Norms

BRIEF domain	Mean *T*-score (*SD*)	*T*-score range	% Clinical[a]	Mean difference (95% CI)	*t*-score	*p*-value	Cohen's *d*[b]
Global Executive Composite	64.61 (14.87)	42-97	47.22	14.61 (9.58 to 19.64)	5.90	.000	1.15
Behavioral Regulation Index	53.22 (11.93)	37-81	19.44	3.22 (-0.82 to 7.26)	1.62	.114	0.29
Inhibit	51.50 (13.08)	35-88	13.88	1.50 (-2.93 to 5.93)	0.69	.496	0.13
Shift	54.81 (12.84)	38-88	25.00	4.80 (0.46 to 9.15)	2.25	.031	0.42
Emotional Control	52.47 (11.17)	37-80	19.44	2.47 (-1.31 to 6.25)	1.33	.193	0.23
Metacognition Index	56.10 (12.52)	36-86	27.77	6.10 (1.82 to 10.29)	2.90	.006	0.55
Initiate	58.44 (12.98)	36-83	36.11	8.44 (4.05 to 12.84)	3.90	.000	0.73
Working Memory	54.14 (10.59)	40-79	16.66	4.14 (0.56 to 7.72)	2.35	.025	0.40
Plan/Organize	55.50 (11.54)	38-77	27.77	5.50 (1.60 to 9.40)	2.86	.007	0.51
Organization Materials	54.61 (11.64)	34-72	25.00	4.61 (0.67 to 8.55)	2.38	.023	0.42
Monitor	53.53 (13.83)	36-91	19.44	3.53 (-1.15 to 8.21)	1.53	.135	0.30

Note. BRIEF = Behavior Rating Inventory of Executive Function; [a]65 or greater;
[b]Small effect size: d = .20, medium effect size: d = .50, large effect size: d = .80

Table 4. Correlations between Executive Functioning, Parent-reported Barriers and Parent-reported Nonadherence

Variables	PMBS DF	PMBS RA	PMBS PR	PMBS Total	Nonadherence
Executive Functioning					
Global Executive Composite	.22	.46**	.56***	.39*	.33
Behavioral Regulation Index	.21	.39*	.50**	.31	.21
Inhibit	.09	.24	.38*	.14	.21
Shift	.06	.27	.48**	.20	.22
Emotional Control	.33	.40*	.41*	.39*	.12
Metacognition Index	.21	.44**	.52***	.42*	.36
Initiate	.32	.30	.32	.40*	.28
Working Memory	.05	.21	.48**	.21	.29
Plan/Organize	.20	.47**	.49**	.41*	.43*
Organization Materials	.25	.40*	.42*	.41*	.02
Monitor	.10	.44**	.52***	.32	.40*

Note. PMBS = Parent Medication Barriers Scale; DF = Disease Frustration; RA = Regimen Adaptation; PR = Parent Reminder; Nonadherence = parent-reported nonadherence; *p < .05; ** p < .01; *** p < .001

Table 5. Correlations between Executive Functioning and Parent-reported Transition Readiness

Variables	RTQ AR	RTQ PI	RTQ Overall
Executive Functioning			
Global Executive Composite	-.36*	.27	-.38*
Behavioral Regulation Index	-.20	.16	-.22
Inhibit	-.26	.09	-.25
Shift	-.14	.27	-.18
Emotional Control	-.15	.11	-.14
Metacognition Index	-.39*	.30	-.40*
Initiate	-.41*	.20	-.33
Working Memory	-.29	.19	-.32
Plan/Organize	-.35*	.28	-.33
Organization Materials	-.29	.29	-.23
Monitor	-.33	.31	-.40*

Note. RTQ = Readiness for Transition Questionnaire; AR = Adolescent Responsibility; PI = Parental Involvement; *$p < .05$

Table 6. Executive Functioning as a Predictor of Parent-Reported Medication Nonadherence

Predictor	R^2	ΔR^2	F	B	SE B	β
Step 1						
Age	.007		.22	.45	.95	.08
Step 2						
Age				.51	.91	.09
PMBS Total	.103	.096	1.79	.27	.15	.31
Step 3						
Age				1.45	.97	.27
PMBS Total				.13	.16	.15
BRIEF Plan/Organize	.226	.123	2.91*	.30	.14	.43*

Note. B = unstandardized coefficients; SE B = standard error of unstandardized coefficients; β = standardized coefficients; PMBS = Parent Medication Barriers Scale; *$p < .05$

Table 7. Executive Functioning as a Predictor of Parent-Reported Transition Readiness

Predictor	R^2	ΔR^2	F	B	SE B	β
Step 1						
Age	.353		18***	.63	.15	.59***
Step 2						
Age				.45	.15	.42**
RTQ – AR	.478	.125	14.65***	.08	.03	.39**
Step 3						
Age				.31	.16	.29
RTQ – AR				.07	.03	.34*
BRIEF GEC	.553	.075	12.81***	-.04	.02	-.32*

Note. B = unstandardized coefficients; SE B = standard error of unstandardized coefficients; β = standardized coefficients; RTQ-AR = Parent-report of Adolescent Responsibility; GEC = Global Executive Composite; *$p < .05$; ** $p < .01$; *** $p < .001$

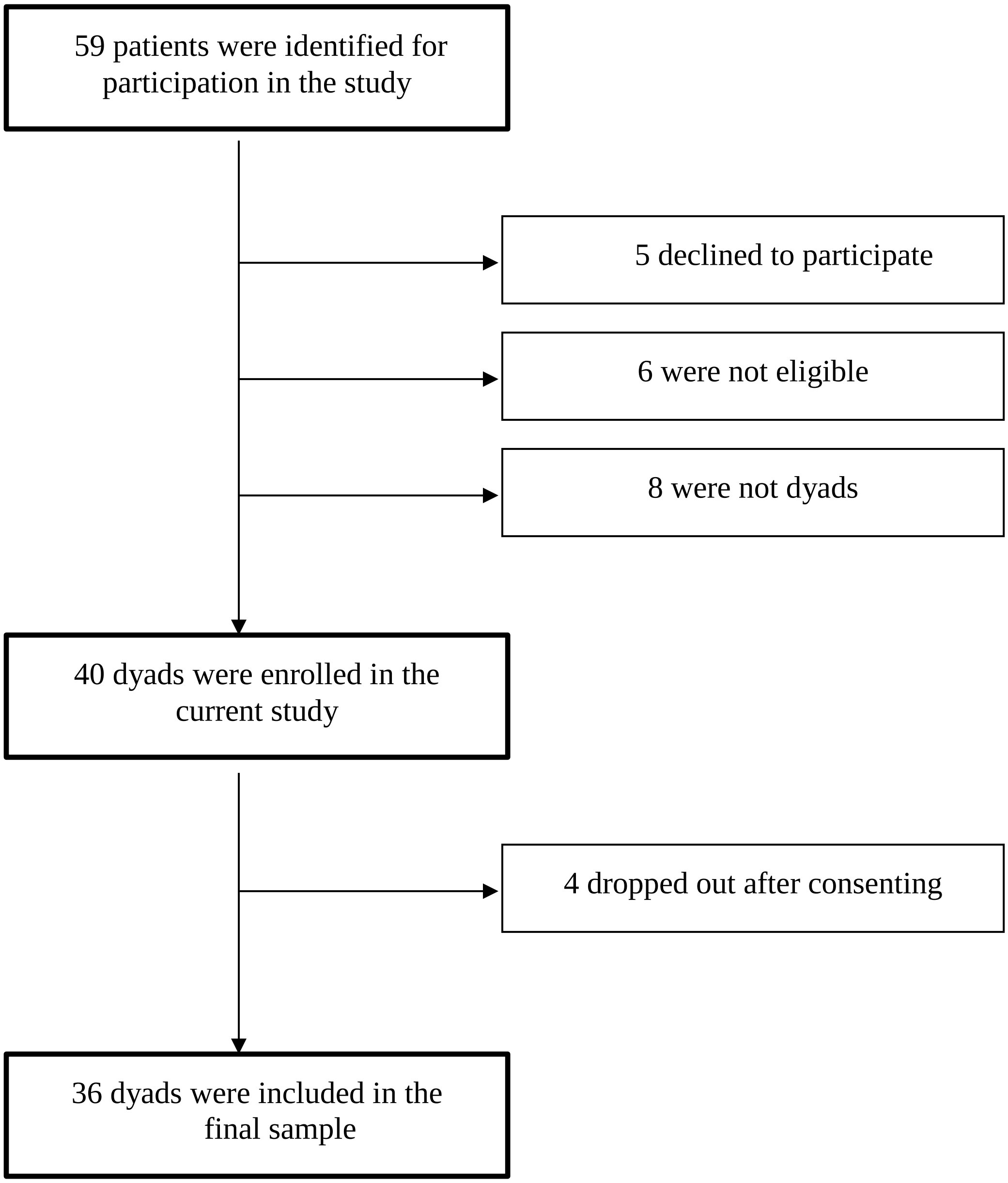

Figure 1. Study recruitment flowchart.