



Published in final edited form as:

J Asthma. 2022 March ; 59(3): 607–615. doi:10.1080/02770903.2020.1856867.

Cognition, symptom perception, and medication non-adherence in older adults with asthma

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Abstract

Background: Cognitive impairment (CI) is highly prevalent in elderly asthmatics and is associated with worse asthma self-management (SM) and outcomes. CI may also explain why older adults may under-perceive asthma symptoms. We hypothesized that CI would be associated with low medication adherence and asthma symptom under-perception (ASP). We also hypothesized that ASP would mediate the relationship between CI and medication adherence.

Methods: Participants of this longitudinal cohort study were asthmatics ($N=334$) 60 years (51% Hispanic, 25% Black). Cognitive measures assessed general cognition, attention, processing speed, executive functioning, memory, and language. Measures of SM were self-reported and electronically measured adherence to controller medications. ASP was assessed for 6 weeks by participants entering estimates of peak expiratory flow (PEF) into a programmable peak flow meter, followed by PEF blows. Participants were blinded to actual PEF values. Percentage of time that participants were in the over-perception zone was calculated as an average.

Results: In regression analyses, those with impairments in memory and general cognition had lower odds ratios (OR) for self-reported non-adherence (OR: 0.96, 95% CI 0.93–0.98 & OR: 0.90, 95% CI 0.83–0.96, respectively). CI was not associated with electronically measured non-adherence or ASP. In structural equation modeling, while CI was associated with adherence ($\beta=0.04$, SE = 0.021, $p=0.04$), ASP did not mediate this relationship.

Conclusions: While results confirmed the importance of cognition in asthma SM, these findings were not linked to ASP. Future analyses are needed to understand the role of confounding factors.

Keywords

Asthma; adherence; cognition; elderly; symptom perception

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Declaration of interest

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

Introduction

The prevalence of cognitive impairment increases with age, particularly in those with certain chronic illnesses (1). There is growing evidence that asthma may be among those illnesses, as it can compromise cerebral oxygenation (2). Some studies have found that older adults with asthma have a 78% increased risk of global cognitive impairment than non-asthmatics, even after controlling for other variables (2). Moreover, older asthmatics who are unable to achieve asthma control are at increased risk for periods of intermittent or prolonged hypoxia, which can have detrimental effects on cerebral functions, and thus, cognition (3). This is particularly concerning given that asthma self-management (SM), including adherence to asthma controller medications, is largely governed by cognitive processes (4). Thus, those most in need of adhering to medications are also more likely to experience a decline in medication-taking capacity.

Despite consistent findings that adequate asthma SM strongly influences asthma outcomes, less than half of older asthmatics regularly adhere to controller medications (5–7). As such, older adults are more prone to worse asthma control and outcomes (8,9), including more asthma-related deaths (10,11), greater risk of hospitalization (12), and worse asthma-related quality of life (5). The most consistently studied cognitive domains for adequate SM appear to be memory and executive functioning (EF) (13,14). EF encompasses cognitive flexibility, working memory, and attentional control (15,16), and allows patients to organize, plan, multi-task, self-monitor, and attend to information effectively (17). Deficits in this area are often predictive of worse SM and adherence behaviors across patient populations (16,18,19).

Effective asthma SM also requires accurate recognition, response, and monitoring of asthma symptoms (20). Upon perception of increased asthma symptoms (e.g. dyspnea, wheezing, coughing), a patient may take a variety of steps, including increasing controller medication dosage, using a rescue inhaler, or taking an oral steroid. Under-perception of asthma symptoms has been linked to elevated risk of near-fatal and fatal asthma attacks, as well as to increased morbidity among middle-aged and younger adults (15,17). It is thus especially concerning that older adults with asthma are substantially less aware of airway obstruction than their younger counterparts (21–24), presenting a significant barrier to implementing important SM strategies.

Studies have shown that beginning around age 60 (25,26), older adults may have reduced sensitivity of chemoreceptors in the lung to hypoxia (27,28), resulting in reduced perception of bronchoconstriction. Asthma in older adults is thus often underdiagnosed and undertreated as a result of both the physiology of ageing and changes in cognitive functioning. Diminished perception may also arise from age- or asthma-related changes in cognition. Studies in children have supported this notion, suggesting that deficits specifically in attention and speed of processing are strong predictors of perceptual accuracy of asthma symptoms (28). Accurate symptom perception involves information processing, awareness of physiological sensations, and monitoring of internal somatic cues, processes that are dependent on cognition (29). Motivation to then respond to such cues and correctly execute and sequence multi-stepped administration of asthma medications are ultimately crucial

components of successful asthma SM (29). While prior studies have shown that correcting symptom under-perception in asthmatic children can improve medication adherence (30), no such studies exist with older adults.

The aim of the present study was to examine the relationship between cognitive functioning, asthma symptom perception, and asthma self-management in a sample of older adults with asthma. Because the literature has consistently identified memory and aspects of EF as necessary for adequate SM (13,14), we first tested the hypothesis that poor performance on these measures would be associated with low medication adherence. We then tested the hypothesis that under-perception of asthma symptoms would be associated with poor performance on measures of general cognitive functioning. Finally, we tested the hypothesis that under-perception of asthma symptoms would mediate the relationship between poor performance on measures of general cognitive functioning and medication non-adherence.

Methods

Procedures

Data for this study were collected cross-sectionally during the baseline visit from a multi-site longitudinal cohort study of asthma symptom perception among older adults. Data were collected between January 2017 to January 2020. The baseline session included administration of cognitive measures by formally trained research assistants. Self-reported medication adherence, demographic information, and other questionnaires assessing asthma control (i.e. Asthma Control Questionnaire, Juniper Asthma Quality of Life Questionnaire) and depression (i.e. Geriatric Depression Scale) were also collected at this visit. Participants then continued 6 weeks of at-home asthma symptom perception and electronic adherence monitoring. The institutional review boards at both Mount Sinai Hospital and the Albert Einstein College of Medicine sites approved this study.

Settings and participants

Participants were adults aged 60 and older ($n=334$) with persistent or severe asthma (i.e. uncontrolled asthma symptoms as defined by the National Heart, Lung, and Blood Institute guidelines (31) and/or taking controller medications) from East Harlem and the Bronx, in New York City. Participants were eligible if they spoke English or Spanish and had a physician diagnosis of asthma. Individuals with a diagnosis of COPD per medical records or other chronic respiratory illnesses, a smoking history of 15 or more pack-years, a physician diagnosis of dementia, or a diagnosis of moderate or severe cardiac disease (including New York Heart Association stages 4 or 5 congestive heart failure) were excluded. Participants dependent on assistance for medication administration and those with uncorrectable visual impairment were also excluded. Participants were recruited from primary care or pulmonology outpatient clinics within Mount Sinai Hospital ($N=155$) or the Albert Einstein College of Medicine ($N=179$). Potentially eligible participants were first identified through electronic medical records at each site, and later contacted by phone to screen for eligibility. Eligible individuals provided in-person written informed consent at the time of the baseline interview.

Measures

Cognitive functioning—Cognitive functioning was evaluated using a battery of well-validated measures with appropriate normative data. Domains assessed included general cognition, aspects of EF (i.e. set-shifting and working memory), processing speed, language (i.e. semantic fluency), and learning and memory. General cognitive functioning was assessed using the Montreal Cognitive Assessment (MoCA) (32), a brief screening tool for mild cognitive impairment.

The MoCA evaluates multiple cognitive domains affected in dementia, including EF, attention, visuospatial abilities, learning and memory, language, and orientation, with a cutoff score below 26 suggestive of impairment (32). Attention and processing speed were assessed using the Trail-Making Test (TMT) (33–35) Part A. TMT-A requires participants to remain vigilant and draw lines connecting numbered dots scattered across a page in order; the score represents the time to completion. EF (i.e. cognitive flexibility/set-shifting) was measured using the TMT Part B. Similar to TMT-A, the TMT-B requires participants to draw lines connecting dots, but alternating between a sequence of numbers and letters. Working memory, another aspect of EF, was assessed using the Wechsler Memory Scale (WMS) (36) Letter-Number Sequencing (LNS), where participants listen to increasingly longer series of numbers and letters, rearrange the information, and repeat it back in numerical and alphabetical order. Language was assessed using the Animal Naming Test, an assessment of semantic fluency in which the participant names as many animals as possible in one minute (37). Finally, verbal memory was assessed using the New York University paragraph recall test (38,39), which consists of an orally presented short paragraph that participants are asked to recall verbatim following immediate (NYU IR) and 5-min delays (NYU DR).

Asthma SM—Adherence to inhaled corticosteroid medications was measured objectively and through self-report. Self-reported adherence was measured in patients who reported prescribed a controller medication, using the Medication Adherence Rating Scale (MARS) (39). The MARS is a 10-item adherence measure that has been validated in English and Spanish. Each item is framed as a negative statement to minimize social desirability bias. It has been shown to have good psychometric properties and correlates well with objective measures of adherence (38,40,41). Patients with scores of >4.5 were classified as adherent (40). Objective adherence was measured by Doser (Meditrack, USA), SmartTouch and SmartDisk (Hailie, New Zealand) devices. These electronic monitoring devices were attached to inhalers at the baseline session and recorded the daily frequency of medication use over 6 weeks following the baseline session. Adherence was calculated as the number of total doses taken per day, divided by the number of prescribed doses for that day across the monitoring period. Objective adherence was classified into three categories on the basis of prior literature (42), low (<50%), moderate (50–80%), and good (>80%). Of note, these data were available for 156 of the 334 participants, as several participants reported not having controller medications ($N=79$). Other reasons included incompatible medications with monitoring devices, loss of devices, or device failures.

Asthma symptom perception—Assessment of asthma symptom perception was performed using the AM2 programmable computerized peak flow monitor (ERT Corporation, Philadelphia, PA). Participants were asked to assess their subjective peak expiratory flow (PEF) from home daily for 6 weeks following the baseline session. Participants' PEF guesses were entered directly into the AM2 device. Research coordinators were trained to coach participants to perform 3 maximal effort blows to record actual PEF. Participants were blinded to the result to avoid a learning effect. A colored sticker was attached to the peak flow monitor showing the participant's predicted PEF values that correspond to the go (green), caution (yellow), and danger (red) zones of asthma control, as per national guidelines (31). AM2 results were included if participants completed 20 valid guesses and PEF measurements. Accuracy of symptom perception was determined by comparison of estimated and actual PEF using a previously validated asthma risk grid (43–47), and the percentage of time that participants performed in the under-perception, over-perception, and accurate zones was calculated. Perception data were available for 249 participants out of 334. Reasons for missing data included having less than 20 data points ($N=48$) and device issues ($N=37$; e.g. loss of the device, device failure).

Additional measures—The baseline assessment also included demographic variables that were collected by self-report. The measure of pulmonary function analyzed for this study was the percent predicted forced expiratory volume in one second (FEV₁% predicted), which is the volume of air that is exhaled during the first second of a forced vital capacity maneuver. Medical comorbidities were calculated based on the Charlson Comorbidity Index (CCI) score (48). All questionnaires were validated in both English and Spanish.

Statistical analyses

Descriptive statistics assessed the distributional characteristics of study participants. Multivariable logistic regression was used for the binary variable of medication adherence (MARS) and ordinal logistic regression for the categorical variable of objective adherence (measured using electronic device). Cognitive impairment was defined as having a z-score of less than or equal to 1.5 standard deviations below the mean of age and education adjusted normative data. Bivariate association between self-reported adherence (MARS) and cognitive variables used Pearson's chi-squared test and Wilcoxon rank sum test for symptom under-perception. Continuous measures of cognitive function were tested in adjusted linear regression models with asthma symptom under-perception. All regression models included adjustments for age, sex, education, race/ethnicity, income, and Charlson comorbidity index. Analyses were performed using SAS statistical software, version 9.4 (SAS Institute, Inc., Cary, NC).

We used structural equation modeling (SEM) to assess the indirect effect that cognition has on medication non-adherence through asthma symptom under-perception. A latent variable was created for cognitive function using the overall scores of the MoCA, TMT A, TMT B, LNS, animal naming, and NYU Paragraph Recall tests as the indicators. Medication adherence was entered into the model as a continuous variable using mean MARS scores. The model was adjusted for age, gender, language, income, race, education and CCI score. SEM was conducted with Mplus7 (Muthen & Muthen, Los Angeles, CA).

Results

Participant descriptive characteristics are displayed in Table 1. The mean age was 67.9 years old (SD: 6.7). The majority of the sample ($N=334$) was female (84.4%), Hispanic (51.2%), or Black, non-Hispanic (24.9%), and 56.2% had some college or higher level of education. A measure of pulmonary function ($FEV_1\%$ predicted = 73.0 ± 19.2) indicated that, on average, asthma was not well controlled. Participants were found to be largely non-adherent to controller medications as assessed by self-report (63.6%) and the objective measure (low adherence 62.8%, moderate adherence 19.9%). However, it should be noted that there was substantial missing data for the objective measure ($N=156$). Further, the self-report measure was only completed by participants who were on controller medications ($N=275$). Asthma symptom under-perception was documented in 24% of assessments.

The association between cognitive impairment and medication adherence is displayed in Table 2. In the unadjusted models, patients with impairments across several domains had lower odds for self-reported non-adherence. Specifically, self-reported non-adherence (i.e. MARS score <4.5) was significantly associated with impairment in several domains, including general cognitive functioning (MoCA), OR = 0.91, 95% CI 0.86–0.96, $p<0.001$, memory (NYU DR), OR = 0.96, 95% CI 0.94–0.98, $p=0.001$, attention/processing speed (TMT A), OR = 1.02, 95% CI 1.00–1.04, $p=0.03$, and working memory (LNS) OR = 0.98, 95% CI 0.95–0.99, $p= .04$. Subjective non-adherence was not significantly associated with TMT B test performance, a measure of executive functioning (OR = 1.02, 95% CI 1.00–1.04, $p=0.09$), or performance on the Animal naming test (OR = 0.99, 95% CI 0.96–1.01, $p=0.25$). Objectively measured non-adherence was not significantly associated with performance on any cognitive domain, in both unadjusted and adjusted models. However, it was significantly correlated with subjectively measured non-adherence ($r=0.42$, $p<0.0001$).

In adjusted analyses, patients with impairments in general cognitive functioning (MoCA, OR = 0.90, 95% CI 0.83–0.96, $p=0.002$) and memory (NYU DR, OR = 0.96, 95% CI 0.93–0.98, $p=0.005$) had lower odds ratios for self-reported non-adherence. However, the adjusted model revealed no association between MARS non-adherence and poor performance on EF (TMT B), OR = 1.01, 95% CI 0.98–1.03, $p=0.60$, working memory (LNS), OR = 0.98, 95% CI 0.95–1.01, $p=0.18$, attention/processing speed (TMT A), OR = 1.02, 95% CI 1.00–1.04, $p=0.13$, or language fluency (Animal naming), OR = 1.00, 95% CI 0.97–1.03, $p=0.88$.

In adjusted analyses, cognitive impairment was not predictive of under-perception of asthma symptoms in any domain (Table 3), including general cognitive functioning (i.e. MoCA), $\beta=0.09$, SE = 0.64, $p=0.89$, memory (i.e. NYU DR), $\beta=0.26$, SE = 0.26, $p=0.96$, EF (i.e. TMT B), $\beta= -0.29$, SE = 0.22, $p=0.20$, working memory (i.e. LNS), $\beta= -0.23$, SE = 0.26, $p=0.38$, attention/processing speed (i.e. TMT A), $\beta=0.14$, SE = 0.21, $p=0.50$, or language (i.e. Animal naming), $\beta=0.09$, SE = 0.25, $p= .73$. This finding did not change in the unadjusted model.

Asthma symptom under-perception was not significantly correlated with self-reported non-adherence (i.e. MARS), $r=0.09$, $p=0.18$, nor with objectively measured non-adherence, $r= -0.07$, $p=.41$. In adjusted multivariable analyses, there was no association between

asthma symptom under-perception and self-reported non-adherence (i.e. MARS), OR = 0.99, 95% CI 0.99–1.00, $p = .25$. Similarly, there was no association between symptom under-perception and objectively measured non-adherence, OR = 1.00, 95% CI 0.99–1.01, $p = .67$. These findings did not change in the unadjusted model.

Using structural equation modeling, we also assessed whether there was a direct path between cognitive functioning and asthma symptom under-perception and non-adherence. We then assessed whether there was an indirect path with symptom under-perception mediating the relationship between cognitive function and non-adherence. We found that while cognition, modeled as a latent variable, was associated with adherence, $\beta=0.04$, SE = 0.021, $p=0.04$, asthma symptom under-perception did not mediate this relationship.

Discussion

The present study moved beyond the existing literature on older adults with asthma to examine the relationship between cognitive impairment, asthma symptom under-perception, and medication adherence. It also provided a unique contribution to the literature by presenting a novel method for assessing asthma symptom perception using the subjective-objective discrepancy of PEF at home in older adults, an approach that was validated from prior studies in children (43).

Our results confirmed the important role of cognition in asthma SM, indicating that poor performance on measures of memory and general cognitive functioning were associated with self-reported medication non-adherence, a finding that echoes prior studies (5,19,49,50). While working memory was predictive of self-reported non-adherence in unadjusted models, the finding that impairments in other aspects of EF were not associated with non-adherence alone or in fully adjusted models was unprecedented. EF encompasses many of the higher-level cognitive skills required to follow a complex medical regimen, including working memory, cognitive flexibility, and inhibitory control. We suspect that our results may be attributed to the fact that adherence to a daily, repetitive regimen of inhaled corticosteroids may not require such high-level abilities. Impairments in memory and general cognition may be more relevant in this context, as deficits in more global functions may indicate greater severity of impairment. In other words, our results suggest that the impact of cognitive impairment on an individual's ability to self-manage may vary depending on the severity of impairment and complexity of the self-management tasks.

We also found that cognition was not associated with symptom under-perception in older adults. This was another surprising but important finding, one that is distinct from studies in asthmatic children (28). For example, Koinis-Mitchell and colleagues (28) previously found a link between better attentional skills and more accurate symptom monitoring, suggesting that children who were distracted by environmental stimuli were also less likely to attend to asthma symptoms, thereby minimizing their likelihood of perceiving serious asthma symptoms. However, in our sample of older adults and with the range of cognitive impairments observed in the study population, cognition does not seem to influence symptom under-perception after all. Future studies could consider a more nuanced

assessment of cognition in relation to asthma symptom perception, particularly for such multi-dimensional constructs as attention and EF.

Our findings also indicated that symptom under-perception had no role in the relationship between cognition and asthma self-management, suggesting that under-perception in fact may not be important for medication adherence. Even patients who can accurately and consistently perceive airway changes will require motivation to act on those changes in order to be successful in asthma self-management. This motivation may be dependent on other factors, including the individual's subjective experience of unpleasant sensations and perhaps other psychological factors, such as stress, depression, or anxiety. Future studies could consider examining these other variables in relation to symptom under-perception.

This study has a number of limitations. First, the inherent drawback to utilizing self-report measures may have contributed to the discrepancy in findings on cognition between the two adherence measures, as those with cognitive impairment may have inaccurate perceptions of their adherence. It is also possible that the objective measures did not adequately capture adherence in participants with cognitive impairment secondary to missing data issues. As reported above, we had valid data for objectively measured adherence in 156 participants in our sample of 334 due to insufficient data points, lost devices, and device failures. It may be that those with cognitive impairment were more likely to misplace their devices, forgot to record sufficient data points, or were unable to use the devices correctly. Adherence to inhaler devices also requires adequate motor control, an ability that may decrease with aging, alongside cognitive capacities. Second, the cross-sectional nature of our analyses is a limitation, as the single measurements of cognitive functioning and asthma SM may be better assessed in a longitudinal fashion to account for any cumulative effects of poor SM on cognitive performance and symptom perception. Third, we did not collect data on time between medical appointments, which could have impacted our results to a degree, as device use training, symptom perception, and medication adherence are typically emphasized at such appointments. Fourth, while our study population was predominantly older adults, the mean age was only 67.9 (SD: 6.7), which challenges the generalizability of our results to more elderly adults who may have greater cognitive impairment. Our sample was also predominantly female and college-educated, which may again limit generalizability. Our exclusion of COPD patients in particular may have skewed our sample toward more female participants as COPD is more frequently diagnosed in elderly men than women (49). Finally, our protocol for measuring asthma symptom perception relies on guessing PEF, which is a numerical task. Future studies should consider using verbal descriptors of dyspnea in older adults as opposed to focusing on numerical values. It may also be prudent to assess asthma symptom reporting and objective measures of pulmonary function such as FEV1, in order to examine discrepancies between asthma symptom reporting and pulmonary function.

Conclusion

In older adults with asthma, cognitive impairment is not associated with asthma symptom perception and symptom perception is not a mediator or moderator of the association of cognitive ability with asthma medication adherence.

Funding

This work was supported by the National Heart Lung and Blood Institute (1R01HL131418 to ADF, JMF, JPW)

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Table 1.

Participant demographic characteristics.

	N	%
Age	<i>N</i> = 334	<i>m</i> = 67.9 (SD: 6.7)
Sex, % Female	<i>N</i> = 282	84.4
Race, %	<i>N</i> = 334	
White, Non-Hispanic	52	15.6
Black, Non-Hispanic	83	24.9
Hispanic	171	51.2
Other	28	8.4
Education, %	<i>N</i> = 329	
Some high school or less	82	24.9
High school degree	62	18.8
Some college	76	23.1
College graduate	109	33.1
Income	<i>N</i> = 312	
\$1500/Month or less, %	171	54.8
Language	<i>N</i> = 334	
Spanish %	94	28.1
Comorbidities, %	<i>N</i> = 274	
Diabetes	71	25.9
Congestive heart failure	5	1.83
Medication Adherence Rating Scale	<i>N</i> = 275	
Adherent	100	36.4
Non-adherent	175	63.6
Objective Controller Adherence %	<i>N</i> = 156	
Good Adherence	27	17.3
Moderate Adherence	31	19.9
Low Adherence	98	62.8
Depression	<i>N</i> = 334	
(≥ 5 on GDS) %	82	24.6
% FEV ₁	<i>N</i> = 309	<i>m</i> = 73.0 (SD: 19.2)
Cognitive Functioning	<i>N</i> = 332	
MoCA < 26, Impaired%	243	73.2
Trails A, Impaired %	94	28.3
Trails B, Impaired %	115	34.7
LNS, Impaired %	98	29.5
Animal Naming, Impaired %	38	11.3
NYU IR, Impaired %	100	30.2
NYU DR, Impaired %	197	59.2
% of Time in Over-Perception Zone	<i>N</i> = 249	<i>m</i> = 13.7 (SD:21.4)
% of Time in Accurate Perception Zone	<i>N</i> = 249	<i>m</i> = 62.8 (SD:24.4)

	N	%
% of Time in Under-Perception Zone	$N = 249$	$m = 23.9$ (SD:25.9)

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Table 2.

Association between cognitive impairment with medication adherence.

	Subjective adherence (MARS)						Objective adherence					
	Unadjusted			Adjusted			Unadjusted			Adjusted		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
General cognition												
MoCA	0.91	0.86–0.96	<.001	0.90	0.83–0.96	.002	0.98	0.92–1.05	.60	0.99	0.91–1.08	.78
EF/working memory												
Trails B	1.02	1.00–1.04	.09	1.01	0.98–1.03	.60	1.01	0.98–1.03	.65	1.00	0.97–1.03	.87
Letter-number sequencing	0.98	0.95–0.99	.04	0.98	0.95–1.01	.18	1.00	0.97–1.04	.95	1.01	0.97–10.6	.52
Attention/processing speed												
Trails A	1.02	1.00–1.04	.03	1.02	1.00–1.04	.13	1.01	0.98–1.03	.62	1.01	0.98–1.04	.76
Memory												
NYU immediate recall	0.97	0.94–0.99	.01	0.98	0.95–1.01	.14	1.00	0.96–1.03	.82	1.01	0.97–1.06	.54
NYU delayed recall	0.96	0.94–0.98	.001	0.96	0.93–0.98	.005	0.98	0.94–1.01	.21	0.99	0.95–1.03	.48
Language												
Animal naming	0.99	0.96–1.01	0.25	1.00	0.97–1.03	.88	1.01	0.97–1.04	.76	1.01	0.97–1.05	.53

Table 3.

Association of cognitive impairment with asthma symptom under-perception.

	Symptom under-perception					
	Unadjusted			Adjusted		
	β	SE	<i>p</i>	β	SE	<i>p</i>
General cognition						
MoCA	0.20	0.54	.71	0.09	0.64	.89
EF/working memory						
Trails B	-0.31	0.19	.09	-0.29	0.22	.20
Letter-number sequencing	-0.04	0.21	.84	-0.23	0.26	.38
Attention/processing speed						
Trails A	0.01	0.18	.93	0.14	0.21	.50
Memory						
NYU immediate recall	0.42	0.24	.09	0.29	0.29	.11
NYU delayed recall	0.06	0.22	.79	0.26	0.26	.96
Language						
Animal naming	0.14	0.22	.53	0.09	0.25	.73