



Exploring the intersection of executive function and medication adherence in school-age children with asthma

Jennifer Sonney & Kathleen C. Insel

To cite this article: Jennifer Sonney & Kathleen C. Insel (2018): Exploring the intersection of executive function and medication adherence in school-age children with asthma, Journal of Asthma, DOI: [10.1080/02770903.2018.1441870](https://doi.org/10.1080/02770903.2018.1441870)

To link to this article: <https://doi.org/10.1080/02770903.2018.1441870>



Published online: 07 Mar 2018.



Submit your article to this journal [↗](#)



Article views: 28



View related articles [↗](#)



View Crossmark data [↗](#)



Exploring the intersection of executive function and medication adherence in school-age children with asthma

Jennifer Sonney, PhD, APRN, Assistant Professor ^a and Kathleen C. Insel, PhD, RN, Professor ^b

^aDepartment of Family and Child Nursing, School of Nursing, University of Washington, Seattle, WA; ^bCollege of Nursing, University of Arizona, Tucson, AZ

ABSTRACT

Asthma is one of the most common chronic diseases of childhood. For children with persistent asthma, asthma control is largely related to controller medication adherence. With increasing calls for children to be involved in their own asthma management, there is a gap in our knowledge about the executive functioning of children with asthma. *Objective:* The purpose of this study was to explore the relationship between executive function, asthma, and medication adherence among school-age children with asthma. *Methods:* Thirty-one children ages 7 to 11 years ($M = 8.9 \pm 1.51$) and one of their parents were enrolled in this study. Parents reported on asthma control while children reported on asthma control, medication beliefs, medication adherence, and completed an executive function battery that assessed inhibition, updating, shifting and planning. *Results:* Compared to the reference sample, children in this study had significantly lower composite scores in inhibition, $t(31) = -3.84, p = .001$, and shifting, $t(30) = -3.73, p = .001$. Controlling for age and asthma control, hierarchical regression analyses revealed that shifting accounted for 16% of the variance in child-reported medication adherence. *Conclusions:* This study revealed lowered executive functioning scores among school-age children with persistent asthma. Furthermore, it appears executive functioning and controller medication adherence are intertwined and warrant future exploration.

ARTICLE HISTORY

Received 16 November 2017
Revised 12 February 2018
Accepted 13 February 2018

KEYWORDS

Shared management;
cognitive function;
self-regulation; controller
medication; inhibition;
updating; shifting

Introduction

Asthma is one of the most prevalent diseases of childhood, affecting over 6 million children in the United States (1). Nearly half of children with asthma experience at least one exacerbation per year; collectively accounting for 571,000 ER visits (2), 136,000 hospitalizations (3), and \$10 billion in healthcare costs (4) annually in the US. Asthma is an incurable, lifelong condition that places children at increased risk for functional impairments including decreased quality of life and school attendance, increased healthcare utilization, and irreversible structural airway remodeling (5–8). Asthma controller medications are the mainstay of treatment for children with persistent disease, with treatment aimed at maintaining asthma control and, by extension, preventing asthma exacerbations (5). However, less than fifty percent of children adhere to their controller medication regimen (7,9). Understanding controller medication adherence represents a critical health need.

Asthma controller medication adherence is complex, with a body of literature that is largely focused on parents as opposed to the children themselves (10). By extension, the majority of medication adherence interventions primarily focus on parents, telling the parent what to

“do” to their child to manage their asthma (11–15). Unfortunately, such approaches disregard the child’s role in asthma management. Moreover, exclusion of the child does not prepare children to learn to manage asthma while under their parent’s supervision, ultimately leading to individuals who are unprepared to assume sole responsibility for their lifelong condition (16). In our prior work, we have argued to reframe child asthma management to that of parent-child shared management, which more accurately reflects the shifting responsibility for asthma management shared between parent and child (10,17). Previously, we reported differences in parent and child-reported asthma beliefs and controller medication adherence (18). This discordance highlights that children are not merely recipients in their asthma care, but indeed do appear to share management responsibility with their parent(s).

The school-age years are a critical time with respect to asthma management, given that children spend increasing time away from their parents while attending school and social activities. Unfortunately, much of the literature related to transfer of asthma management responsibility focuses on adolescents. From a developmental perspective, adolescence is often when peer conformity,

invincibility, and a desire for normalcy are prevalent (19). It is not surprising, therefore, that nonadherence to management regimens peaks in adolescence along with poor asthma control and related morbidity (20–22). In contrast, the school years represent a natural period of management transition, as school-age children are typically rule-driven, understand right and wrong, and are able to problem solve; all of which support their capacity to be active participants in their own asthma management (17,19,23–27). Asthma management is complex and involves a broad range of executive functioning processes. Given the pervasive issue of controller medication nonadherence among children with asthma, we chose to explore the relationship between child executive functioning processes and medication adherence among school-age children.

Simply defined, executive functioning relates to numerous cognitive processes that contribute to planning, organization, monitoring and self-regulation of goal-directed behavior (28,29). Miyake et al. (30) proposed a framework for understanding executive function comprised of three foundational processes: *inhibition*, *updating*, and *shifting* (30). *Inhibition* refers to the ability to suppress automatic, predisposed responses or interfering stimuli (29,30). *Updating*, often linked to working memory, is the ability to monitor, manipulate and update information of relevance to specific tasks (29–31). *Shifting*, also known as task switching or cognitive flexibility, refers to the ability to shift between multiple tasks or operations (28,30). Together, *inhibition*, *updating* and *shifting* are distinguishable but related processes that collectively contribute to more complex executive function processes (e.g., self-monitoring and planning) (30). Numerous studies have demonstrated that *inhibition*, *updating* and *shifting* have distinct developmental trajectories toward adult-level performance (32–34). Typically developing children attain adult-level performance of *inhibition* in early adolescence, *shifting* during adolescence, and *updating* in young adulthood (29,33).

Executive functioning of children with asthma is a relatively understudied area. Much of the literature focuses on intelligence and academic achievement (35–37). Despite increased absences among children with asthma, most teams report no differences in academic achievement among children with asthma compared to their healthy peers (35–39). Few studies have examined the relationship between asthma and more specific executive function processes. While some teams report no relationship between neurocognitive functioning and asthma (38,39), others have found that children with asthma do perform worse on specific processes such as *inhibition*, sustained attention and processing speed (40). Note, while processing speed is not an executive function

process, it supports executive functioning. The challenge in comparing across studies lies in what Miyake et al. describe as task impurity, in that many executive function tests actually measure numerous processes, therefore it is unclear which process(es) relate to asthma management (30). We addressed this knowledge gap by selecting an executive function battery with subtests targeting specific executive function processes. Our aims for this paper are to 1) describe executive functioning of school-age children with asthma; 2) examine the associations among child executive functioning, asthma beliefs, and asthma controller medication adherence; and 3) examine executive function as a predictor of child medication beliefs and controller medication adherence.

Methods

Sample

Thirty-one children with asthma ages 7 to 11 years participated in this cross-sectional descriptive study. Participants were recruited from the Arizona Respiratory Center research database, comprised of children and their families who have participated in other studies and/or expressed interest in participating in asthma research. The study team did not have access to the electronic health records of prospective participants, therefore our eligibility criteria depended on parental report. Children were eligible for the study if they had a persistent asthma, which we defined as a prescription for daily asthma medication. Children were excluded if their parents reported a history of developmental delay, traumatic brain injury, Attention Deficit Hyperactivity Disorder, Obstructive Sleep Apnea, or an asthma exacerbation requiring oral corticosteroids within the prior 30 days. These exclusion criteria were selected as each could negatively affect performance on the executive function measures. Each child had one parent participate in the study who was able to speak and read English and reside with the child at least 50% of the time.

Procedure

The University of Arizona Human Subjects Protection Program approved this study. Staff from the Arizona Respiratory Center generated a list of prospective study participants from the research database. Parents of prospective participants were called on the telephone by Respiratory Center staff using a recruitment script. After describing the study and reviewing eligibility, interested subjects were referred to the Principal Investigator to discuss participation and schedule a one-time study visit. Parent-child dyads met with a study representative at the University of Arizona College of Nursing research suite where

parents signed informed consent and children assented to participate. During the two-hour session, parents sat in an adjacent sitting room while study personnel read survey questions to the children and then administered the executive function battery.

Measures

Subtests were selected from three cognitive batteries, NEPSYII (41), Wide Range Assessment of Memory and Learning – Second Edition (WRAML2) (42), and Woodcock-Johnson III Tests of Cognitive Abilities (WJ III) (43). Each of the cognitive batteries use established normative data based on national, stratified random samples of children (41–43). The NEPSYII subtests are associated with several executive function processes; the selected battery of NEPSYII subtests included Animal Sorting, Auditory Attention and Response Set, Clocks, Design Fluency and Inhibition (41). *Updating* was assessed using selected subtests of the WRAML2 (42). Processing speed, or the speed in which one completes a mental task, was assessed using selected subtests of the WJ III (43). See Table 1 for a summary of executive function processes assessed by each subtest. We acknowledge that task impurity may be present among some subtests; that is, subtests may assess more than one executive function process. When subtests assess more than one executive function process, the higher-level process was selected (e.g., *shifting* was selected over *updating*).

The NEPSY II subtests that test *inhibition*, or the suppression of automatic, predisposed responses (30) included Auditory Attention, Inhibition-Naming and Inhibition-Inhibition. Auditory Attention assesses selective and sustained attention as a child listens to a series of words and responds to a specified target word. The inhibition subtest has three phases: naming, inhibition and switching. For Inhibition-Naming, the child names a series of black and white shapes followed by naming the direction of a series of arrows. Inhibition-Inhibition

involves giving an alternate response (e.g., saying circle when seeing a square, and square when seeing a circle).

NEPSYII subtests associated with *shifting*, or the ability to shift back and forth between multiple tasks or operations (30), include Animal Sorting, Design Fluency, Inhibition-Switching and Response Set. Animal Sorting assesses the child's ability to use self-determined criteria to create as many unique card sorts as they can under time constraints. Design Fluency subtest tests the child's ability to generate unique designs connecting five dots under time constraints. Response Set, a subtest of Auditory Attention, assesses the ability of the child to inhibit the previously learned response and respond in a different way to a target word. Inhibition-Switching involves inhibiting a learned response while a conflicting response is given. The Clocks measure assesses both visual and drawing items and is associated with planning, a higher order executive function process. For visual items, the child reads the time on clocks with or without numbers present. For drawing items, the child draws analog clocks to represent a time provided by the examiner. The selected battery included paper and pencil activities, answering questions, and playing games. All subtests have established reliability and validity. Subtest age-adjusted standardized scores are computed by the NEPSY II computer-scoring program, with a mean scaled score of ten and a standard deviation of three.

Updating, closely related to working memory, refers to monitoring, revising, and the dynamically manipulating relevant information (30). *Updating* was assessed using the Finger Windows and Number Letter subtests of the WRAML2 (42). Finger windows involves the examiner presenting predetermined sequences of inserting the blunt end of a pencil through holes in a plastic template, then the child reproduces the sequence. Number Letter asks the child to orally reorder digits and letters in numerical order and alphabetical order when initially given in no particular order. The WRAML2 has established reliability and validity. Raw subtest scores are converted to age-adjusted standard scores and a standardized working memory index (composite) score with a mean of 100 and a standard deviation of 15.

Processing speed, or the speed in which one completes a mental task, was assessed using the Visual Matching and Decision Speed subtests of the WJ III (43). While not an executive function, processing speed supports cognitive processes. Visual Matching consists of two rows of numbers and the child selects the two that match. Similarly, Decision Speed consists of the child selecting the two pictures that are similar from an array. Both subtests were conducted under time constraints. The WJIII computer-scoring program computes age-adjusted standard scores for each subtest and a standardized

Table 1. Subtests and associated executive function processes.

	Inhibition	Updating	Shifting	Planning
NEPSYII				
Animal Sorting			X	
Auditory Attention	X			
Clocks				X
Design Fluency			X	
Inhibition-Naming	X			
Inhibition-Inhibition	X			
Inhibition-Switching			X	
Response Set			X	
WRAML2				
Finger Windows		X		
Number Letter		X		

Note: WRAML2, Wide Range Assessment of Memory and Learning – Second Edition

processing speed composite. Scores have a mean of 100 and a standard deviation of 15.

The children in our sample all had an established asthma diagnosis and had initiated controller medication therapy, which precluded assessment of asthma severity. Instead, as recommended by the National Heart, Lung, and Blood Institute (NHLBI) Guidelines for the Diagnosis and Management of Asthma (5), we assessed asthma control using the Childhood Asthma Control Test (C-ACT) (44), a 7-item instrument using child and parent report to classify asthma control in children aged 4 to 11 years. Children completed the four child-reported items with a study representative while parents independently completed the three parent-reported items. The summed scores can range from zero to 27, with higher scores indicating better asthma control. Validated cut-points for C-ACT scores of ≥ 20 indicate well-controlled asthma, 13–19 not well controlled, and ≤ 12 as poorly controlled. The C-ACT has established validity and reliability. The Cronbach's alpha was .65 for the present study.

The Medication Adherence Report Scale for Asthma (MARS-A) (45) is a 10-item instrument that assess intentional avoidance and reduction of asthma controller medication use, particularly symptom-driven nonadherence. The MARS-A uses a 5-point scale (one = always, five = never). Scores for the 10 items are averaged, with an average score of >4.5 indicating high adherence. The MARS-A does not reflect actual medication adherence, but rather individual beliefs and behaviors related to medication adherence. We chose to have child participants complete the MARS-A, as opposed to their parents, given our interest in understanding child beliefs and behaviors. Examples include “I only use my [controller medication] when I need it” and “I take it less than instructed”. The MARS-A has been validated in adults with asthma, but this was a novel use of MARS-A in children with asthma. The estimated literacy level of MARS-A was second grade, and the Cronbach's alpha was .70.

The Beliefs about Medicines Questionnaire (BMQ) – Specific is a 10-item self-report questionnaire that assesses the domains of medication necessity and concerns (46). The BMQ uses a 5-point scale (one = strongly disagree, five = strongly agree), with five items assessing perceived medication necessity and five items assessing medication concerns. Domain scores are summed, and the Necessity-Concern differential is calculated by subtracting the concern score from the necessity score. A positive Necessity-Concern differential indicates that necessity outweighs medication concern whereas a negative score indicates concerns outweigh necessity. The BMQ has been previously used in children down to age 7 years (47). The Cronbach's alpha was .79.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) software version 19 was used for analysis. All variables met assumptions for parametric analyses. A p value of $<.05$ was used as the criterion for statistical significance. Descriptive statistics (mean, range, standard deviation) were used to describe the demographic characteristics, medication adherence, medication beliefs, and age-adjusted standard scores on cognitive measures. Mann-Whitney U and Kruskal-Wallis tests were used to assess for differences in cognitive performance and gender, race, ethnicity and asthma status. We calculated separate executive function composite scores for *inhibition*, *updating*, *shifting* and processing speed. *Inhibition* and *shifting* composite scores were calculated by averaging subtest scores for each executive function process. *Updating* and processing speed composite scores were calculated via the computerized scoring software for WRAML2 (*updating*) and WJ III (processing speed).

One-sample t -tests were used to compare normative sample means with the study sample means for each cognitive subtest and composite score. Pearson correlation coefficients (two-tailed) were used to examine associations between cognitive variables, medication adherence, medication beliefs, and asthma control. Hierarchical linear regression was used to examine associations between selected cognitive processes, medication beliefs and medication adherence. There was one instance of missing data, which occurred when a child declined to complete a particular subtest.

Results

Forty-one children ages 7–11 years who met study eligibility criteria were contacted by Arizona Respiratory Center staff using a recruitment script. Four were eliminated due to exclusion criteria, and an additional six declined to participate. The remaining thirty-one children ages 7–11 years ($M = 8.9 \pm 1.51$) enrolled in this cross sectional study. The demographic characteristics of the sample are summarized in Table 2. Of the 31 children in this study, 81% had well-controlled asthma and 19% not well controlled per the C-ACT. The medication Necessity-Concern differential ranged from -3 – 16 ($M = 6.97$, $SD 5.63$), indicating that overall the sample felt that asthma controller medication necessity outweighed concerns. Reported medication adherence ranged from 1.6–4.9 ($M = 3.49$, ± 0.74), indicating medication adherence below the adherent threshold of 4.5. A series of Mann-Whitney U Tests showed no difference in cognitive

Table 2. Demographic characteristics of the sample.

Demographic Characteristics	N (%)
Gender	
Male	20 (64.5)
Female	11 (35.5)
Ethnic origin	
Hispanic or Latino	18 (58.1)
Not Hispanic or Latino	12 (38.7)
Prefer Not to Say	1 (3.2)
Race	
American Indian or Alaska Native	2 (6.5)
Black or African American	2 (6.5)
Caucasian or White	19 (61.3)
Mixed race	3 (9.7)
Prefer Not to Say	5 (16.1)
Asthma Status	
Well Controlled	25 (80.6)
Not Well Controlled	6 (19.4)

performance by gender nor among children with well-controlled and not well-controlled asthma. Similarly, a series of Kruskal-Wallis tests showed no difference in cognitive performance by race.

Executive function and processing speed subtests and composite scores

Child executive function and processing speed performance is summarized in Table 3. Child participant performance differed significantly from the reference sample means on numerous subtests, particularly NEPSY II subtests that assess *inhibition* and *shifting*. The study sample did have significantly lower composite scores compared to the reference sample in *inhibition*, $t(31) = -3.84$, $p =$

.001, and *shifting*, $t(30) = -3.73$, $p = .001$ (see Table 3), indicating lower executive functioning compared to the reference sample. There were no significant differences between the study sample and the reference sample on the *updating* and processing speed composite scores.

Correlations between child executive function and asthma control, medication beliefs and adherence

There were no significant associations between executive functioning and child asthma control or medication beliefs (see Table 4). There was a significant association between the *shifting* composite score and the clocks subtest (planning) ($r = .75$, $p < .001$), indicating that higher *shifting* scores was highly associated with higher capacity for planning. Child-reported medication adherence was significantly correlated with both planning ($r = .38$, $p = .04$) and the *shifting* composite score ($r = .42$, $p = .02$), such that children with higher *shifting* and planning composite scores had higher medication adherence.

Executive function as a predictor of medication beliefs and medication adherence

To assess executive function as a predictor of asthma medication beliefs and adherence, we used two separate hierarchical regression analyses (see Table 5). For both models, age and asthma level of control (C-ACT) were used as a control (step one) given that age and asthma control have a known association with both asthma medication beliefs and adherence. The *shifting* composite

Table 3. Summary of executive function and processing speed subtest and composite scores and comparison with reference sample scores.

Instrument	N	Mean (SD)	Observed Range	t-test† t (sig)	95% CI of Difference	
					Lower	Upper
Inhibition						
Auditory attention	31	10.39 (2.65)	5–15	.81 (.423)	–.59	1.36
Inhibition-naming	31	8.39 (2.69)	3–14	–3.34 (.002)**	–2.60	–.63
Inhibition-inhibition	31	8.10 (2.76)	2–14	–3.84 (.001)**	–2.92	–.89
Inhibition composite	31	8.96 (1.51)	5.67–11.67	–3.84 (.001)**	–1.60	–.49
Updating						
Finger windows	31	9.74 (2.62)	4–17	–.55 (.587)	–1.22	.70
Number Letter	31	11.10 (2.94)	3–16	2.08 (.046)**	0.20	2.17
Updating composite	29	103.38 (11.45)	85–126	1.59 (.12)	–.98	7.73
Shifting						
Animal sorting	31	7.68 (2.81)	3–13	–4.60 (<.001)**	–3.35	–1.29
Design fluency	31	8.39 (3.04)	2–17	–2.95 (.006)**	–2.73	–.50
Response set	31	10.13 (2.85)	4–14	.25 (.803)	–.92	1.17
Inhibition-switching	30	8.90 (2.80)	3–17	–2.16 (.040)**	–2.14	–.06
Shifting composite	30	8.80 (1.76)	5.25–13.25	–3.73 (.001)**	–1.86	–.54
Planning						
Clocks	31	9.55 (3.27)	1–17	–.77 (.449)	–1.65	.75
Processing Speed						
Visual Matching	31	93.32 (15.05)	64–123	–2.47 (.019)**	–12.20	–1.16
Decision Speed	31	99.84 (17.13)	71–138	–.052 (.959)	–6.45	6.12
Processing Speed composite	30	96.40 (16.97)	63–135	–1.16 (.26)	–9.94	2.74

Note: SD, Standard Deviation; CI, Confidence Interval

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

† sample mean in comparison with reference sample mean

Table 4. Correlations between executive function, medication beliefs and medication adherence.

Variable	1	2	3	4	5	6	7	8
1. Inhibition composite	—							
2. Updating composite	.32	—						
3. Shifting Composite	.25	.36	—					
4. Planning	.03	.22	.75**	—				
5. Processing Speed composite	.38*	.26	.21	.14	—			
6. Asthma control (C-ACT)	.08	-.22	.10	-.03	-.17	—		
7. Medication Beliefs	.25	.06	.31	.30	.02	.49**	—	
8. Adherence (MARS-A)	.18	.02	.42*	.38*	-.01	.26	.48**	—

Note: C-ACT, Child Asthma Control Test; MARS-A, Medication Adherence Report Scale for Asthma

* $p < .05$

** $p < .01$

score was used as the predictor in step two of the analyses based on the significant correlations identified in Table 4.

In the first model, *shifting* was used to predict child medication beliefs, controlling for child age and asthma control. While age was not a significant predictor of child medication beliefs, we were not surprised that child asthma control was significant ($\beta = .52, p < .01$). The squared semi-partial correlations indicate that child asthma control explained 27% of the variance in reported medication beliefs. Addition of the *shifting* composite score in step two was not significant at the conventional $p < .05$ level, though the squared semi-partial correlations indicate that *shifting* explained 7% of the variance in medication beliefs and collectively resulted in a statistically significant model, $F(3, 26) = 5.6, p < .01$.

In the second model, *shifting*, controlling for age and asthma control, was used to predict child-reported controller medication adherence. In step one of the analysis, neither age or asthma control were significant predictors of medication adherence. However, the *shifting* composite score in step two accounted for 16% of the variance in

medication adherence, which was statistically significant, $F(3, 26) = 3.23, p < .05$.

Discussion

This pilot study sought to describe executive functioning of school-age children with persistent asthma and to explore the relationship of executive functioning, medication beliefs and controller medication adherence. With respect to aim one, to describe the executive functioning of children with persistent asthma, findings of the present study show that compared to healthy peers, children with asthma demonstrated impairments in *inhibition* and *shifting*. *Updating*, planning and processing speed did not differ from the reference sample. Hajek et al. (40) explored the same executive functions and processing speed in 6–14 year old children with asthma ($n = 15$), and found that children with asthma performed below the normative population in *inhibition*, working memory (*updating*) and processing speed (40). While not in complete agreement, both teams found that children with asthma appear to

Table 5. Linear regression models using shifting as predictor of asthma medication beliefs and adherence.

Model	R ²	R ² Δ	β	sr ²
Predicted: Medication Beliefs				
Model 1 predictors: Age, Asthma control (C-ACT)	.33*	.33*	—	—
Age	—	—	.17	.03
Asthma Control	—	—	.52**	.27
Model 2 predictors: Age, Asthma control (C-ACT), Shifting Composite	.39**	.07	—	—
Age	—	—	.17	.03
Asthma Control	—	—	.50**	.24
Shifting Composite	—	—	.26	.07
Predicted: Medication Adherence				
Model 1 predictors: Age, Asthma control (C-ACT)	.12	.12	—	—
Age	—	—	.19	.03
Asthma Control	—	—	.26	.07
Model 2 predictors: Age, Asthma Control (C-ACT), Shifting Composite	.27*	.16*	—	—
Age	—	—	.19	.04
Asthma Control	—	—	.22	.05
Shifting Composite	—	—	.40*	.16

* $p < .05$ ** $p < .01$, C-ACT, Childhood Asthma Control Test; R², Coefficient of determination; R² Δ, coefficient of determination change; β, beta coefficient; sr², squared semi-partial correlation (portion of variance in the dependent variable [Medication Beliefs or Medication Adherence] that is uniquely explained by the independent variable [predictors]).

experience impairments in executive function processes. Interestingly, Rajabi et al. (48) also reported impairments in inhibition, attention and shifting among 30 adults with asthma (48). Collectively, despite the use of varying executive function batteries among the study teams, these findings suggest that individuals with asthma appear to underperform in select executive function processes compared to reference samples.

Aim two sought to identify associations among child executive functioning processes, asthma beliefs, and asthma controller medication adherence. The association between processing speed and inhibition did not surprise us, given that processing speed supports executive functioning. Similarly, we have previously reported on the associations among asthma control, medication beliefs and medication adherence (18). The association between *shifting* and medication adherence as well as planning and medication adherence was very interesting. To our knowledge, this is the first study to associate medication adherence in children with asthma with an executive function process, *shifting*, and a more complex executive function, planning. In our study, higher executive functioning scores were associated with greater reported medication adherence.

Shifting reflects an individual's ability to switch between tasks, operations and strategies, as well as inhibit previously established rules (49). Similarly, planning is related to goal-directed behavior as well as an individual's ability to anticipate consequences (32,49,50). As such, *shifting* may contribute to planning. For example, following an asthma exacerbation, a child may inhibit a previously held belief that controller medications are only useful during an exacerbation and switch to a new rule that controller medications may be important even outside of an exacerbation (*shifting*). As such, the child evaluates the prior nonadherent behavior and plans to be adherent in the future (planning). In other words, *shifting* may play a supportive role to one's overall planning ability, which certainly is plausible in our study where *shifting* and planning were highly correlated.

Our final aim was to examine executive function as a predictor of child medication beliefs and controller medication adherence. *Shifting* did not emerge as a significant predictor of child asthma medication beliefs. Coupled with the lack of correlation among any of the executive function processes and medication beliefs in aim two; it appears that in this sample, executive function does not have a significant relationship with medication beliefs. Similar findings were recently reported by Soones et al. (51), who found among their sample of adults ages 60 years and older ($n = 433$), executive functioning did not have a significant relationship with medication beliefs (51). *Shifting* did emerge as a significant predictor

of child asthma controller medication adherence in our sample, such that children with lower shifting scores had lower medication adherence. Medication adherence is complex, requiring remembering to take the medications despite competing demands, planning, organizing and self-regulating. As such, findings from the present study reflect this complexity in that children with more capacity for complex executive function (e.g., *shifting*, planning) reported higher adherence.

Given the exploratory nature of this pilot study, we may only speculate about possible mechanisms that might account for asthma-related executive function underperformance compared to normative samples. Based on a review of the literature, possible mechanisms include asthma severity and control, cumulative insults related to intermittent hypoxia, sleep disturbances, and glucocorticoid use. Asthma control and severity have been associated with cognitive deficits among adults with asthma such that worse asthma control is associated with poorer cognitive functioning (51–54). In our study, asthma control (measured by C-ACT) did not emerge as a significant predictor of medication adherence. However, the majority of children in our sample had well-controlled asthma, therefore it is possible we experienced a ceiling effect that explains why we did not find a significant relationship in our analysis. One strategy to address this in the future is to use stratified sampling in order to achieve a wider range in asthma control among the sample.

Hypoxia is another possible mechanism to explain asthma-related executive function underperformance compared to normative samples, particularly for those who have a history of severe exacerbations. Asthma-induced intermittent hypoxia has been linked to impaired learning and memory in immature rodents (55,56). Findings in older adults are mixed (57), though there is a lack of evidence exploring intermittent hypoxia and executive functioning in children. More research is needed to determine the whether there is a cumulative effect of intermittent hypoxic episodes on child executive functioning and whether executive function normalizes over time. Recent articles report executive functioning impairments in adults with asthma, suggesting that such insults may endure (48,58).

Sleep and glucocorticoid use may also be important considerations with respect to asthma-associated executive functioning impairment. Children with asthma experience a high rate of sleep disturbances (59,60), particularly those with poor asthma control, and such disturbances may also impair executive functioning (51,61). Our small sample size precluded analyzing possible covariates, but sleep should be considered in future studies. The long-term cognitive effects of glucocorticoid use may also be relevant. Rajabi et al. (48) reported that

adults who received regular corticosteroid therapy had better cognitive performance compared to adults who did not, and suggested inflammation as a possible mechanism (48). Oxidative stress may be another potential mechanism to explore. Clearly, asthma is a complex, multifactorial disease, and additional research is needed to disentangle the contributions of various mechanisms on child executive function.

Interestingly, executive function deficits and association with poorer treatment adherence may not be unique to asthma, as similar findings have also been reported among children and adolescents with type 1 diabetes (62,63). Similarly, executive function deficits have also been reported among children with cystic fibrosis (64), though to our knowledge the relationship with treatment adherence has not been explored. Among adults across numerous chronic conditions, executive functioning has also been reported as a predictor of medication adherence, suggesting that executive function may be an important predictor of adherence across ages and chronic conditions (65).

Limitations

Several limitations of this pilot study should be considered when interpreting findings. We used retrospective recall of asthma control and controller medication use; spirometry and a medication-tracking device would have improved the reliability of those data. The majority of the children in our study reported well-controlled asthma, and thus medication adherence among these children may be of less importance than for those who are poorly controlled. We also recruited subjects from a respiratory center research database, suggesting that our sample had access to subspecialty care, though 35% reported receiving asthma care from community providers. Our small sample size was insufficient to pursue more complex analyses and covariates. We also could not infer causation due to the correlational design.

Conclusion

This study revealed lowered executive functioning scores among school-age children with persistent asthma compared to a normative sample. We also found significant associations between shifting, planning and controller medication adherence. If the present findings are longitudinally replicated, executive functioning may emerge as an important consideration in childhood asthma self/shared management. For intervention researchers, executive functioning may provide a new avenue for targeted interventions aimed at improving asthma self/shared management. Similarly, clinical

providers may elect to incorporate executive functioning when developing asthma self/shared asthma management plans. In summary, it appears that among children with persistent asthma, executive functioning and controller medication adherence may be intertwined; further elucidation is needed such that future interventions may be designed to be within the cognitive capacity of children with asthma.

Acknowledgements

The authors gratefully acknowledge Drs. Ki Moore, Lynn Gerald, and Chris Segrin for their assistance with the study design, implementation, and analysis; Dr. Jamie Goodwin and Argelia Benavides of the Arizona Respiratory Center for their assistance with recruitment; Ms. Rachelle Begay for her assistance with recruitment and data collection; and Ms. Kari Koerner Marano for her expertise and assistance with data collection.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

ORCID

Jennifer Sonney  <http://orcid.org/0000-0002-0766-2918>

Kathleen C. Insel  <http://orcid.org/0000-0001-7620-9933>

References

- Centers for Disease Control and Prevention. Most recent asthma data: national data Atlanta, GA: U.S. Department of Health & Human Services. 2017 [cited 2017]. Available from: https://www.cdc.gov/asthma/most_recent_data.htm.
- National Center for Health Statistics and Centers for Disease Control and Prevention. National hospital ambulatory medical care survey: 2013 Emergency department summary tables: National center for health statistics. 2013 [April 20, 2017]. Available from: https://www.cdc.gov/nchs/data/ahcd/nhamcs_emergency/2013_ed_web_tables.pdf
- Centers for Disease Control and Prevention. Most recent asthma data Atlanta, GA: US Department of Health and Human Services. 2017 [April 20, 2017]. Available from: https://www.cdc.gov/asthma/most_recent_data.htm.
- Jang J, Gary Chan KC, Huang H, Sullivan SD. Trends in cost and outcomes among adult and pediatric patients with asthma: 2000–2009. *Annals of Allergy, Asthma and Immunology*. 2013;111(6):516–22. doi:10.1016/j.anai.2013.09.007. PMID:24267362.
- National Asthma Education Prevention Program (NAEPP). Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma-Summary Report 2007. *J Allergy Clin Immunol*. 2007;120(5

- Suppl):S94–138. doi:10.1016/j.jaci.2007.09.043. PMID:17983880.
6. Li Z, Huang IC, Thompson L, Tuli S, Huang SW, DeWalt D, et al. The relationships between asthma control, day-time sleepiness, and quality of life among children with asthma: A path analysis. *Sleep Med.* 2013;14(7):641–7. doi:10.1016/j.sleep.2013.04.002. PMID:23684939.
 7. Celano MP, Linzer JF, Demi A, Bakeman R, Smith CO, Croft S, Kobrynski LJ. Treatment adherence among low-income, African American children with persistent asthma. *J Asthma.* 2010;47(3):317–22. Epub 2010/04/17. doi:10.3109/02770900903580850. PMID:20394517.
 8. Grainge CL, Lau LC, Ward JA, Dulay V, Lahiff G, Wilson S, Holgate S, Davies DE, Howarth PH. Effect of bronchoconstriction on airway remodeling in asthma. *N Engl J Med.* 2011;364(21):2006–15. doi:10.1056/NEJMoa1014350. PMID:21612469.
 9. Elkout H, Helms PJ, Simpson CR, McLay JS. Adequate levels of adherence with controller medication is associated with increased use of rescue medication in asthmatic children. *PLoS ONE.* 2012;7(6):1–6. doi:10.1371/journal.pone.0039130.t001.
 10. Sonney JT, Gerald LB, Insel KC. Parent and child asthma illness representations: a systematic review. *J Asthma.* 2016;53(5):510–6. doi:10.3109/02770903.2015.1116088. PMID:26785738.
 11. Nelson KA, Heighstein GR, Garbutt J, Trinkaus K, Fisher EB, Smith SR, et al. A randomized controlled trial of parental asthma coaching to improve outcomes among urban minority children. *Archives of Pediatric Adolescent Medicine.* 2011;165(6):520–6.
 12. Chan AH, Stewart AW, Harrison J, Camargo CA Jr, Black PN, Mitchell EA. The effect of an electronic monitoring device with audiovisual reminder function on adherence to inhaled corticosteroids and school attendance in children with asthma: A randomised controlled trial. *Lancet Respiratory Medicine.* 2015;3(3):210–9. Epub 2015/01/27. doi:10.1016/s2213-2600(15)00008-9. PMID:25617215.
 13. Bender BG, Cvietusa PJ, Goodrich GK, Lowe R, Nuanes HA, Rand C, Shetterly S, Tacinas C, Vollmer WM, Wagner N. Pragmatic trial of health care technologies to improve adherence to pediatric asthma treatment: A randomized clinical trial. *JAMA Pediatr.* 2015;169(4):317–23. doi:10.1001/jamapediatrics.2014.3280. PMID:25664620.
 14. Vasbinder EC, Janssens HM, Rutten-van Molken MP, van Dijk L, de Winter BC, de Groot RC, Vulto AG, van den Bemt PM, e-MATIC Study Group. e-Monitoring of Asthma Therapy to Improve Compliance in children using a real-time medication monitoring system (RTMM): the e-MATIC study protocol. *BMC Med Inform Decis Mak.* 2013;13:38. Epub 2013/03/22. doi:10.1186/1472-6947-13-38. PMID:23514242.
 15. Chiang LC, Huang JL, Yeh KW, Lu CM. Effects of a self-management asthma educational program in Taiwan based on PRECEDE-PROCEED model for parents with asthmatic children. *J Asthma.* 2004;41(2):205–15.
 16. Kieckhefer GM, Trahms CM. Supporting development of children with chronic conditions: From compliance toward shared management. *Pediatr Nurs.* 2000;26(4):354–63. PMID:12026469.
 17. Sonney JT, Insel KC. Reformulating the Common Sense Model of Self-Regulation: Toward Parent-Child Shared Regulation. *Nurs Sci Q.* 2016;29(2):154–9. doi:10.1177/0894318416630091. PMID:26980895.
 18. Sonney J, Insel KC, Segrin C, Gerald LB, Moore IM. Association of asthma illness representations and reported controller medication adherence among school-aged children and their parents. *J Pediatr Health Care.* 2017 in press.
 19. Newton JT, Harrison V. The cognitive and social development of the child. *Dent Update.* 2005;32(1):33–8. PMID:15739662.
 20. Brandt S, Dickinson B. Time and risk preferences and the use of asthma controller medication. *Pediatrics.* 2013;131(4):e1204–10. Epub 2013/03/13. doi:10.1542/peds.2011-2982. PMID:23478866.
 21. Desai M, Oppenheimer JJ. Medication adherence in the asthmatic child and adolescent. *Curr Allergy Asthma Rep.* 2011;11(6):454–64. doi:10.1007/s11882-011-0227-2. PMID:21968618.
 22. Henriksen JM. Adolescence asthma and transition. *Clinical Respiratory Journal.* 2009;3(2):67–88. doi:10.1111/j.1752-699X.2009.00133.x. PMID:20298379.
 23. Olson LM, Radecki L, Frintner MP, Weiss KB, Korfmacher J, Siegel RM. At what age can children report dependably on their asthma health status? *Pediatrics.* 2007;119(1):e93–102. doi:10.1542/peds.2005-3211. PMID:17200264.
 24. Rebok G, Riley AW, Forrest CB, Starfield B, Green BL, Robertson J, et al. Elementary school aged children's reports of their health: A cognitive interviewing study. *Qual Life Res.* 2001;10(1):59–70.
 25. Riley AW. Evidence that school-age children can self-report on their health. *Ambul Pediatr.* 2004;4(4 Suppl):371–6. doi:10.1367/A03-178R.1. PMID:15264962.
 26. Kieckhefer GM, Trahms CM. Supporting development of children with chronic conditions: from compliance toward shared management. *Pediatr Nurs.* 2000;26(4):354–63. PMID:12026469.
 27. Malerstein AJ, Ahern MM. Piaget's stages of cognitive development and adult character structure. *Am J Psychother.* 1979;33(1):107–18. PMID:464161.
 28. Best JR, Miller PH, Naglieri JA. Relations between Executive Function and Academic Achievement from Ages 5 to 17 in a Large, Representative National Sample. *Learn Individ Differ.* 2011;21(4):327–36. doi:10.1016/j.lindif.2011.01.007. PMID:21845021.
 29. Huizinga M, Dolan CV, van der Molen MW. Age-related change in executive function: Developmental trends and a latent variable analysis. *Neuropsychologia.* 2006;44(11):2017–36. doi:10.1016/j.neuropsychologia.2006.01.010. PMID:16527316.
 30. Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD. The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: A latent variable analysis. *Cognit Psychol.* 2000;41(1):49–100. doi:10.1006/cogp.1999.0734. PMID:10945922.
 31. Diamond A. Executive functions. *Annu Rev Psychol.* 2013;64:135–68. doi:10.1146/annurev-psych-113011-143750. PMID:23020641.

32. Juric LC, Richards MM, Introzzi I, Andres ML, Urquijo S. Development patterns of executive functions in children. *Span J Psychol*. 2013;16:E41. doi:10.1017/sjp.2013.44. PMID:23866237.
33. Pennequin V, Sorel O, Fontaine R. Motor planning between 4 and 7 years of age: changes linked to executive functions. *Brain Cogn*. 2010;74(2):107–11. doi:10.1016/j.bandc.2010.07.003. PMID:20678848.
34. Lehto JE, Juujarvi P, Kooistra L, Pulkkinen L. Dimensions of executive functioning: Evidence from children. *British Journal of Developmental Psychology*. 2003;21:59–80. doi:10.1348/026151003321164627. PMID:WOS:000181910000005.
35. Gutstadt LB, Gillette JW, Mrazek DA, Fukuhara JT, LaBrecque JF, Strunk RC. Determinants of school performance in children with chronic asthma. *Am J Dis Child*. 1989;143(4):471–5. Epub 1989/04/01. PMID:2929529.
36. Lindgren S, Lokshin B, Stromquist A, Weinberger M, Nassif E, McCubbin M, et al. Does asthma or treatment with theophylline limit children's academic performance? *N Engl J Med*. 1992;327(13):926–30.
37. Taras H, Potts-Datema W. Childhood asthma and student performance at school. *J Sch Health*. 2005;75(8):296–312.
38. Annett RD, Aylward EH, Lapidus J, Bender BG, DuHamel T. Neurocognitive functioning in children with mild and moderate asthma in the Childhood Asthma Management Program. *J Allergy Clin Immunol*. 2000;105(4):717–24. doi:10.1067/mai.2000.105226.
39. Rietveld S, Colland VT. The impact of severe asthma on schoolchildren. *J Asthma*. 1999;36(5):409–17. Epub 1999/08/26. PMID:10461930.
40. Hajek CA, Yeates KO, Anderson V, Mackay M, Greenham M, Gomes A, Lo W. Cognitive outcomes following arterial ischemic stroke in infants and children. *J Child Neurol*. 2014;29(7):887–94. doi:10.1177/0883073813491828. PMID:23760990.
41. Korkman M, Kirk U, Kemp S. Administration Manual. NEPSY II. 2nd Edition. San Antonio, TX: PsychCorp; 2007.
42. Sheslow D, Adams W. Wide Range Assessment of Memory and Learning, Second Edition: PAR, Inc.; 2012 [April 27, 2014]. Available from: <http://www4.parinc.com/Products/Product.aspx?ProductID=WRAML2>.
43. Strauss E, Sherman EMS, Spreen O. Woodcock-Johnson III Tests of Cognitive Abilities (WJ III COG). A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary, 3rd edition. Oxford, UK: Oxford University Press; 2006. p. 351–62.
44. Liu AH, Zeiger R, Sorkness C, Mahr T, Ostrom N, Burgess S, Rosenzweig JC, Manjunath R. Development and cross-sectional validation of the Childhood Asthma Control Test. *J Allergy Clin Immunol*. 2007;119(4):817–25. Epub 2007/03/14. doi:10.1016/j.jaci.2006.12.662. PMID:17353040.
45. Cohen JL, Mann DM, Wisnivesky JP, Horne R, Leventhal H, Musumeci-Szabo TJ, et al. Assessing the validity of self-reported medication adherence among inner-city asthmatic adults: The Medication Adherence Report Scale for Asthma. *Annals of Allergy, Asthma and Immunology*. 2009;103:325–31.
46. Horne R, Weinman J, Hankins M. The Beliefs about Medicines Questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and Health*. 1999;14(1):1–24.
47. Yilmaz O, Eroglu N, Ozalp D, Yuksel H. Beliefs about medications in asthmatic children presenting to emergency department and their parents. *J Asthma*. 2012;49(3):282–7. Epub 2012/02/07. doi:10.3109/02770903.2011.654021. PMID:22303961.
48. Rajabi S, Keshavarz E, Dehghani Y, Keshavarz M, AliMoradi K. Comparing executive functions between patients with chronic asthma and healthy subjects. *J Asthma*. 2017;1–8. doi:10.1080/02770903.2017.1337786. PMID:28708949.
49. Best JR, Miller PH, Jones LL. Executive Functions after Age 5: Changes and Correlates. *Dev Rev*. 2009;29(3):180–200. doi:10.1016/j.dr.2009.05.002. PMID:20161467.
50. Unterrainer JM, Kaller CP, Loosli SV, Heinze K, Ruh N, Paschke-Muller M, Rauh R, Biscaldi M, Rahm B. Looking ahead from age 6 to 13: a deeper insight into the development of planning ability. *Br J Psychol*. 2015;106(1):46–67. doi:10.1111/bjop.12065. PMID:24417408.
51. Soones TN, Lin JL, Wolf MS, O'Connor R, Martynenko M, Wisnivesky JP, Federman AD. Pathways linking health literacy, health beliefs, and cognition to medication adherence in older adults with asthma. *J Allergy Clin Immunol*. 2017;139(3):804–9. doi:10.1016/j.jaci.2016.05.043. PMID:27555454.
52. Irani F, Barbone JM, Beausoleil J, Gerald L. Is asthma associated with cognitive impairments? A meta-analytic review. *J Clin Exp Neuropsychol*. 2017;1–14. doi:10.1080/13803395.2017.1288802. PMID:28325118.
53. Bozek A, Krajewska J, Jarzab J. The improvement of cognitive functions in patients with bronchial asthma after therapy. *J Asthma*. 2010;47(10):1148–52. Epub 2010/11/03. doi:10.3109/02770903.2010.513077. PMID:21039205.
54. Ray M, Sano M, Wisnivesky JP, Wolf MS, Federman AD. Asthma control and cognitive function in a cohort of elderly adults. *J Am Geriatr Soc*. 2015;63(4):684–91. doi:10.1111/jgs.13350. PMID:25854286.
55. Guo RB, Sun PL, Zhao AP, Gu J, Ding X, Qi J, Sun XL, Hu G. Chronic asthma results in cognitive dysfunction in immature mice. *Exp Neurol*. 2013;247:209–17. doi:10.1016/j.expneurol.2013.04.008. PMID:23639832.
56. O'Brien LM, Gozal D. Behavioural and neurocognitive implications of snoring and obstructive sleep apnoea in children: facts and theory. *Paediatr Respir Rev*. 2002;3:3–0. doi:10.1054/prrv.2002.0177.
57. Moss M, Franks M, Briggs P, Kennedy D, Scholey A. Compromised arterial oxygen saturation in elderly asthma sufferers results in selective cognitive impairment. *J Clin Exp Neuropsychol*. 2005;27(2):139–50. doi:10.1080/13803390490515450. PMID:15903147.
58. O'Connor R, Wolf MS, Smith SG, Martynenko M, Vencio DP, Sano M, Wisnivesky JP, Federman AD. Health literacy, cognitive function, proper use, and adherence to inhaled asthma controller medications among older adults with asthma. *Chest*. 2015;147(5):1307–15. doi:10.1378/chest.14-0914. PMID:25275432.
59. Mirabelli MC, Hsu J, Gower WA. Comorbidities of asthma in U.S. children. *Respir Med*. 2016;116:34–40. doi:10.1016/j.rmed.2016.05.008. PMID:27296818.
60. Sonney J, Segrin C, Ward T. Associations among behavioral sleep disturbance, family functioning, and controller

- medication adherence in children with asthma. *J Dev Behav Pediatr.* [2017](#);38:208–14.
61. O'Brien LM. The neurocognitive effects of sleep disruption in children and adolescents. *Child Adolesc Psychiatr Clin N Am.* [2009](#);18(4):813–23.
 62. Goethals ER, de Wit M, Van Broeck N, Lemiere J, Van Liefferinge D, Böhler S, et al. Child and parental executive functioning in type 1 diabetes: Their unique and interactive role toward treatment adherence and glycemic control. *Pediatr Diabetes.* [2017](#);1–7. doi:[10.1111/pedi.12552](#). PMID:28758314.
 63. Perez KM, Patel NJ, Lord JH, Savin KL, Monzon AD, Whittemore R, Jaser SS. Executive Function in Adolescents With Type 1 Diabetes: Relationship to Adherence, Glycemic Control, and Psychosocial Outcomes. *J Pediatr Psychol.* [2017](#);42(6):636–46. doi:[10.1093/jpepsy/jsw093](#). PMID:28008003.
 64. Piasecki B, Turska-Malinska R, Matthews-Brzozowska T, Mojs E. Executive function in pediatric patients with cystic fibrosis, inflammatory bowel disease and in healthy controls. *Eur Rev Med Pharmacol Sci.* [2016](#);20(20):4299–304. PMID:27831643.
 65. Stillely CS, Bender CM, Dunbar-Jacob J, Sereika S, Ryan CM. The impact of cognitive function on medication management: three studies. *Health Psychol.* [2010](#);29(1):50–5. doi:[10.1037/a0016940](#). PMID:20063935.