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Executive function fails to predict smoking outcomes in a clinical trial to motivate smokers to quit

Andrew T. Fox, Ph.D.[a], **Laura E. Martin, Ph.D.**[a,h], **Jared Bruce, Ph.D.**[b], **Jose L. Moreno, Ph.D.**[c], **Vincent S. Staggs, Ph.D.**[d,e], **Hyoung S. Lee, Ph.D.**[f], **Kathy Goggin, Ph.D**[d,e], **Kari Jo Harris, Ph.D.**[g], **Kimber Richter, Ph.D.**[h], **Christi Patten, Ph.D.**[i], and **Delwyn Catley, Ph.D.**[j]

[a]Hoglund Brain Imaging Center, University of Kansas Medical Center, Kansas City, KS 66160, USA

[b]Department of Psychology, University of Missouri – Kansas City, 5030 Cherry Hall, Room 313, Kansas City, MO, 64110

[c]Department of Psychiatry, University of Texas Health Science Center - San Antonio, 7703 Floyd Curl Drive, San Antonio, Texas 78229-3900

[d]Health Services and Outcomes Research, Children's Mercy Kansas City, 2401 Gillham Road, Kansas City, MO 64108

[e]School of Medicine, University of Missouri – Kansas City, 2411 Holmes Street Kansas City, MO 64108

[f]Interdisciplinary Arts and Sciences, University of Washington Tacoma, 1900 Commerce St, Tacoma, WA 98402-3100

[g]School of Public and Community Health Sciences, University of Montana, Skaggs Building Room 352, Missoula, MT 59812

[h]Department of Preventive Medicine and Public Health, University of Kansas Medical Center, Kansas City, KS 66160

[i]Department of Psychology and Psychiatry, Mayo Clinic, 200 First St SW, Rochester, MN 55905

[j]Center for Children's Healthy Lifestyles and Nutrition, Children's Mercy Kansas City, 2401 Gillham Rd., Kansas City, MO 64108

Abstract

Background—Executive function (EF) is considered an important mediator of health outcomes. It is hypothesized that those with better EF are more likely to succeed in turning their intentions into actual health behaviors. Prior studies indicate EF is associated with smoking cessation. Experimental and longitudinal studies, however, have yielded mixed results. Few studies have examined whether EF predicts post-treatment smoking behavior. Fewer still have done so *prospectively* in a large trial. We sought to determine if EF predicts quit attempts and cessation

Corresponding Author: Andrew T. Fox, Hoglund Brain Imaging Center, University of Kansas Medical Center, Mail Stop 1052, 3901 Rainbow Blvd, Kansas City, KS 66160; afox3@kumc.edu.

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among community smokers in a large randomized trial evaluating the efficacy of motivational interventions for encouraging cessation.

Methods—Participants (N=255) completed a baseline assessment that included a cognitive battery to assess EF (Oral Trail Making Test B, Stroop, Controlled Oral Word Association Test). Participants were then randomized to 4 sessions of Motivational Interviewing or Health Education or one session of Brief Advice to quit. Quit attempts and cessation were assessed at weeks 12 and 26.

Results—In regression analyses, none of the EF measures were statistically significant predictors of quit attempts or cessation (all *p*s > 0.20).

Conclusions—Our data did not support models of health behavior that emphasize EF as a mediator of health outcomes. Methodological shortcomings weaken the existing support for an association between EF and smoking behavior. We suggest methodological improvements that could help move this potentially important area of research forward.

Keywords

Smoking cessation; motivational interviewing; health education; executive function; clinical trial; community sample

1. Introduction

Executive function (EF), which comprises cognitive processes like working memory, attention, and inhibition along with higher-order processes like self-regulation and planning (Goldstein et al., 2014), is associated with improved health. EF contributes to dietary (Allan et al., 2010, 2011) and exercise (Hall et al., 2008) adherence, maintaining healthy weight (Menon et al., 2013), antiretroviral therapy adherence (Avants et al., 2001; Solomon and Halkitis, 2008), and non-smoking status (Brega et al., 2008; Menon et al., 2013; Moss et al., 2009).

Smokers show poorer EF than non-smokers and ex-smokers (Durazzo et al., 2012; Glass et al., 2009; Nestor et al., 2011; Sabia et al., 2012; Starr et al., 2007), which could be an effect of smoking or both a cause and an effect. The few studies with longitudinal or experimental designs better suited to establishing whether EF predicts smoking behavior have yielded mixed results. For example, EF deficits in children with ADHD did not predict later cigarette smoking (Wilens et al., 2011). In smokers with schizophrenia, one of three EF assessments predicted treatment success (Moss et al., 2009) while in a study of community smokers one of two EF measures was associated with success in a laboratory relapse model (Mueller et al., 2009). Taken together these studies involving different populations, measures, and outcomes provide limited evidence that EF predicts smoking behavior. Further examination of this relationship in prospective studies, especially in large, diverse samples of smokers, is warranted.

We conducted a randomized controlled trial of Motivational Interviewing (MI) for inducing quit attempts and cessation in smokers with low interest in quitting (Catley et al., 2016), which included baseline measures of EF. Because no study has prospectively examined the

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influence of EF on smoking outcomes in a large treatment trial among a diverse community sample, we conducted such an analysis using our data. We hypothesized that individuals with higher levels of EF at baseline would be more likely to attempt quitting and achieve abstinence because quitting smoking is a multi-step process (Lee et al., 2014) and both planning and executing plans are executive functions (Miller and Cohen, 2001).

2. Methods

Our data came from a clinical trial (ClinicalTrials.gov #NCT01188018) described in detail elsewhere (Catley et al., 2016; Catley et al., 2012). The study protocol was approved by the Institutional Review Board of the University of Missouri–Kansas City (#0978).

2.1. Participants

Participants (N = 255, 110 women) were recruited from the community. The sample was predominantly Black (65%), low-income (58% <$1000/mo.), and high school educated or less (84%) (see Catley et al. (2016) for full demographics). Primary inclusion criteria were: age ≥18 (mean 45.8), self-reported smoking of ≥1 cigarette per day (mean 17.1), not using cessation medication, and low desire to quit (≤6 on a 10-point scale; mean 1.9).

2.2. Study Arms

Participants were randomized in a 2:2:1 ratio to MI, Health Education (HE), or Brief Advice (BA). In MI and HE, participants received four 20-min sessions of in-person (baseline, week 12) or over-the-phone (weeks 6, 18) cessation counseling. In BA participants experienced one 5-min session of direct advice to quit smoking.

2.3. Psychological Assessments

Baseline measures were assessed via computer or trained research staff and included demographics, smoking characteristics, and psychological variables. Nicotine dependence was assessed with the Heavy Smoking Index (HSI) (Kozlowski et al., 1994). EF measures were chosen for efficient administration and coverage of several facets of EF. We chose the Oral Trail Making Test (OTMT) (Ricker and Axelrod, 1994; Ricker et al., 1996) for general executive function, the “Victoria” Stroop task (Troyer et al., 2006) for response inhibition, and the Controlled Oral Word Association Test (COWAT-FAS) (Reitan and Wolfson, 1985) for verbal fluency. Detailed description and validation of these tests are available (Reitan and Wolfson, 1985; Ricker and Axelrod, 1994; Ricker et al., 1996; Troyer et al., 2006). OTMT score was defined as time to complete “B” section, Stroop as the interference score (color word sheet time/color dots sheet time), and COWAT-FAS as total valid words spoken.

2.4. Other Assessments

Other assessments included the Wechsler Test of Adult Reading (WTAR; proxy for IQ) (The Psychological Corporation, 2001); the Center for Epidemiologic Studies - Depression scale (CES-D) (Radloff, 1977); the Neuroticism and Extroversion components of the Eysenck Personality Questionnaire—Brief Version (EPQ) (Sato, 2005); and the Symbol Digit Modalities Test (SDMT) (Smith, 2002).

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2.5. Outcome Variables

Main outcomes were quit attempts at baseline, 12 weeks, and 26 weeks defined as a self-reported quit attempt of at least 24 hours (Boardman et al., 2005; Zhou et al., 2009) within the past 3 months and smoking cessation, defined as self-reported abstinence at 12 weeks and cotinine-verified 7-day point-prevalence abstinence at 26 weeks (Benowitz et al., 2002; Hughes et al., 2003). Readiness to quit ["Contemplation Ladder" (Biener and Abrams, 1991)], measured at baseline and weeks 12 and 26 was a secondary outcome.

2.6. Data Analysis

Results of preliminary factor analysis of the EF measures did not justify creating an EF composite; this approach was not pursued further. To avoid multicollinearity among the EF measures, we fit separate models for each EF variable-outcome combination.

Odds of a quit attempt were modeled using mixed logistic regression. For each explanatory EF variable (Stroop, OTMT-B, COWAT-FAS) we fit the following four models and compared them using the Bayesian Information Criterion (BIC): A base model (predictors: arm, week, arm*week), a base + EF predictor model (predictors: arm, week, arm*week, EF predictor), a base + EF + EF*arm model, and finally a full model which added seven covariates (age, HSI, CES-D, WTAR, SDMT, EPQ Neuroticism, EPQ Extroversion) to the best-fitting (i.e., lowest-BIC) of the previous three models.

Odds of quitting smoking (verified cessation) were modeled using Firth logistic regression. Due to few quitters, the only covariate included was study arm. We repeated this analysis limited to participants reporting a quit attempt to determine if effects of EF on cessation differ between those who do and do not make a quit attempt.

Contemplation Ladder was modeled in the same way as quit attempts except with Gaussian rather than logistic mixed models.

3. Results

Control variables were mostly similar between quit attempters and non-quit attempters (Table 1). Mean differences on the EF measures were <0.3 SD apart and not statistically significant (Wilcoxon test ps > 0.3). The same was true when comparing quitters versus non-quitters (Table 1). Bivariate correlations between the EF measures and outcome variables were uniformly small ($|r| < 0.14$; Table 2).

In the quit attempt modeling, the best model per BIC for all three EF variables was the full model including the 7 covariates and the EF predictor, but not the EF*arm interaction. We found no statistically significant relation between odds of making a quit attempt and Stroop (aOR=1.07, 95% CI [0.70, 1.63], $p = .761$), OTMT-B (aOR=1.26, 95% CI [0.77, 2.07], $p = .356$), or COWAT-FAS (aOR= 1.29, 95% CI [0.77, 2.17], $p = .331$).

Similarly, we did not find significant associations between smoking cessation and Stroop (aOR=1.43, 95% CI [0.81, 2.51], $p = .217$), OTMT-B (aOR=0.83, 95% CI [0.44, 1.60], $p = .584$), or COWAT-FAS (aOR= 0.84, 95% CI [0.47, 1.49], $p = .539$). Limiting the analysis to

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only those reporting a quit attempt yielded similar, non-significant results (aORs 1.44, 0.82, and 0.77 for Stroop, OTMT-B, and COWAT-FAS, respectively).

For the models predicting Contemplation Ladder the full model was not selected for any EF variable. COWAT-FAS was a significant predictor of Contemplation Ladder ($\beta = 0.38$, 95% CI [0.09, 0.66], $p = .010$), but neither Stroop ($\beta = 0.10$, 95% CI [−0.21, 0.40], $p = .532$) nor OTMT-B ($\beta = 0.08$, 95% CI [−0.26, 0.41], $p = .659$) were significant.

The BIC indicated improved likelihood-based fit when the EF predictors were added to the base models for quit attempt and Contemplation Ladder. However, changes in generalized R^2 for all three outcomes were uniformly negligible: OTMT-B and Stroop never increased R^2 by more than 0.01, and the largest effect on R^2 for COWAT-FAS was a 0.03 increase for Contemplation Ladder. The addition of COWAT-FAS and Stroop both worsened likelihood-based fit in verified cessation modeling. Additionally, OTMT-B and Stroop improved likelihood-based fit in quit attempt modeling, but their regression effects were both in the opposite direction than we would expect if EF is positively associated with quit attempts.

4. Discussion

We explored whether baseline executive function predicted quit attempts and cessation in a large community sample of unmotivated-to-quit smokers. EF did not predict quit attempts or cessation and only one of three EF tests was significantly associated with Contemplation Ladder. A second analysis of cessation limited only to those who reported a quit attempt also yielded null results. In total, only one of twelve EF-outcome relationships was statistically significant. Although EF measures improved likelihood-based fit (i.e., BIC) in most models, generalized R^2 values suggest these measures make negligible contributions to predictive power.

The unexpected null results may be due to a weak or null relationship between EF and smoking behavior change or due to limitations in our study methods. One possibility is that we failed to use the “right” measure of EF; however, the best way to measure EF is not clear, and two of our measures were similar to ones that were significant predictors elsewhere: Moss et al. (2009) showed Trail Making Test B scores predicted cessation, and Mueller et al. (2009) found Stroop interference scores predicted short-term abstinence. But neither measure correlated with smoking behavior in our sample.

Another possibility is that EF may not predict who *attempts* to quit but instead predicts *success* in quitting. Our follow-up analysis on successful cessation among those reporting quit attempts yielded the same null results although this analysis had limited statistical power due to few quitters. EF could be a better predictor of the ability to control urges, say, than of deciding to initiate goal-directed behavior.

A third possibility is that our EF measures were possibly not sufficiently sensitive for a healthy community sample, resulting in ceiling effects. However, one study found significant effects using the Stroop test in a healthy population (Mueller et al., 2009).

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Although our results were null they add to a general picture of inconsistent evidence for EF as a predictor of smoking and smoking cessation. An important problem with the literature is that EF is defined and measured differently across studies. In smoking studies, EF has been operationalized using a paper-and-pencil scale (Brega et al., 2008), as a composite of scores on several cognitive tasks (Wilens et al., 2011), and as scores from several separate cognitive tasks (Moss et al., 2009; Mueller et al., 2009). Inconsistent defining/measuring EF is well documented; Goldstein et al. (2014) identified 33 definitions and 9 theoretical models. Additionally, studies involve different populations: older adults, adolescents, people with schizophrenia, and, in the present study, unmotivated-to-quit community smokers. It remains unclear how these sample differences may be impacting results; however, results appear to be consistently weak.

Another issue is that researchers sometimes conclude EF is an important predictor when only one scale out of a battery produced a statistically significant result. Often, no rationale is given for considering the one significant measure a better predictor than the others. In the two prior studies examining smoking outcomes combined only 2 of 5 EF predictors were significant (Moss et al., 2009; Mueller et al., 2009). We know of no published study reporting an entire battery of EF-primary outcome associations as null as in the present case. One explanation is that having at least one statistically significant predictor serves as a *de facto* threshold for publication.

4.1. Conclusions

Our null findings highlight that evidence for the association between EF and smoking cessation remains weak. While our results may be due to EF being less strongly related to quit attempts than cessation or other methodologic limitations, future research should confirm this and employ improved methods by: pre-registering specific EF measure-outcome hypotheses, conducting prospective and experimental studies, using more stable measurements including factor analysis to generate composite measures of EF, measuring EF neurobiology using brain imaging, and reporting null findings.

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Table 1

Means for Executive Function and Control Variables across Quit/Quit Attempt Status

	0 Quit Attempts		>0 Quit Attempts		Did Not Quit		Quit	
	Mean (SD)	**n**	**Mean (SD)**	**n**	**Mean (SD)**	**n**	**Mean (SD)**	**n**
EF Variables								
Stroop *	2.4 (0.8)	105	2.6 (0.9)	138	2.5 (0.9)	203	2.7 (0.8)	11
OTMT-B	46.2 (30.6)	100	50.2 (31.8)	129	49.4 (31.7)	194	40.3 (23.6)	10
COWAT-FAS	35.4 (12.8)	108	36.9 (12.3)	140	36.7 (12.5)	207	34.4 (8.9)	11
Other Variables								
Age	45.0 (10.5)	111	46.3 (11.2)	144	46.3 (10.7)	213	47.8 (11.6)	11
Heavy Smoking Index	3.3 (1.3)	111	3.1 (1.3)	144	3.2 (1.3)	213	2.5 (0.9)	11
CES-D	15.8 (10.7)	111	16.9 (10.1)	144	16.0 (10.1)	213	23.7 (11.3)	11
WTAR	90.2 (17.2)	96	88.8 (15.8)	121	89.0 (16.7)	183	91.2 (16.5)	9
SDMT	45.1 (11.2)	108	43.0 (10.1)	141	43.7 (10.4)	208	41.9 (11.9)	11
EPQ Neuroticism	16.4 (10.9)	111	16.5 (9.6)	144	16.4 (10.1)	213	21.0 (10.5)	11
EPQ Extroversion	26.2 (8.7)	111	28.7 (8.4)	144	28.2 (8.7)	213	28.0 (7.9)	11
Contemplation Ladder, BL	2.4 (2.1)	111	3.2 (2.2)	144	2.8 (2.2)	213	3.4 (2.3)	11

Abbreviations: OTMT = Oral Trail Making Test; COWAT = Controlled Oral Word Association Test; CES – D = Center for Epidemiologic Studies – Depression scale; WTAR = Wechsler Test of Adult Reading; SDMT = Symbol Digit Modalities Test; EPQ = Eysenck Personality Questionnaire.

* Interference score (time to complete color word sheet/time to complete color dots sheet)

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Table 2

Correlation matrix

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1. Stroop	--															
2. OTMT-B	0.13	--														
3. COWAT	−0.13	−0.44	--													
4. Age	0.14	0.08	0.03	--												
5. HSI	0.08	0.07	−0.17	−0.05	--											
6. CES-D	0.06	0.02	−0.11	−0.06	0.07	--										
7. WTAR	−0.37	−0.49	0.60	0.02	−0.18	−0.09	--									
8. SDMT	−0.27	−0.41	0.44	−0.37	−0.09	−0.11	0.43	--								
9. EPQ-N	0.02	−0.07	0.05	−0.13	0.02	0.68	0.05	0.03	--							
10. EPQ-E	0.12	0.01	0.17	−0.02	0.04	−0.25	0.05	0.04	−0.15	--						
11. CL BL	0.00	−0.04	0.17	−0.03	−0.25	0.13	0.17	0.07	0.08	0.03	--					
12. CL W12	0.03	0.01	0.11	0.08	−0.15	0.04	0.14	−0.06	0.07	0.01	0.38	--				
13. CL W26	−0.07	0.02	0.14	0.00	−0.13	0.07	0.16	0.05	0.09	0.03	0.33	0.62	--			
14. QA BL	0.11	0.14	−0.06	0.02	−0.07	0.07	−0.17	−0.18	0.00	0.06	0.23	0.15	0.12	--		
15. QA W12	0.02	0.10	−0.05	0.00	−0.04	0.16	−0.21	−0.15	0.12	0.03	0.14	0.43	0.31	0.28	--	
16. QA W26	0.06	0.09	0.05	0.02	−0.04	0.09	0.00	−0.12	0.00	0.13	0.24	0.57	0.59	0.23	0.51	--
17. Cessation	0.04	−0.06	−0.04	0.03	−0.12	0.16	0.03	−0.04	0.10	−0.00	0.05	0.26	0.30	0.05	0.15	0.21

Abbreviations: OTMT = Oral Trail Making Test; COWAT = Controlled Oral Word Association Test; HSI = Heavy Smoking Index; CES – D = Center for Epidemiologic Studies – Depression scale; WTAR = Wechsler Test of Adult Reading; SDMT = Symbol Digit Modalities Test; EPQ-N/E = Eysenck Personality Questionnaire – Neuroticism/Extroversion scales; CL = Contemplation Ladder; QA = Quit Attempt

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