Daily Activities: The Impact of COPD and Cognitive Dysfunction

Amanda M. Brunette¹, Kelsey Warner^{2,3}, Kristen E. Holm^{4,5}, Kimberly Meschede⁴,
Frederick S. Wamboldt^{4,6}, Elizabeth Kozora^{4,6}, David J. Moser², Barry J. Make^{4,7}, James D. Crapo^{4,7},
Kerrie L. Moreau^{7,8}, Howard D. Weinberger^{4,7}, Russell Bowler^{4,7}, Karin F. Hoth^{2,4,9,*}

¹University of Iowa, Department of Psychological and Brain Sciences, Iowa City, IA 52242, USA

²University of Iowa Carver College of Medicine, Department of Psychiatry, Iowa City, IA 52242, USA

³Hennepin Healthcare, Department of Speech-Language Pathology, Minneapolis, MN 55404, USA

⁴National Jewish Health, Department of Medicine, Denver, CO 80206, USA

⁵Colorado School of Public Health, Department of Community and Behavioral Health, Aurora, CO 80045, USA

⁶University of Colorado School of Medicine at the Anschutz Medical Campus, Department of Psychiatry, Aurora, CO 80045, USA

⁷University of Colorado School of Medicine at the Anschutz Medical Campus, Department of Medicine, Aurora, CO 80045, USA

⁸Denver Veterans Administration Medical Center, Geriatric Research Education and Clinical Center, Denver, CO 80220 USA

⁹University of Iowa, Iowa Neuroscience Institute, Iowa City, IA 52242, USA

*Corresponding author at: University of Iowa Carver College of Medicine, Department of Psychiatry, 200 Hawkins Dr., W278GH, Iowa City, IA 52242. Tel: 319-356-0544; fax: 319-353-8656; E-mail address: Karin-hoth@uiowa.edu

Accepted 16 September 2020

Abstract

Objective: Chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation; however, pulmonary function does not fully account for patients' functional difficulties. The primary aim of the study was to determine the association between several domains of cognition and daily activity among those with COPD.

Method: Eighty-nine former smokers completed a neuropsychological battery including measures across multiple domains of cognition, pulmonary function measures, and daily activity questionnaires. Using a cross-sectional design, we compared daily activity between former smokers with and without COPD using two measures (St. George's Respiratory Questionnaire [SGRQ] Activity Subscale and Lawton Instrumental Activities of Daily Living [IADL] Scale) and examined the association between cognition and daily activity among those with COPD.

Results: As expected, former smokers with COPD reported more difficulty than those without COPD on both activity measures (SGRQ Activity Subscale $p < .001$; Lawton IADL Scale $p = .040$). Among former smokers with COPD, poorer delayed recall was associated with more difficulty with daily activities (SGRQ Activity Subscale) ($p = .038$) while adjusting for severity of airflow limitation, exercise tolerance, oxygen use, dyspnea, and symptoms of anxiety and depression.

Conclusion: The findings suggest that cognition is associated with daily activity in patients with COPD. Future research should examine whether cognitive interventions may help to maximize patients' engagement in daily activities.

Keywords: Lung disease; Activities of daily living; SGRQ; Neuropsychology; Cognition

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation that is not fully reversible, but it involves multiple systems and comorbidities. A history of cigarette smoking is the primary risk factor for COPD, although inhaled environmental toxins also may contribute. COPD is the third leading cause of death in the USA (Xu, Murphy, & Kochanek, 2015), with prevalence rates increasing with older age (Akgiin, Crothers, & Pisani, 2012). Treatment for COPD focuses on reducing the impact of symptoms (such as fatigue and dyspnea) on patients' lives, reducing acute exacerbations of symptoms, and improving exercise tolerance (Global Initiative for Chronic Obstructive Lung Disease, 2019).

Patients with COPD have impairments in a range of daily tasks. Basic activities of daily living (ADLs) are affected (Braido et al., 2015; Kanervisto et al., 2010; Liu et al., 2014), which include activities necessary for self-care such as bathing, dressing, grooming, and eating (Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963). Individuals with COPD also have impairments in instrumental ADLs (IADLs) (Braido et al., 2015; Kanervisto et al., 2010; Liu et al., 2014; Rodriguez Gonzalez-Moro et al., 2009). IADLs are complex abilities that allow one to adapt to the environment in order to live independently, such as handling finances, preparing food, using the telephone, and engaging in accurate medication use (Lawton & Brody, 1969). COPD severity (staged based on airflow limitation measured using spirometry) has been found to be associated with the ability to manage ADLs and IADLs, with individuals at more advanced stages demonstrating more impairment in the management of daily activities (Hajiro, Nishimura, Tsukino, Ikeda, & Oga, 2000; Kanervisto et al., 2010; Rodriguez Gonzalez-Moro et al., 2009). Disease-specific measures that target the impact of respiratory symptoms specifically are most commonly used to assess the impact of COPD on daily functioning (Hajiro et al., 2000; Janaudis-Ferreira, Beauchamp, Robles, Goldstein, & Brooks, 2014; Miravittles et al., 2009; Peruzza et al., 2003; Rodriguez Gonzalez-Moro et al., 2009). Examples of disease-specific measures include the London Chest Activity of Daily Living Scale (Garrod, Bestall, Paul, Wedzicha, & Jones, 2000), the St. George's Respiratory Questionnaire (SGRQ) Activity Subscale (Jones, Quirk, Baveystock, & Littlejohns, 1992), and the Pulmonary Functional Status and Dyspnea Questionnaire (Lareau, Carrieri-Kohlman, Janson-Bjerklie, & Roos, 1994). The total score of the SGRQ has traditionally been used to measure health-related quality of life, though examining the Activity Subscale allows the assessment of how daily activity is affected due to respiratory disease.

Research has previously examined the associations between pulmonary measures (including airflow limitation, exercise intolerance, and shortness of breath) and problems performing daily activities in COPD. Some studies have found significant relationships between pulmonary measures and daily functioning (Engstrom, Persson, Larsson, & Sullivan, 2001; Incalzi et al., 2001; Liang et al., 2008; Peruzza et al., 2003; Seemungal et al., 1998; van Helvoort, Willems, Dekhuijzen, van Hees, & Heijdra, 2016). Other studies had variable findings across different pulmonary measures (Garrod et al., 2000; Kapella, Larson, Covey, & Alex, 2011; Marin et al., 2011; Özge, Özge, & Ünal, 2006; Ozsoy et al., 2019). One study did not find significant relationships (Osman, Godden, Friend, Legge, & Douglas, 1997). When effect sizes were provided, they ranged from no effect to large. The inconsistent findings may be due to differences in the severity of the COPD population included in the study (Ozsoy et al., 2019), or individual differences in patients' response to symptoms (Kapella et al., 2011; Leidy, 1994) with some people choosing to manage less activities given their pulmonary symptoms, whereas others choose to maintain their management of daily activities despite increased pulmonary symptoms.

Identifying additional causes of functional limitation beyond pulmonary factors alone is necessary. Functional disability predicts mortality and nursing home placement (Bharucha, Pandav, Shen, Dodge, & Ganguli, 2004; Inouye et al., 1998) and this risk is even higher for older persons who have COPD (Liu et al., 2014). Understanding factors that contribute to decreased daily activity in COPD could lead to improved patient care. Cognition is an understudied area in COPD and cognitive functioning is an additional clinical factor that may influence daily activity in COPD.

Studies in the neuropsychology literature have found that cognition is more strongly associated with the ability to complete IADLs than basic ADLs. Cognitive difficulties interfere with the ability to manage IADLs in healthy older adults (Cahn-Weiner, Boyle, & Malloy, 2002; Cahn-Weiner, Malloy, Boyle, Marran, & Salloway, 2000; Gross, Rebok, Unverzagt, Willis, & Brandt, 2011; Lahav & Katz, 2020), populations with chronic medical conditions such as patients with heart failure and cardiovascular disease (Alosco et al., 2012; Jefferson, Paul, Ozonoff, & Cohen, 2006), and patients with neurological disease (Baum, Edwards, Yonan, & Storandt, 1996; Cahn-Weiner et al., 2007; Gold, 2012; Goverover, Genova, Hillary, & DeLuca, 2007; Goverover & Hinojosa, 2002; Hansen et al., 2018; Katz, Hartman-Maeir, Ring, & Srooker, 2000; Schmitter-Edgecombe, Woo, & Greeley, 2009; Toglia et al., 2017).

Some previous studies have found a relationship between cognition and daily activity (i.e., basic ADLs, IADLs, and disease-specific measures of daily activity) in COPD. However, the focus has been on the association between global cognitive functioning rather than specific cognitive domains (Martinez, Richardson, Han, & Cigolle, 2014; Özge et al., 2006; Yazar et al., 2017). Antonelli-Incalzi et al. (2008) found that level of global cognition (i.e., high, medium, and low) was positively associated with both basic and IADLs in patients with COPD. Studies using a disease-specific measures (i.e., Activity Subscale of the SGRQ) have found variable results regarding the relationship between cognition and daily activity (Cleutjens, Spruit, et al., 2017b; Incalzi et al., 2001; Park & Larson, 2015). Overall, although some research has observed a relationship between cognition and functional abilities in patients with COPD, research has not examined a broad range of neuropsychological domains in relation to functional abilities in patients with COPD.

Comprehensive neuropsychological assessment could reveal which cognitive domains are related to difficulties in daily activities among patients with COPD. This is especially relevant in this population because patients with COPD experience most pronounced reductions in executive functioning (Cleutjens, Franssen, et al., 2017a; Dodd, Getov, & Jones, 2010; Kozora et al., 2008; Liesker et al., 2004; Villeneuve et al., 2012), processing speed (Cleutjens, Franssen, et al., 2017a;

Dodd et al., 2010; Kozora et al., 2008; Liesker et al., 2004; Prigatano, Parsons, Levin, Wright, & Hawryluk, 1983), and memory (Dodd et al., 2010; Kozora et al., 2008; Prigatano et al., 1983; Stuss, Peter, Guzman, Guzman, & Troyer, 1997) in the context of intact performance on global cognitive screening measures. Research suggests that in general more advanced COPD (via Global Initiative for Chronic Obstructive Lung Disease [GOLD] stage) is associated with poorer cognitive performance (Crews et al., 2001; Fix, Golden, Daughton, And, & Bell, 1982; Hoth et al., 2020; Liesker et al., 2004; Prigatano et al., 1983; Stuss et al., 1997). Examining cognition and daily functioning is important in individuals with COPD, given that even subtle difficulties in various domains of cognitive functioning may impact the ability to manage daily activities.

The first aim of the current analysis was to compare engagement in daily activities between former smokers with COPD and former smokers without COPD. Since daily activity has been examined in multiple ways in previous research, we chose to include both a general measure of functional abilities (Lawton IADL) and a disease-specific measure of daily activity (Activity Subscale of the SGRQ). We hypothesized that former smokers with COPD would report more impairment in daily activity as measured by the SGRQ Activity subscale and Lawton IADL Scale. The second and primary aim was to determine the association between domains of cognition and daily activity among those with COPD. We hypothesized that poorer cognitive performance in memory, executive functioning, and processing speed would be associated with more impairment in daily activity in former smokers with COPD. The domains of memory, executive functioning, and processing speed were examined because they are the domains of cognition that are primarily affected in patients with COPD, and as a result are most likely to be related to difficulty with daily functioning. Additional cognitive domains were also included in this study to be comprehensive.

Methods

Study Population

Participants were recruited from the cohort of individuals in the COPDGene study at National Jewish Health (NJH) in Denver, CO (Regan et al., 2010) to participate in an ancillary study focused on examining cardiovascular physiology and cognition in smokers with and without COPD (NIH K23 HL095658; further information about the ancillary study can be found Hoth et al. (2020)). Participants were limited to former smokers because current smoking acutely alters vascular function, which was a primary measure in that study. The current study is a secondary analysis of the ancillary study data. All procedures involving human participants were approved by the Institutional Review Board at NJH (#2278A). All participants provided written documentation of informed consent before participating in the study. The study was performed in accordance with the ethical standards of the Declaration of Helsinki. Study visits occurred between March 2011 and April 2013.

Participants were required to be between 55 and 85 years old, have at least a 10 pack-year smoking history at the time of their enrollment in the COPDGene study, have at least an 8th-grade education, speak English at the level of a native speaker, and have normal corrected vision and hearing. Exclusion criteria were determined based on self-report through a phone screen prior to the study. Exclusion criteria were as follows: previous diagnosis of mild cognitive impairment or dementia, previous diagnosis of a neurological disorder (e.g., stroke or movement disorder), traumatic brain injury with loss of consciousness greater than 10 min, major psychiatric disorder (e.g., schizophrenia, bipolar disorder, alcohol or other substance use disorder besides tobacco), history of treatment for alcohol or substance use (other than tobacco use), recent change in treatment for depression or anxiety, major medical condition other than COPD or asthma (e.g., renal failure, uncontrolled cancer, previous radiation treatment for cancer), certain specific cardiovascular conditions (i.e., arrhythmia, left sided heart failure), COPD exacerbation within the past month that required a physician or ER visit and/or treatment with antibiotics or oral corticosteroids. Exclusion criteria for the current study were designed to reduce confounding medical conditions that impact cognition in older adults. One hundred and one participants enrolled in the ancillary study. Twelve participants were excluded from the current analyses for the following reasons: three endorsed exclusion criteria during study visits that were not endorsed upon screening (one active illicit substance use, two traumatic brain injury), three participants were missing data for some of the cognitive measures, one participant was an outlier regarding education, and five participants were outliers with regard to young age (and were removed a priori to age match the groups).

The most common approach to staging the severity of COPD is described by the GOLD (Global Initiative for Chronic Obstructive Lung Disease, 2019). The presence of persistent airflow limitation on spirometry has been the core of the GOLD definition of COPD since 2001 (i.e., mild [Stage 1] to very severe [Stage 4] airflow limitation). In the current manuscript we grouped participants based on classification of airflow limitation (No COPD, Stage 1–2, and Stage 3–4) (Global Initiative for Chronic Obstructive Lung Disease, 2019) so that the severity variable reflected a unitary construct for ease of interpretation in the models. In an effort to enroll a representative sample, the study allowed for the enrollment of patients with a wide range of COPD severity. The current sample included 31 former smokers without COPD and 58 with COPD based on airflow limitation (33 mild–moderate airflow limitation [4 GOLD stage 1 and 29 GOLD stage 2] and 25 severe–very severe airflow limitation

[14 GOLD stage 3 and 11 GOLD stage 4]). All participants were former smokers, but the groups differed in terms of qualifying for a diagnosis of COPD based on airflow limitation measured by spirometry. The sample size was set based on power analysis for the primary aims of the grant (NIH K23 HL095658) focused on cardiopulmonary mechanisms that affect cognition in COPD. The current analysis utilized activity measures that were collected for secondary data analysis.

Procedures and Measures

The study is a cross-sectional design. Participants completed all measures included in the current analysis on the same day. A study flow diagram can be found in [Fig. 1](#).

Daily Activity Measures

Participants completed the Lawton Instrumental Activities of Daily Living (IADL) Scale (Lawton & Brody, 1969). The Lawton IADL Scale is a general self-report measure of functional abilities and has been used across many populations, including older adults (Cahn-Weiner et al., 2002), patients with mild cognitive impairment (Burton, Strauss, Bunce, Hunter, & Hultsch, 2009; Tabert et al., 2002), and patients with dementia (Boyle, Cohen, Paul, Moser, & Gordon, 2002; Boyle et al., 2003; Green, Mohs, Schmeidler, Aryan, & Davis, 1993; Włodarczyk, Brodaty, & Hawthorne, 2004). The Lawton IADL Scale contains the following eight items: telephone use, shopping, food preparation, house-keeping, laundry, transport, medication use, and finance management. Responses were dichotomized (i.e., coded to indicate the presence or absence of any reported IADL difficulty).

The SGRQ Activity Subscale was used as a disease-specific measure of daily activities (Jones et al., 1992). The SGRQ Activity Subscale has been utilized extensively in patients with COPD (Ferrer et al., 1997; Garrod et al., 2000; Liang et al., 2008; Marin et al., 2011; Menn, Weber, & Holle, 2010; Mostert, Goris, Weling-Scheepers, Wouters, & Schols, 2000). The SGRQ Activity Subscale is a self-report measure of daily activities that cause or are limited by breathlessness. Questions address how breathlessness interferes with activities such as dressing, walking up a flight of stairs, completing housework, and engaging in exercise. Scores on the SGRQ Activity Subscale can range from 0 to 100, with higher scores indicating greater limitation of daily activities due to breathlessness.

COPD Severity

Spirometry was performed with the EasyOne spirometer (nidd, Medical Technologies Inc., Andover, MA), in accordance with ATS guidelines. After baseline forced vital capacity (FVC) testing, two puffs of albuterol (180 mg) were administered from a metered dose inhaler with a spacer. After 20 min the participants were prompted to perform three additional acceptable FVC maneuvers. Any results of questionable quality (rating of C or below) were reviewed by a study pulmonologist (BJM). Primary measures were postbronchodilator forced expiratory volume in 1 s (FEV1) percent predicted and FEV1/FVC ratio. For three of the participants, previous spirometry results were obtained and entered due to suboptimal quality of testing.

Neuropsychological Performance

The cognitive measures used in this study were chosen because they are frequently used in clinical and experimental neuropsychology research and have normative data for healthy individuals. The cognitive tests were administered and scored by a trained research assistant using standard administration and scoring criteria under the supervision of a neuropsychologist. The research assistant was blind to the hypothesis of the current analysis. Consistent with common practice in neuropsychological assessment, single word reading ability was used to estimate premorbid intellectual functioning. In this study, single word reading ability as assessed using the WRAT4 Reading Standard Score (mean of 100 and SD of 15). The WRAT4 was included for descriptive purposes and not as a primary cognitive measure. Scores for cognitive functioning were grouped into the following domains: (i) executive functioning/processing speed, (ii) memory recall, (iii) language, and (iv) visuospatial functioning. The executive functioning/processing speed domain include the Trail Making Test Part B (Tombaugh, Rees, & McIntyre, 1998), the Controlled Word Associated Test (COWA) (Tombaugh, Kozak, & Rees, 1998), and the Wechsler Adult Intelligence Scale Fourth Edition (WAIS-IV) Coding subtest (Wechsler, 2008). The memory domain included the California Verbal Learning Test Second Edition (CVLT-II) Long Delay Free Recall (Delis, Kramer, Kaplan, & Ober, 2000) and the Brief Visuospatial Memory Test (BVM-T) Delayed Recall (Benedict, 1997). The language domain included the Boston Naming Test (Kaplan, Goodglass, & Weintraub, 2001) and category fluency (specifically animal fluency) (Gladsjo et al., 1999). The visuospatial functioning domain included the WAIS-IV Block Design subtest (Wechsler, 2008) and the Hooper Visual Organization Test (Hooper, 1983). Raw test scores were transformed into T-scores that have a mean of 50 and standard deviation of 10 using previously published

Fig. 1. Study flow diagram.

age-referenced normative data for healthy adults. Cognitive domain scores were calculated as the arithmetic mean of normatively derived T-scores for all of the tests in that domain. Thus, a domain score of 50 indicates exactly average performance, with a score of 40, for example, indicating performance that is 1 SD below the mean relative to healthy age-matched peers. For more detail on the cognitive measures used in this study, see the supplementary material.

Additional Measures

The Hospital Anxiety and Depression Scale (HADS) was used to determine severity of symptoms of depression and anxiety. The HADS has been used in studies of COPD (Laurin, Moullec, Bacon, & Lavoie, 2011; Ng et al., 2007). There are 14 items in this measure. The total score can range from 0 to 42 with scores below 14 typically considered “normal.” In the current sample, Cronbach’s alpha for the HADS total score was .84. The Modified Medical Research Council (MMRC) Dyspnea Scale is a one item self-report measure of breathlessness that can range from 0 to 4, with a higher score indicating more breathlessness (Fletcher, Elmes, Fairbairn, & Wood, 1959).

The 6-minute Walk Test (6MWT) was used as an indicator of exercise intolerance. This test measures the distance walked in 6 min and was administered according to ATS guidelines (“ATS statement: Guidelines for the six-minute walk test, 2002”).

Data Analysis

First, characteristics of the COPD group relative to the comparison group were examined using *t*-tests for continuous variables and chi-square (χ^2) tests for dichotomous variables. Second, Pearson correlations, *t*-tests, and chi-square (χ^2) tests were used to identify demographic, clinical, and cognitive variables associated with the two activity measures (SGRQ Activity Subscale and Lawton IADL Scale) in former smokers with COPD including: age, sex, education, WRAT4 Word Reading, pack-years, HADS total score (which addresses both depression and anxiety symptoms), FEV1% Predicted, 6MWT meters walked, MMRC, oxygen use, memory recall, executive functioning/processing speed, language, and visuospatial functioning. Third, demographic and clinical variables that were related to either activity measure (i.e., SGRQ Activity Subscale or IADL problems) were entered into simultaneous regression models conducted in former smokers with COPD with activity as the dependent variable (one linear regression for the SGRQ Activity Subscale and one logistic regression for Lawton IADL Scale). We included the same covariates in all regression models to ease interpretation. All analyses examining the relationship between cognition and daily activities were conducted only in former smokers with COPD because this population had been shown to present with impairments in daily activities. Given that the primary aim was to examine cognitive function in relation to daily activity, separate regression models were run for each cognitive domain that was significantly related to the activity measures.

Some data were missing in the study. One individual with COPD did not complete the MMRC dyspnea rating for unknown reasons. One individual with COPD was unable to complete the 6MWT due to a physical injury. Four individuals skipped one item on the HADS (three individuals with COPD and one individual without COPD), and as a result their total score was prorated. Three individuals without COPD did not complete over four items on the SGRQ, and as a result the Activity Subscale could not be calculated. The SGRQ manual indicates that the activity component can only tolerate a maximum of four missed items.

Results

Former smokers with COPD reported a more extensive smoking history, more breathlessness, and more symptoms of depression and anxiety than the comparison group (Table 1). Individuals with COPD also were more likely to use oxygen and walked a shorter distance on the 6MWT. Overall, the mean cognitive performance of both groups was within the average range. However, individuals with COPD performed significantly worse on the executive functioning/processing speed domain than those without COPD ($p = .007$; Table 1). With regard to daily activities, former smokers with COPD reported more difficulty with daily activities due to breathlessness on the SGRQ Activity Subscale compared to those without COPD ($t = -5.786$, $p < .001$), and a significantly greater proportion of former smokers with COPD reported difficulty with one or more IADLs relative to patients without COPD ($\chi^2 = 4.23$, $p = .040$; 52% vs. 29%, respectively, see Table 1).

Bivariate analyses revealed a significant association between memory (delayed recall) and the SGRQ Activity Subscale ($p = .011$; Table 2). There was also a significant association between language and difficulty on IADLs ($p = .010$; Table 2). Based on the bivariate associations presented in Table 2, the following covariates were included in linear and logistic regression models because they had a statistically significant association with the SGRQ Activity Subscale OR IADL problems in bivariate

Table 1. Demographic and clinical characteristics, daily activity, and neuropsychological performance

	No COPD <i>n</i> = 31		COPD <i>n</i> = 58		95% CI	P	Effect size D or phi**
	Mean (SD)	(<i>n</i>) %	Mean (SD)	(<i>n</i>) %			
Demographic and clinical characteristics							
Age (years)	67.7 (5.7)		70.2 (7.1)		(−5.49, 0.40)	.089	0.39
Sex (<i>n</i> /% female)		(14) 45.2		(24) 41.4		.731	0.04
Years of education	14.8 (2.3)		13.9 (2.1)		(−0.06, 1.89)	.066	0.41
Race (<i>n</i> /% Black)		(1) 3.2		(6) 10.3		.235	0.13
Ethnicity (<i>n</i> /% Hispanic or Latino)		(1) 3.2		(0) 0		.169	0.15
Estimated premorbid IQ (WRAT 4)	101.1 (8.3)		101.9 (6.7)		(−4.05, 2.42)	.617	0.11
Smoking history (pack-years)	36.4 (21.5)		59.5 (36.1)		(−35.31, −11.03)	<.001	0.78
Depression and anxiety (HADS)	5.0 (3.6)		7.5 (5.2)		(−4.61, −0.42)	.019	0.56
Post-Bronchodilator Spirometry							
FEV1/FVC(%)	77.9 (4.8)		52.5 (11.9)		(20.92, 29.77)	*	
FEV1% Predicted	92.0 (18.3)		52.3 (20.1)		(31.03, 48.25)	*	
6MWT distance (m)	501.6 (91.9)		394.3 (102.6)		(63.41, 151.25)	<.001	1.10
Breathlessness (MMRC Dyspnea Scale)	0.4 (0.7)		1.5 (1.1)		(−1.50, −0.74)	<.001	1.19
Any oxygen use		(4) 12.9		(39) 67.2		<.001	0.52
Neuropsychological performance ⁺							
Memory recall	50.8 (9.4)		47.7 (8.1)		(−0.67, 6.89)	.105	0.35
Executive functioning/processing speed	51.4 (6.4)		47.5 (6.4)		(1.08, 6.74)	.007	0.61
Language	54.2 (6.9)		51.4 (6.7)		(−0.14, 5.88)	.062	0.41
Visuospatial functioning	52.5 (7.4)		52.4 (5.9)		(−2.72, 3.00)	.922	0.01
Daily activity							
SGRQ Activity Subscale	20.0 (22.1)		52.9 (25.8)		(−44.19, −21.58)	<.001	1.37
Lawton IADL Scale (any reported problem)		(9) 29.0		(30) 51.7		.040	0.22

Note: *The two groups of patients with and without COPD were created based on these variables, thus the statistical comparison is not relevant. **Cohen's *D* was used as the effect size for continuous variables and ϕ was used as the effect size for categorical variable. [†]Neuropsychological performance measures were examined using T-scores. T-scores for each cognitive domain are age-corrected average values for the tests in that domain, with a mean of 50 and a standard deviation of 10. CI = confidence interval. Race categories included White and Black participants. Ethnicity categories included Hispanic or Latino and not Hispanic or Latino.

analyses: FEV1% predicted ($p < .001$), 6MWT Distance ($p < .001$), oxygen use (yes vs. no) ($p < .001$), MMRC Dyspnea score ($p < .001$), HADS Total Score ($p = .019$).

A total of four regression models were calculated, two linear regressions with the SGRQ Activity Subscale as the dependent variable (one including memory and one including language) and two logistic regressions with self-reported IADL problems (Yes or No) as the dependent variable (one including memory and one including language). The association between memory (delayed recall) and daily activities on the SGRQ Activity Subscale ($b = -0.610$, $p = .038$) remained statistically significant after adjusting for demographic and clinical covariates (Table 3). Therefore, poorer memory performance was associated with more difficulty with daily activities on the SGRQ Activity Subscale in individuals with COPD. Language was not significantly associated with difficulties with daily activity on the SGRQ Activity Subscale ($p > .05$) in the fully adjusted model. Neither delayed recall nor language remained statistically significantly associated with IADL problems ($p > .05$) after adjusting for demographic and clinical covariates.

Discussion

This study examines specific domains of cognitive functioning in relation to daily activity in patients with COPD. We considered both a disease-specific measure of daily activity that assesses daily activity due to breathlessness (as it is most typically assessed in COPD using the SGRQ Activity Subscale) and a general measure of instrumental daily activities (as measured by the Lawton IADL Scale). As expected, former smokers with COPD reported more difficulty with daily activities on both the SGRQ Activity Subscale and on the Lawton IADL Scale compared to those without COPD. We found that worse performance on an objective cognitive memory measure (delayed recall) was associated with more difficulties with daily activity (i.e., SGRQ Activity Subscale) in former smokers with COPD. The association between poorer delayed recall and difficulty with daily activities was significant after adjusting for the effects of airflow limitation, exercise tolerance (i.e., 6MWT distance), oxygen use, breathlessness, and symptoms of depression and anxiety.

Follow-up analyses were completed to examine the correlations between each memory test and the SGRQ Activity Subscale to help clarify our significant model further. Among former smokers with COPD, poorer delayed visual recall (BVM-T delayed recall) was associated with more difficulty with daily activities (SGRQ Activity Subscale) ($r = -.285$, $p = .030$). Delayed verbal

Table 2. Bivariate association of demographic, clinical, and cognitive variables with daily activity in participants with GOLD defined COPD

Variable	SGRQ Activity Subscale		Lawton IADL Scale (any reported problem)	
	<i>r</i> or <i>t</i>	<i>P</i>	<i>t</i> or χ^2	<i>p</i>
Age	<i>r</i> = −.21	.110	<i>t</i> = −1.46	.149
Sex	<i>t</i> = −1.40	.167	χ^2 = 1.66	.198
Years of education	<i>r</i> = .03	.835	<i>t</i> = 0.84	.406
Estimated premorbid IQ (WRAT 4)	<i>r</i> = −.16	.230	<i>t</i> = −0.22	.830
Smoking history (pack-years)	<i>r</i> = .03	.830	<i>t</i> = 0.60	.553
FEV1% Predicted	<i>r</i> = −.58	<.001	<i>t</i> = −1.12	.267
6MWT distance (Meters)	<i>r</i> = −.57	<.001	<i>t</i> = 1.05	.300
Any oxygen use	<i>t</i> = −7.27	<.001	χ^2 = 0.09	.923
Breathlessness (MMRC Dyspnea Scale)	<i>r</i> = .61	<.001	<i>t</i> = −0.75	.454
Depression and anxiety (HADS)	<i>r</i> = .31	.019	<i>t</i> = −0.53	.597
Executive functioning/processing speed	<i>r</i> = −.10	.449	<i>t</i> = 0.69	.493
Memory recall	<i>r</i> = −.33	.011	<i>t</i> = 1.33	.188
Language	<i>r</i> = −.06	.677	<i>t</i> = 2.65	.010
Visuospatial functioning	<i>r</i> = −.13	.325	<i>t</i> = −0.80	.430

Note: 6MWT = 6-minute walk test. MMRC = Modified Medical Research Council. HADS = Hospital Anxiety and Depression Scale. SGRQ = St. George's Respiratory Questionnaire. Difficulties with IADLs were measured by the Lawton IADL Scale. Variables are bolded if they have a $p < .05$. Pearson correlations, *t*-tests, and chi-square (χ^2) tests were used to identify demographic, clinical, and cognitive variables associated with the two activity measures (SGRQ Activity Subscale and Lawton IADL Scale) in former smokers with COPD. Pearson correlations (*r*) were used when examining the relationship between two continuous variables, *t*-tests were used when examining the relationship between a continuous variable and dichotomous variable, and a chi-square (χ^2) test was used when examining the relationship between two dichotomous variables. Notably, the Lawton IADL Scale was dichotomized (i.e., coded to indicate the presence or absence of any reported IADL difficulty). These analyses were completed in participants with COPD, and $n = 58$ except in situations where there were missing data (as outlined at the end of the Methods section).

Table 3. Linear regression for SGRQ activity among former smokers with GOLD defined COPD

Independent variable	Unstandardized b	SE	P
FEV1% predicted	−0.311	0.128	.019
6MWT distance (m)	−0.017	0.028	.553
Any oxygen use			
No	Reference		
Yes	18.869	6.251	.004
Breathlessness (MMRC Dyspnea Scale)	4.560	2.500	.074
Depression and anxiety (HADS)	0.533	0.427	.218
Memory recall	−0.610	0.286	.038

Note: In bold if significant. A higher score on the SGRQ Activity Subscale indicates greater limitation in activity.

recall (CVLT-II delayed free recall) was not significantly associated with daily activities (SGRQ Activity Subscale), though the finding trended toward significance ($r = -.232$, $p = .080$). As a result, our finding may not be specific to verbal or visual memory.

Our findings suggest that memory was significantly associated with a disease-specific measure of daily activities, and not related to a general measure of IADLs (Lawton IADL). The SGRQ Activity Subscale is a disease-specific self-report measure of daily activities limited by breathlessness (e.g., dressing, walking up a flight of stairs, completing housework, and engaging in exercise). The Lawton IADL assesses independent living skills more broadly, such as ability to prepare food and handle finances. It is possible memory was significantly related to the SGRQ Activity Subscale because this measure more adequately captured the difficulties with daily activities seen in patients with COPD. For example, the effect size for the SGRQ Activity Subscale when comparing patients with and without COPD was 1.37, whereas the effect size was 0.22 for the Lawton IADL measure.

The study was designed to investigate whether mild weaknesses in cognition affected daily living in participants who had not previously come to clinical attention as having cognitive difficulties. By including multiple clinical variables known to impact activity (e.g., airflow limitation, exercise tolerance, shortness of breath) in the model, we were able to examine whether cognition had an independent association with daily activity. Strengths of this study were that we examined specific cognitive domains in relation to daily functioning in contrast with previous studies that have focused on global cognition. We also adjusted for disease severity and use two functional ability measures (i.e., SGRQ Activity Subscale and Lawton IADL Scale respectively).

Limitations of the study must be considered when interpreting the findings. Participants in our study endorsed minimal problems completing daily activities on the Lawton IADL Scale (e.g., cooking, using the telephone). As a result, the IADL

score was dichotomized into participants with no concerns and those with some reported concern (i.e., 0 vs. 1 score). The Lawton IADL Scale has been examined in this manner in other studies (Jefferson et al., 2006; Steffens, Bosworth, Provenzale, & MacFall, 2002), but the limited endorsement of problems suggests that the items do not ideally capture the IADL difficulties that are most relevant for this population. The measure has most frequently been used in patients with dementia who have notable cognitive impairment (Green et al., 1993). The fact that associations between cognitive performance and IADL difficulties were no longer significant in models that were fully adjusted for key demographic and clinical variables may be due to limitations of the Lawton IADL measure's sensitivity. Future research investigating activity engagement in patients with COPD should explore measures that capture a broader range of functioning, such as the Everyday Cognition Scale (Farias et al., 2008), which includes more complex and higher order daily tasks than the Lawton IADL Scale. There is some indication in the literature that patients with COPD tend to underreport their symptoms (Langsetmo, Platt, Ernst, & Bourbeau, 2008; Wilkinson, Donaldson, Hurst, Seemungal, & Wedzicha, 2004), thus, in future studies it would be useful to collect information from informants as they may have more insight into the patient's everyday functioning.

Future research could also examine performance-based and naturalistic measures of daily functioning. Utilizing tasks that mimic naturalistic settings have been developed with the goal of better capturing real-world functional abilities (Burgess et al., 2006; Robertson & Schmitter-Edgecombe, 2017). Some performance-based measures of daily functioning include Executive Function Performance Test (EFPT) (Baum, 2003), the Weekly Calendar Planning Activity (Toglia, 2015), the Actual Realities Test (Goverover & DeLuca, 2018), the Performance Assessment of Self-Care Skills (PASS) (Chisholm, Toto, Raina, Holm, & Rogers, 2014), the Kitchen Task Assessment (Baum & Edwards, 1993), the Kettle test (Hartman-Maeir, Harel, & Katz, 2009), and various versions of the Multiple Errands Test (Antoniak et al., 2019; Burns et al., 2019; Dawson et al., 2009; Rand, Rukan, Weiss, & Katz, 2009; Shallice & Burgess, 1991). Using measures that capture more complex IADLs from both the patient and an informant would add to our understanding of the relationship between specific cognitive domains and daily activity in patients with COPD.

An additional limitation is that the participants self-reported their medical and substance use history to determine exclusion criteria, and it is possible they inaccurately reported their history or had an undiagnosed medical condition. Those participants who agreed to participate in our study, which required attending two visits, may have had higher cognitive and physical functional abilities than those who declined to participate. Our study involved secondary data analyses and future studies are needed that directly and prospectively address the relationship between cognition and daily functioning in COPD. Additionally, our sample included only former smokers given the study was a secondary analysis of data from a grant focused on former smokers. Thus, we cannot be sure that the findings generalize to all individuals with COPD from different causes. Future research is needed that includes smoking status to better understanding the impact of cognitive function on ADLs. The sample had limited diversity in terms of ethnicity and race, and this restricts the generalizability of the findings. Lastly, it is important to note that depression and anxiety symptom severity was minimal in our sample. Future studies should examine the impact of mood symptoms on the relationship between cognition and daily functioning in COPD.

Our original hypothesis was that poorer performance in memory, executive functioning, and processing speed would be associated with more difficulty with daily activities in former smokers with COPD. Despite the limitations of our activity measures in this population, we did observe that memory performance was associated with daily activity in patients with COPD. This association is supported by previous research in healthy older adults (Gross et al., 2011), patients with mild cognitive impairment (Schmitter-Edgecombe et al., 2009), and patients with dementia (Cahn-Weiner et al., 2007).

We anticipated that executive functioning and processing speed performance would also be associated with daily activity. This hypothesis was based on past research findings (Cahn-Weiner et al., 2002) and the fact that patients with COPD experience weaknesses in executive functioning and processing speed early in the disease progression (Dodd et al., 2010; Kozora et al., 2008; Liesker et al., 2004; Villeneuve et al., 2012). Instead, in our sample memory was associated with activity beyond the effects of traditional measures of disease severity, but executive functioning/processing speed was not significantly associated with activity. Our findings suggest that cognition is associated with daily activity, but also highlight the need for future research to use activity measures that capture a wider range of more complex everyday activities.

There are clinical implications of the association between cognition and daily activities in COPD. First, the findings provide clinicians with further understanding of the factors that contribute to impairments in daily functioning in patients with COPD. If a patient with COPD presents with difficulty completing daily activities, clinicians could consider cognition as contributing to these problems. Second, the findings underscore the importance of attending to cognitive functioning when treating patients with COPD. Understanding the domains of cognition that may contribute to management of daily activities in patients with COPD can help inform how cognitive rehabilitation is applied. Our findings suggest that memory aids are likely to be particularly important. Previous research has shown that cognitive interventions (such as teaching strategies to compensate for cognitive weaknesses) resulted in improved engagement in daily activities in stroke patients (Carter, Oliveira, Duponte, & Lynch, 1988) and in patients with mild cognitive impairment (Kurz, Pohl, Ramsenthaler, & Sorg, 2009). Other interventions may aid in

maintaining cognitive functioning, such as exercise (Kramer, Erickson, & Colcombe, 2006), healthy eating (Gomez-Pinilla, 2008), and social support (Seeman, Lusignolo, Albert, & Berkman, 2001). Since patients in the earlier stages of COPD do report changes in daily activities (Miravittles et al., 2009), a cognitive intervention may be most effective early in the disease and prevent further decline in activity engagement. However, this study is cross-sectional and further research is needed to justify the implementation of these interventions in patients with COPD.

Overall, cognition is associated with daily activity in patients with COPD. Our study supports that even among individuals with mild cognitive weaknesses, poorer memory was associated with more difficulty with daily activities. In addition to focusing on the effect of physical symptoms like dyspnea on difficulties with daily activities, clinicians should also consider the impact of cognition on management of daily activities in patients with COPD.

Acknowledgments

We thank Ann Depew, M.A. and Christina Schnell, B.A. for assistance with participant recruitment and Trudi Madigan, Ronnie Calzada, Steven Belcher, and James Thorpe for assistance with data collection. Thank you to James Murphy PhD for assistance with study design and Anne Hunting, Lyndsay Lev, B.S., and Anna Croghan, M.A. for administrative support. Study data were collected and managed using REDCap electronic data capture tools hosted at the University of Colorado. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies.

Funding

This work was supported by the National Institutes of Health [K23 HL095658, R01 HL089897, R01 HL089856] and the NIH/NCATS Colorado CTSI Grant [UL1 TR001082]. Contents are the authors' sole responsibility and do not necessarily represent official NIH views. The COPDGene study [NCT00608764] is also supported by the COPD Foundation through contributions made to an Industry Advisory Board comprised of AstraZeneca, Boehringer-Ingelheim, Novartis, Pfizer, GlaxoSmithKline, Siemens and Sunovion.

Conflict of Interest

None declared

References

- Akgün, K. M., Crothers, K., & Pisani, M. (2012). Epidemiology and management of common pulmonary diseases in older persons. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 67(3), 276–291. doi: 10.1093/gerona/glr251.
- Alosco, M. L., Spitznagel, M. B., Cohen, R., Sweet, L., Colbert, L. H., Josephson, R., et al. (2012). Cognitive impairment is independently associated with reduced instrumental ADLs in persons with heart failure. *The Journal of Cardiovascular Nursing*, 27(1), 44. doi: 10.1097/JCN.0b013e318216a6cd.
- Antonelli-Incalzi, R., Corsonello, A., Trojano, L., Acanfora, D., Spada, A., Izzo, O., et al. (2008). Correlation between cognitive impairment and dependence in hypoxemic COPD. *Journal of Clinical and Experimental Neuropsychology*, 30(2), 141–150. doi: 10.1080/13803390701287390.
- Antoniak, K., Clores, J., Jensen, D., Nalder, E., Rotenberg, S., & Dawson, D. R. (2019). Developing and validating a big-store multiple errands test. *Frontiers in Psychology*, 10, 2575. doi: 10.3389/fpsyg.2019.02575.
- ATS statement: Guidelines for the six-minute walk test (2002). *American Journal of Respiratory and Critical Care Medicine*, 166(1), 111–117.
- Baum, C., Edwards, D., Yonan, C., & Storandt, M. (1996). The relation of neuropsychological test performance to performance of functional tasks in dementia of the Alzheimer type. *Archives of Clinical Neuropsychology*, 11(1), 69–75.
- Baum, C., & Edwards, D. F. (1993). Cognitive performance in senile dementia of the Alzheimer's type: The kitchen task assessment. *American Journal of Occupational Therapy*, 47(5), 431–436.
- Baum, C. M., Morrison, T., Hahn, M., & Edwards, D. F. (2003). *Test manual: Executive function performance test*. St. Louis, MO: Washington University.
- Benedict, R. (1997). *Brief visuospatial memory test revised*. Lutz, FL: Psychological Assessment Resources, Inc.
- Bharucha, A. J., Pandav, R., Shen, C., Dodge, H. H., & Ganguli, M. (2004). Predictors of nursing facility admission: A 12-year epidemiological study in the United States. *Journal of the American Geriatrics Society*, 52(3), 434–439. doi: 10.1111/j.1532-5415.2004.52118.x.
- Boyle, P. A., Cohen, R. A., Paul, R., Moser, D., & Gordon, N. (2002). Cognitive and motor impairments predict functional declines in patients with vascular dementia. *International Journal of Geriatric Psychiatry*, 17(2), 164–169.
- Boyle, P. A., Malloy, P. F., Salloway, S., Cahn-Weiner, D. A., Cohen, R., & Cummings, J. L. (2003). Executive dysfunction and apathy predict functional impairment in Alzheimer disease. *The American Journal of Geriatric Psychiatry*, 11(2), 214–221.
- Braido, F., Baiardini, I., Scichilone, N., Sorino, C., Di Marco, F., Corsico, A., et al. (2015). Disability in moderate chronic obstructive pulmonary disease: Prevalence, burden and assessment - results from a real-life study. *Respiration*, 89(2), 100–106. doi: 10.1159/000368365.
- Burgess, P. W., Alderman, N., Forbes, C., Costello, A., LAURE, M. C., Dawson, D. R., et al. (2006). The case for the development and use of "ecologically valid" measures of executive function in experimental and clinical neuropsychology. *Journal of the International Neuropsychological Society*, 12(2), 194–209.

- Burns, S. P., Dawson, D. R., Perea, J. D., Vas, A., Pickens, N. D., & Neville, M. (2019). Development, reliability, and validity of the multiple errands test home version (MET-home) in adults with stroke. *American Journal of Occupational Therapy*, 73(3), 7303205030p1–7303205030p10.
- Burton, C. L., Strauss, E., Bunce, D., Hunter, M. A., & Hultsch, D. F. (2009). Functional abilities in older adults with mild cognitive impairment. *Gerontology*, 55(5), 570–581.
- Cahn-Weiner, D. A., Boyle, P. A., & Malloy, P. F. (2002). Tests of executive function predict instrumental activities of daily living in community-dwelling older individuals. *Applied Neuropsychology*, 9(3), 187–191.
- Cahn-Weiner, D. A., Farias, S. T., Julian, L., Harvey, D. J., Kramer, J. H., Reed, B. R., et al. (2007). Cognitive and neuroimaging predictors of instrumental activities of daily living. *Journal of the International Neuropsychological Society*, 13(05), 747–757. doi: [10.1017/S1355617707070853](https://doi.org/10.1017/S1355617707070853).
- Cahn-Weiner, D. A., Malloy, P. F., Boyle, P. A., Marran, M., & Salloway, S. (2000). Prediction of functional status from neuropsychological tests in community-dwelling elderly individuals. *The Clinical Neuropsychologist*, 14(2), 187–195.
- Carter, L. T., Oliveira, D. O., Dupont, J., & Lynch, S. V. (1988). The relationship of cognitive skills performance to activities of daily living in stroke patients. *The American Journal of Occupational Therapy*, 42(7), 449–455.
- Chisholm, D., Toto, P., Raina, K., Holm, M., & Rogers, J. (2014). Evaluating capacity to live independently and safely in the community: Performance assessment of self-care skills. *British Journal of Occupational Therapy*, 77(2), 59–63.
- Cleutjens, F., Spruit, M. A., Ponds, R., Vanfleteren, L., Franssen, F. M. E., Gijzen, C., et al. (2017a). Cognitive impairment and clinical characteristics in patients with chronic obstructive pulmonary disease. *Chronic Respiratory Disease* 1479972317709651. doi: [10.1177/1479972317709651](https://doi.org/10.1177/1479972317709651).
- Cleutjens, F. A., Franssen, F. M., Spruit, M. A., Vanfleteren, L. E., Gijzen, C., Dijkstra, J. B., et al. (2017b). Domain-specific cognitive impairment in patients with COPD and control subjects. *International Journal of Chronic Obstructive Pulmonary Disease*, 12, 1–11. doi: [10.2147/copd.S119633](https://doi.org/10.2147/copd.S119633).
- Crews, W. D., Jefferson, A. L., Bolduc, T., Elliott, J. B., Ferro, N. M., Broshek, D. K., et al. (2001). Neuropsychological dysfunction in patients suffering from end-stage chronic obstructive pulmonary disease. *Archives of Clinical Neuropsychology*, 16(7), 643–652.
- Dawson, D. R., Anderson, N. D., Burgess, P., Cooper, E., Krpan, K. M., & Stuss, D. T. (2009). Further development of the multiple errands test: Standardized scoring, reliability, and ecological validity for the Baycrest version. *Archives of Physical Medicine and Rehabilitation*, 90(11), S41–S51.
- Delis, D., Kramer, J., Kaplan, E., & Ober, B. (2000). *California verbal learning test* (2nd ed.). San Antonio, TX: Psychological Corporation.
- Dodd, J., Getov, S., & Jones, P. (2010). Cognitive function in COPD. *The European Respiratory Journal*, 35(4), 913–922. doi: [10.1183/09031936.00125109](https://doi.org/10.1183/09031936.00125109).
- Engstrom, C. P., Persson, L. O., Larsson, S., & Sullivan, M. (2001). Health-related quality of life in COPD: Why both disease-specific and generic measures should be used. *The European Respiratory Journal*, 18(1), 69–76.
- Farias, S. T., Mungas, D., Reed, B. R., Cahn-Weiner, D., Jagust, W., Baynes, K., et al. (2008). The measurement of everyday cognition (ECog): Scale development and psychometric properties. *Neuropsychology*, 22(4), 531. doi: [10.1037/0894-4105.22.4.531](https://doi.org/10.1037/0894-4105.22.4.531).
- Ferrer, M., Alonso, J., Morera, J., Marrades, R. M., Khalaf, A., Aguar, M. C., et al. (1997). Chronic obstructive pulmonary disease stage and health-related quality of life. *Annals of Internal Medicine*, 127(12), 1072–1079.
- Fix, A. J., Golden, C. J., Daughton, D., And, I. K., & Bell, C. W. (1982). Neuropsychological deficits among patients with chronic obstructive pulmonary disease. *International Journal of Neuroscience*, 16(2), 99–105.
- Fletcher, C. M., Elmes, P. C., Fairbairn, A. S., & Wood, C. H. (1959). The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. *British Medical Journal*, 2(5147), 257–266.
- Garrod, R., Bestall, J., Paul, E., Wedzicha, J., & Jones, P. (2000). Development and validation of a standardized measure of activity of daily living in patients with severe COPD: The London chest activity of daily living scale (LCADL). *Respiratory Medicine*, 94(6), 589–596.
- Gladsjo, J. A., Schuman, C. C., Evans, J. D., Peavy, G. M., Miller, S. W., & Heaton, R. K. (1999). Norms for letter and category fluency: Demographic corrections for age, education, and ethnicity. *Assessment*, 6(2), 147–178.
- Global Initiative for Chronic Obstructive Lung Disease. (2019). Retrieved from <http://www.goldcopd.org/>
- Gold, D. A. (2012). An examination of instrumental activities of daily living assessment in older adults and mild cognitive impairment. *Journal of Clinical and Experimental Neuropsychology*, 34(1), 11–34. doi: [10.1080/13803395.2011.614598](https://doi.org/10.1080/13803395.2011.614598).
- Gomez-Pinilla, F. (2008). Brain foods: The effects of nutrients on brain function. *Nature Reviews Neuroscience*, 9(7), 568–578. doi: [10.1038/nrn2421](https://doi.org/10.1038/nrn2421).
- Goverover, Y., & DeLuca, J. (2018). Assessing everyday life functional activity using actual reality in persons with MS. *Rehabilitation Psychology*, 63(2), 276.
- Goverover, Y., Genova, H. M., Hillary, F. G., & DeLuca, J. (2007). The relationship between neuropsychological measures and the timed instrumental activities of daily living task in multiple sclerosis. *Multiple Sclerosis Journal*, 13(5), 636–644.
- Goverover, Y., & Hinojosa, J. (2002). Categorization and deductive reasoning: Predictors of instrumental activities of daily living performance in adults with brain injury. *American Journal of Occupational Therapy*, 56(5), 509–516.
- Green, C. R., Mohs, R. C., Schmeidler, J., Aryan, M., & Davis, K. L. (1993). Functional decline in Alzheimer's disease: A longitudinal study. *Journal of the American Geriatrics Society*, 41(6), 654–661.
- Gross, A. L., Rebok, G. W., Unverzagt, F. W., Willis, S. L., & Brandt, J. (2011). Cognitive predictors of everyday functioning in older adults: Results from the ACTIVE cognitive intervention trial. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, 66(5), 557–566. doi: [10.1093/geronb/gbr033](https://doi.org/10.1093/geronb/gbr033).
- Hajiro, T., Nishimura, K., Tsukino, M., Ikeda, A., & Oga, T. (2000). Stages of disease severity and factors that affect the health status of patients with chronic obstructive pulmonary disease. *Respiratory Medicine*, 94(9), 841–846. doi: [10.1053/rmed.2000.0804](https://doi.org/10.1053/rmed.2000.0804).
- Hansen, M., De Amicis, N. K., Anderson, N. D., Binns, M. A., Clark, A. J., & Dawson, D. R. (2018). Cognitive contributors to multiple errands test (MET) performance. *American Journal of Occupational Therapy*, 72(6), 7206205050p1–7206205050p7.
- Hartman-Maeir, A., Harel, H., & Katz, N. (2009). Kettle test—A brief measure of cognitive functional performance: Reliability and validity in stroke rehabilitation. *American Journal of Occupational Therapy*, 63(5), 592–599.
- Hooper, H. (1983). *Hooper visual organization test manual*. Los Angeles, CA: Western Psychological Services.
- Hoth, K. F., Moreau, K. L., Weinberger, H. D., Holm, K. E., Meschede, K., Crapo, J. D., et al. (2020). Carotid artery stiffness is associated with cognitive performance in former smokers with and without chronic obstructive pulmonary disease. *Journal of American Heart Association*, e014862. doi: [10.1161/jaha.119.014862](https://doi.org/10.1161/jaha.119.014862).
- Incalzi, R. A., Bellia, V., Catalano, F., Scichilone, N., Imperiale, C., Maggi, S., et al. (2001). Evaluation of health outcomes in elderly patients with asthma and COPD using disease-specific and generic instruments: The salute Respiratoria nell'Anziano (Sa.R.a.) study. *Chest*, 120(3), 734–742.

- Inouye, S. K., Peduzzi, P. N., Robison, J. T., Hughes, J. S., Horwitz, R. I., & Concato, J. (1998). Importance of functional measures in predicting mortality among older hospitalized patients. *Journal of the American Medical Association*, 279(15), 1187–1193.
- Janaudis-Ferreira, T., Beauchamp, M. K., Robles, P. G., Goldstein, R. S., & Brooks, D. (2014). Measurement of activities of daily living in patients with COPD: A systematic review. *Chest*, 145(2), 253–271. doi: [10.1378/chest.13-0016](https://doi.org/10.1378/chest.13-0016).
- Jefferson, A. L., Paul, R. H., Ozonoff, A., & Cohen, R. A. (2006). Evaluating elements of executive functioning as predictors of instrumental activities of daily living (IADLs). *Archives of Clinical Neuropsychology*, 21(4), 311–320. doi: [10.1016/j.acn.2006.03.007](https://doi.org/10.1016/j.acn.2006.03.007).
- Jones, P. W., Quirk, F. H., Baveystock, C. M., & Littlejohns, P. (1992). A self-complete measure of health status for chronic airflow limitation. The St. George's respiratory questionnaire. *American Review of Respiratory Disease*, 145(6), 1321–1327. doi: [10.1164/ajrccm/145.6.1321](https://doi.org/10.1164/ajrccm/145.6.1321).
- Kanervisto, M., Saarelainen, S., Vasankari, T., Jousilahti, P., Heistaro, S., Heliövaara, M., et al. (2010). COPD, chronic bronchitis and capacity for day-to-day activities: Negative impact of illness on the health-related quality of life. *Chronic Respiratory Disease*, 7(4), 207–215. doi: [10.1177/1479972310368691](https://doi.org/10.1177/1479972310368691).
- Kapella, M. C., Larson, J. L., Covey, M. K., & Alex, C. G. (2011). Functional performance in chronic obstructive pulmonary disease declines with time. *Medicine and Science in Sports and Exercise*, 43(2), 218.
- Kaplan, E., Goodglass, H., & Weintraub, S. (2001). *Boston Naming Test* (2nd ed.). Philadelphia: Lippincott Williams & Wilkins.
- Katz, N., Hartman-Maeir, A., Ring, H., & Soroker, N. (2000). Relationships of cognitive performance and daily function of clients following right hemisphere stroke: Predictive and ecological validity of the LOTCA battery. *The Occupational Therapy Journal of Research*, 20(1), 3–17.
- Katz, S., Ford, A. B., Moskowitz, R. W., Jackson, B. A., & Jaffe, M. W. (1963). Studies of illness in the aged. The index of ADL: A standardized measure of biological and psychosocial function. *Journal of the American Medical Association*, 185, 914–919.
- Kozora, E., Emery, C., Kaplan, R. M., Wamboldt, F. S., Zhang, L., & Make, B. J. (2008). Cognitive and psychological issues in emphysema. *Proceedings of the American Thoracic Society*, 5(4), 556–560. doi: [10.1513/pats.200708-123ET](https://doi.org/10.1513/pats.200708-123ET).
- Kramer, A. F., Erickson, K. I., & Colcombe, S. J. (2006). Exercise, cognition, and the aging brain. *Journal of Applied Physiology*, 101(4), 1237–1242. doi: [10.1152/jappphysiol.00500.2006](https://doi.org/10.1152/jappphysiol.00500.2006).
- Kurz, A., Pohl, C., Ramsenthaler, M., & Sorg, C. (2009). Cognitive rehabilitation in patients with mild cognitive impairment. *International Journal of Geriatric Psychiatry*, 24(2), 163–168. doi: [10.1002/gps.2086](https://doi.org/10.1002/gps.2086).
- Lahav, O., & Katz, N. (2020). Independent older Adult's IADL and executive function according to cognitive performance. *OTJR: Occupation, Participation and Health*, 40(3), 1539449220905813.
- Langsetmo, L., Platt, R. W., Ernst, P., & Bourbeau, J. (2008). Underreporting exacerbation of chronic obstructive pulmonary disease in a longitudinal cohort. *American Journal of Respiratory and Critical Care Medicine*, 177(4), 396–401. doi: [10.1164/rccm.200708-1290OC](https://doi.org/10.1164/rccm.200708-1290OC).
- Lareau, S. C., Carrieri-Kohlman, V., Janson-Bjerklie, S., & Roos, P. J. (1994). Development and testing of the pulmonary functional status and dyspnea questionnaire (PFSDQ). *Heart & Lung*, 23(3), 242–250.
- Laurin, C., Moullec, G., Bacon, S. L., & Lavoie, K. L. (2011). The impact of psychological distress on exacerbation rates in COPD. *Therapeutic Advances in Respiratory Disease*, 5(1), 3–18. doi: [10.1177/1753465810382818](https://doi.org/10.1177/1753465810382818).
- Lawton, M. P., & Brody, E. M. (1969). Assessment of older people: Self-maintaining and instrumental activities of daily living. *The Gerontologist*, 9(3), 179–186.
- Leidy, N. K. (1994). Functional status and the forward progress of merry-go-rounds: Toward a coherent analytical framework. *Nursing Research*, 43(4), 196–202.
- Liang, W.-M., Chen, J.-J., Chang, C.-H., Chen, H.-W., Chen, S.-L., Hang, L.-W., et al. (2008). An empirical comparison of the WHOQOL-BREF and the SGRQ among patients with COPD. *Quality of Life Research*, 17(5), 793–800. doi: [10.1007/s11136-008-9326-5](https://doi.org/10.1007/s11136-008-9326-5).
- Liesker, J. J. W., Postma, D. S., Beukema, R. J., ten Hacken, N. H. T., van der Molen, T., Riemersma, R. A., et al. (2004). Cognitive performance in patients with COPD. *Respiratory Medicine*, 98(4), 351–356. doi: [10.1016/j.rmed.2003.11.004](https://doi.org/10.1016/j.rmed.2003.11.004).
- Liu, Y., Croft, J. B., Anderson, L. A., Wheaton, A. G., Presley-Cantrell, L. R., & Ford, E. S. (2014). The association of chronic obstructive pulmonary disease, disability, engagement in social activities, and mortality among US adults aged 70 years or older, 1994–2006. *International Journal of Chronic Obstructive Pulmonary Disease*, 9, 75–83. doi: [10.2147/COPD.S53676](https://doi.org/10.2147/COPD.S53676).
- Marin, J. M., Cote, C. G., Diaz, O., Lisboa, C., Casanova, C., Lopez, M. V., et al. (2011). Prognostic assessment in COPD: Health related quality of life and the BODE index. *Respiratory Medicine*, 105(6), 916–921. doi: [10.1016/j.rmed.2011.01.007](https://doi.org/10.1016/j.rmed.2011.01.007).
- Martinez, C. H., Richardson, C. R., Han, M. K., & Cigolle, C. T. (2014). Chronic obstructive pulmonary disease, cognitive impairment, and development of disability: The health and retirement study. *Annals of the American Thoracic Society*, 11(9), 1362–1370. doi: [10.1513/AnnalsATS.201405-187OC](https://doi.org/10.1513/AnnalsATS.201405-187OC).
- Menn, P., Weber, N., & Holle, R. (2010). Health-related quality of life in patients with severe COPD hospitalized for exacerbations-comparing EQ-5D, SF-12 and SGRQ. *Health and Quality of Life Outcomes*, 8(1), 1. doi: [10.1186/1477-7525-8-39](https://doi.org/10.1186/1477-7525-8-39).
- Miravittles, M., Soriano, J. B., Garcia-Rio, F., Muñoz, L., Duran-Tauleria, E., Sanchez, G., et al. (2009). Prevalence of COPD in Spain: Impact of undiagnosed COPD on quality of life and daily life activities. *Thorax*, 64(10), 863–868. doi: [10.1136/thx.2009.115725](https://doi.org/10.1136/thx.2009.115725).
- Mostert, R., Goris, A., Welting-Scheepers, C., Wouters, E., & Schols, A. (2000). Tissue depletion and health related quality of life in patients with chronic obstructive pulmonary disease. *Respiratory Medicine*, 94(9), 859–867.
- Ng, T., Niti, M., Tan, W., Cao, Z., Ong, K., & Eng, P. (2007). Depressive symptoms and chronic obstructive pulmonary disease: Effect on mortality, hospital readmission, symptom burden, functional status, and quality of life. *Archives of Internal Medicine*, 167(1), 60–67. doi: [10.1001/archinte.167.1.60](https://doi.org/10.1001/archinte.167.1.60).
- Osman, I. M., Godden, D. J., Friend, J. A., Legge, J. S., & Douglas, J. G. (1997). Quality of life and hospital re-admission in patients with chronic obstructive pulmonary disease. *Thorax*, 52(1), 67–71.
- Özge, C., Özge, A., & Ünal, Ö. (2006). Cognitive and functional deterioration in patients with severe COPD. *Behavioural Neurology*, 17(2), 121–130. doi: [10.1155/2006/848607](https://doi.org/10.1155/2006/848607).
- Ozsoy, I., Ozcan Kahraman, B., Acar, S., Ozalevli, S., Akkoclu, A., & Savci, S. (2019). Factors influencing activities of daily living in subjects with COPD. *Respiratory Care*, 64(2), 189–195. doi: [10.4187/respcare.05938](https://doi.org/10.4187/respcare.05938).
- Park, S. K., & Larson, J. L. (2015). Cognitive function as measured by trail making test in patients with COPD. *Western Journal of Nursing Research*, 37(2), 236–256. doi: [10.1177/0193945914530520](https://doi.org/10.1177/0193945914530520).
- Peruzza, S., Sergi, G., Vianello, A., Pisent, C., Tiozzo, F., Manzan, A., et al. (2003). Chronic obstructive pulmonary disease (COPD) in elderly subjects: Impact on functional status and quality of life. *Respiratory Medicine*, 97(6), 612–617.

- Prigatano, G. P., Parsons, O., Levin, D. C., Wright, E., & Hawryluk, G. (1983). Neuropsychological test performance in mildly hypoxemic patients with chronic obstructive pulmonary disease. *Journal of Consulting and Clinical Psychology*, 51(1), 108.
- Rand, D., Rukan, S. B.-A., Weiss, P. L., & Katz, N. (2009). Validation of the virtual MET as an assessment tool for executive functions. *Neuropsychological rehabilitation*, 19(4), 583–602.
- Regan, E. A., Hokanson, J. E., Murphy, J. R., Make, B., Lynch, D. A., Beaty, T. H., et al. (2010). Genetic epidemiology of COPD (COPDGene) study design. *COPD*, 7(1), 32–43. doi: [10.3109/15412550903499522](https://doi.org/10.3109/15412550903499522).
- Robertson, K., & Schmitter-Edgecombe, M. (2017). Naturalistic tasks performed in realistic environments: A review with implications for neuropsychological assessment. *The Clinical Neuropsychologist*, 31(1), 16–42.
- Rodriguez Gonzalez-Moro, J., de Lucas Ramos, P., Izquierdo Alonso, J., López-Muñiz Ballesteros, B., Antón Díaz, E., et al. (2009). Impact of COPD severity on physical disability and daily living activities: EDIP-EPOC I and EDIP-EPOC II studies. *International Journal of Clinical Practice*, 63(5), 742–750. doi: [10.1111/j.1742-1241.2009.02040.x](https://doi.org/10.1111/j.1742-1241.2009.02040.x).
- Schmitter-Edgecombe, M., Woo, E., & Greeley, D. R. (2009). Characterizing multiple memory deficits and their relation to everyday functioning in individuals with mild cognitive impairment. *Neuropsychology*, 23(2), 168. doi: [10.1037/a0014186](https://doi.org/10.1037/a0014186).
- Seeman, T. E., Lusignolo, T. M., Albert, M., & Berkman, L. (2001). Social relationships, social support, and patterns of cognitive aging in healthy, high-functioning older adults: MacArthur studies of successful aging. *Health Psychology*, 20(4), 243–255. doi: [10.1037//0278-6133.20.4.243](https://doi.org/10.1037//0278-6133.20.4.243).
- Seemungal, T. A., Donaldson, G. C., Paul, E. A., Bestall, J. C., Jeffries, D. J., & Wedzicha, J. A. (1998). Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*, 157(5 Pt 1), 1418–1422. doi: [10.1164/ajrccm.157.5.9709032](https://doi.org/10.1164/ajrccm.157.5.9709032).
- Shallice, T., & Burgess, P. W. (1991). Deficits in strategy application following frontal lobe damage in man. *Brain*, 114(2), 727–741.
- Steffens, D. C., Bosworth, H. B., Provenzale, J. M., & MacFall, J. R. (2002). Subcortical white matter lesions and functional impairment in geriatric depression. *Depression and Anxiety*, 15(1), 23–28. doi: [10.1002/da.1081](https://doi.org/10.1002/da.1081).
- Stuss, D., Peter, I., Guzman, D., Guzman, C., & Troyer, A. (1997). Chronic obstructive pulmonary disease: Effects of hypoxia on neurological and neuropsychological measures. *Journal of Clinical and Experimental Neuropsychology*, 19(4), 515–524. doi: [10.1080/01688639708403741](https://doi.org/10.1080/01688639708403741).
- Tabert, M. H., Albert, S. M., Borukhova-Milov, L., Camacho, Y., Pelton, G., Liu, X., et al. (2002). Functional deficits in patients with mild cognitive impairment prediction of AD. *Neurology*, 58(5), 758–764.
- Toglia, J. (2015). *Weekly calendar planning activity (WCPA): a performance test of executive function*. Bethesda, Maryland: AOTA Press.
- Toglia, J., Askin, G., Gerber, L. M., Taub, M. C., Mastrogiovanni, A. R., & O'Dell, M. W. (2017). Association between 2 measures of cognitive instrumental activities of daily living and their relation to the Montreal cognitive assessment in persons with stroke. *Archives of Physical Medicine and Rehabilitation*, 98(11), 2280–2287.
- Tombaugh, T., Kozak, J., & Rees, L. (1998). Normative data for the controlled oral word association test. In O. Spreen, E. Strauss (Eds.), *A compendium of neuropsychological test. Administration, norms, and commentary* (pp. 453–457). New York: Oxford University Press.
- Tombaugh, T., Rees, L., & McIntyre, N. (1998). Normative data for the trail making test. Personal communication cited in Spreen and Strauss. In O. Spreen, E. Strauss (Eds.), *A compendium of neuropsychological tests: Administration, norms and commentary*. (pp. 540). New York: Oxford University Press.
- van Helvoort, H. A., Willems, L. M., Dekhuijzen, P. R., van Hees, H. W., & Heijdra, Y. F. (2016). Respiratory constraints during activities in daily life and the impact on health status in patients with early-stage COPD: A cross-sectional study. *NPJ Primary Care Respiratory Medicine*, 26, 16054. doi: [10.1038/npjpcrm.2016.54](https://doi.org/10.1038/npjpcrm.2016.54).
- Villeneuve, S., Pepin, V., Rahayel, S., Bertrand, J. A., de Lorimier, M., Rizk, A., et al. (2012). Mild cognitive impairment in moderate to severe COPD: A preliminary study. *Chest*, 142(6), 1516–1523. doi: [10.1378/chest.11-3035](https://doi.org/10.1378/chest.11-3035).
- Wechsler, D. (2008). *Wechsler adult intelligence scale* (4th ed.). San Antonio, TX: Pearson.
- Wilkinson, T. M., Donaldson, G. C., Hurst, J. R., Seemungal, T. A., & Wedzicha, J. A. (2004). Early therapy improves outcomes of exacerbations of chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*, 169(12), 1298–1303. doi: [10.1164/rccm.200310-1443O](https://doi.org/10.1164/rccm.200310-1443O).
- Włodarczyk, J. H., Brodaty, H., & Hawthorne, G. (2004). The relationship between quality of life, mini-mental state examination, and the instrumental activities of daily living in patients with Alzheimer's disease. *Archives of Gerontology and Geriatrics*, 39(1), 25–33. doi: [10.1016/j.archger.2003.12.004](https://doi.org/10.1016/j.archger.2003.12.004).
- Xu, J. Q., Murphy, S. L., & Kochanek, K. D. (2015). Deaths: Final data for 2013. *National Vital Statistics Reports*, 64(2), 1.
- Yazar, E. E., Aydin, S., Gunluoglu, G., Kamat, S., Gungen, A. C., & Yildiz, P. (2017). Clinical effects of cognitive impairment in patients with chronic obstructive pulmonary disease. *Chronic Respiratory Disease* 1479972317743757. doi: [10.1177/1479972317743757](https://doi.org/10.1177/1479972317743757).