

Executive function and other cognitive deficits are distal risk factors of generalized anxiety disorder 9 years later

Original Article

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Abstract

Objective. The cognitive model (Hirsch & Mathews, 2012) and attentional control theory (Eysenck & Derakshan, 2011) postulate that compromised executive function (EF) and other cognitive constructs are negatively linked to increased excessive and uncontrollable worry, the core symptom of generalized anxiety disorder (GAD). However, the prospective link between neuropsychological constructs and GAD are not well understood.

Methods. A nationally representative sample of 2605 community-dwelling adults whose average age was 55.20 (s.d. = 11.41, range 33–84; 56.31% females) participated at baseline and 9-year follow-up. Baseline neuropsychological function and symptoms were measured using the Brief Test of Adult Cognition by Telephone and Composite International Diagnostic Interview – Short Form. Multivariate Poisson and negative binomial regression analyses were conducted with 11 baseline covariates entered simultaneously: age, gender, years of formal education, perceived control, hypertension/diabetes, body mass index, exercise status, as well as GAD severity, panic disorder severity, and depression severity. Those with baseline GAD were also removed.

Results. Lower Time 1 composite global cognition z-score independently predicted higher Time 2 GAD severity and diagnosis [odds ratio (OR) 0.60, 95% confidence interval (CI) 0.40–0.89, $p = 0.01$]. Poor inhibition, set-shifting, working memory (WM) updating, inductive reasoning, and global cognition sequentially forecasted heightened GAD. However, processing speed, verbal WM, verbal fluency, and episodic memory did not predict future GAD.

Conclusion. Global cognition, inductive reasoning, inhibition, set-shifting, and WM updating EF impairments may be distal risk factors for elevated GAD nearly a decade later.

Executive function (EF) is conceptualized as a multidimensional goal-directed system, often linked to the brain's prefrontal cortex (PFC) which modulates human cognitive and behavioral processes (Miyake & Friedman, 2012). These processes empower us to effectively overcome habits, weigh benefits and costs, prioritize goals, decide strategically, and respond adaptively. Multiple EF components have been linked consistently to numerous facets of human functioning, physical health, and interpersonal distress (Wright *et al.* 2014). EF and general cognitive capacities are also considered key features in the research domain criteria (RDoC; Cuthbert & Insel, 2013) for mental illness, such as depression (Snyder, 2013) and anxiety (Beaudreau *et al.* 2013).

Two theories have posited that cognitive capacities might be linked to pathological worry, the cardinal symptom of generalized anxiety disorder (GAD). Attentional control theory posits that poor EF and related processes produce worrying (Eysenck & Derakshan, 2011). Similarly, the cognitive model theorizes that unconscious processing biases (threat representations) and voluntary processing abilities (e.g. attention), increase the probability of developing verbal-linguistic worry (Hirsch & Mathews, 2012). These theories thus assume that inhibition, set-shifting, and working memory (WM) updating deficits are related to worry.

Inhibition is the ability to refrain volitionally from autopilot responses in order to select a less conventional and more task-pertinent response (Miyake *et al.* 2000). On several tasks (e.g. Stroop, go-no-go, Flanker tasks), participants with higher trait worry and GAD (*v.* controls) displayed poorer inhibition (Beaudreau & O'Hara, 2009; Price *et al.* 2012; Hallion *et al.* 2017). Engagement in worry also led to impaired inhibition (Righi *et al.* 2009; Waters & Valvoi, 2009; Larson *et al.* 2013; Hallion *et al.* 2014), and inhibition deficits uniquely predicted worry topic frequency (Kircanski *et al.* 2015). Set-shifting (degree of versatility to change between cognitive sets) builds on inhibition. Set-shifting was worse in GAD (*v.* controls) (Tempesta *et al.* 2013), and negatively predicted GAD 12 years later (Zhang *et al.* 2015). Collectively, these findings led us to hypothesize that inhibition and set-shifting deficits would predict future GAD.

WM refers to the maintenance and manipulation of task-relevant material. Theoretically, verbal WM deficits are inextricably intertwined with worry (Hirsch & Mathews, 2012). Overall, studies that found WM differences when comparing GAD to controls used complex WM tasks that required recognizing, recalling, rearranging, and creating novel stimuli online (e.g. letter-number sequencing, task-irrelevant unpleasant stimuli, random number generation paradigm; Hayes *et al.* 2008; Butters *et al.* 2011; Leigh & Hirsch, 2011; MacNamara & Proudfit, 2014; Moon & Jeong, 2015). However, simpler backward digit span performance (Wechsler,

1997) was equivalent among older adults with and without high trait anxiety (Wetherell *et al.* 2002) and GAD (Price & Mohlman, 2007). We thus forecasted that verbal WM as indexed by the *digit span* would not significantly predict GAD.

WM *updating* is the capacity to use WM maintenance to monitor for and swiftly and accurately incorporate new task-specific information. Individuals with GAD (*v.* controls) and high (*v.* low) worriers were slower on WM updating tasks (e.g., n-back; Stefanopoulou *et al.* 2014; Gustavson & Miyake, 2016; Vytal *et al.* 2016; Balderston *et al.* 2017), which prospectively predicted higher worry severity (Bredemeier & Berenbaum, 2013). Moreover, worry led to inefficiencies in swiftly eliminating non-pertinent data and determining whether target cues corresponded with material maintained in WM (Gustavson & Miyake, 2016). Further, high (*v.* low-) worriers also showed higher general switch costs on several switch tasks (Beckwé *et al.* 2014; Gustavson *et al.* 2017). Based on this evidence, we posited that WM updating deficits indexed by general switch costs would predict future GAD.

Understudied non-EF cognitive capacity constructs in GAD include global cognition, inductive reasoning, processing speed, verbal fluency, and episodic memory (EM). Prospectively, global cognition negatively predicted GAD in one study (Zhang *et al.* 2015) but not others (De Beurs *et al.* 2000; Schoevers *et al.* 2005). We hence made no *a priori* hypothesis with regard to whether global cognition predicted future GAD. Inductive reasoning refers to the ability to use present observations to make sensible predictions about novel cases. Inductive reasoning is thus important for making rational decisions and regulating emotions effectively. Despite the absence of direct studies of inductive reasoning in GAD, higher trait anxiety uniquely accounted for poor cognitive abstraction (Yochim *et al.* 2013) and adults with GAD (*v.* controls) showed weaker concept formation (Butters *et al.* 2011). Further, individuals with (*v.* without) GAD tended to construe benign/ambiguous stimuli as threatening/negative (Hirsch *et al.* 2016), suggesting deficiencies in accurately deducing data. Accordingly, we surmised that inductive reasoning would negatively forecast future GAD.

With regard to verbal fluency, in community-dwelling older adults (Beaudreau & O'Hara, 2009; Yochim *et al.* 2013) and general adults (Airaksinen *et al.* 2005), it was similar between high and low anxious persons. Also, processing speed (Trail Making Test A) did not differ between elderly with and without GAD (Mantella *et al.* 2007). Processing speed measured by simple time-pressured tests (e.g. backward counting; Lachman *et al.* 2014) would hence probably not differ between GAD and controls. Plausibly, we hypothesized that verbal fluency and processing speed would *not* predict GAD. EM requires consciously remembering events. Most studies found no link between EM and worry/anxiety (e.g. Beaudreau & O'Hara, 2009; Yochim *et al.* 2013), especially when the Rey Auditory Verbal Learning Test (Rey, 1964) was tested on anxious youths (Günther *et al.* 2004) and adults (20–64 years; Airaksinen *et al.* 2005). Therefore, we postulated that EM deficits would not sequentially predict GAD.

In summary, *specific* impairments in EF and non-EF constructs were hypothesized based on theory and research to predate the *onset* of pathological worry (Eysenck & Derakshan, 2011; Hirsch & Mathews, 2012). However, no studies have used comprehensive cognitive measures (e.g. Brief Test of Adult Cognition by Telephone; Lachman *et al.* 2014) to prospectively examine the neuropsychological-GAD link and test the core tenets of attentional control theory and the cognitive model of worry. Thus far, the bulk of literature on anxiety disorders has focused mainly on 'hot'

affect-laden cognition (e.g. see meta-analysis by Bar-Haim *et al.* 2007). However, there is a dearth of studies on 'cold' cognition in GAD. We attempted to fill this knowledge gap. For primary analyses, we predicted that inhibition, set-shifting, and WM updating deficits would predate the onset of GAD. However, we made no predictions with regard to whether accuracy and/or latency would strongly predict GAD, as the nascence of these topics precluded us from making such *a priori* hypotheses. Also, we hypothesized that verbal WM (*digit span*) would not significantly forecast GAD. For secondary analyses, we explored the possibility that global cognition may be linked to GAD in later life. We predicted that inductive reasoning (*number series*) would be negatively sequentially related to GAD. However, we hypothesized that processing speed (30-seconds-and-counting task), verbal fluency (*category*), and EM (*word list recall*) would not predict GAD.

Method

Participants

Participants were members of the Midlife Development in the United States (MIDUS) study at waves two and three (Brim *et al.* 2004; Ryff & Lachman, 2017; Ryff *et al.* 2017). Of the initial 4206 participants, 2605 had complete data of the neuropsychological tests and symptoms at Time 1 and of symptoms at Time 2. Compared with non-completers, completers were significantly more likely to be younger [odds ratio (OR) 0.99, 95% confidence interval (CI) 0.98–0.99], $p < 0.0001$), female (χ^2 (df = 1) = 12.34, $p = 0.00047$), educated (OR 1.14, 95% CI 1.11–1.17, $p < 0.0001$), and had better global cognition (OR 1.57, 95% CI 1.47–1.70, $p < 0.0001$). However, they did not significantly differ in terms of GAD (OR 1.00, 95% CI 0.93–1.08, $p = 0.97$), panic disorder (OR 0.96, 95% CI 0.91–1.02, $p = 0.96$), and major depressive disorder diagnosis (OR 0.97, 95% CI 0.94–1.01, $p = 0.097$) at baseline.

Table 1 demonstrates baseline descriptive study variables. Overall, 56.31% were female, 92.21% were Caucasians, 2.70% were African American, and 4.40% were Asian, Pacific Islander, and other ethnicities. Mean age was 55.20 (s.d. = 11.41, range = 33–84). 71.60% received education beyond high school. Among 1.73% of participants who met criteria for baseline GAD, 77.78% and 24.44% presented with comorbid major depressive disorder and panic disorder respectively. Among 1.61% of respondents who met GAD criteria at Time 2, 73.81% and 40.48% had comorbid major depressive disorder and panic disorder. The second assessment took place after 9.11 years on average (s.d. = 0.53, range = 6–11). At Time 2, respondents had a mean age of 64.32 years (s.d. = 11.42, range = 42–93).

Measures

Measures of inhibition, set-shifting, WM updating, verbal WM, global cognition, inductive reasoning, processing speed, verbal fluency, and EM were administered only at baseline. Diagnoses were attained at both baseline and 9-year follow-up.

Brief test of adult cognition by telephone (Tun & Lachman, 2006; Lachman et al. 2014)

Subtests were administered in the following sequence: Word List Recall–Immediate, Backward Digit Span, Category Fluency, Stop-and-Go Switch Task, Number Series, 30-Seconds-and-Counting-Test, and Word List Recall–Delayed. EM was assessed by the ability to correctly recall as many words read aloud from a 15-word list

Table 1. Descriptive and Pearson's correlations of study variables at baseline

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. Age	-														
2. Female	-0.01	-													
3. Education	-0.14**	-0.12**	-												
4. GAD T1	-0.067**	0.084**	-0.093**	-											
5. MDD T1	-0.10**	0.14**	-0.051**	0.34**	-										
6. PD T1	-0.085**	0.13**	-0.048*	0.11**	0.26**	-									
7. GC T1	-0.39**	-0.12**	0.43**	-0.033	-0.037	-0.021	-								
8. EM T1	-0.27**	0.24**	0.17**	0.016	0.032	0.053**	0.37**	-							
9. HTN	-0.29**	-0.024	0.10**	-0.031	-0.051**	-0.045*	0.18**	0.11**	-						
10. DM	-0.14**	0.055**	0.085**	-0.029	-0.011	-0.044*	0.14**	0.11**	0.20**	-					
11. Exercise	0.028	-0.14**	-0.107**	-0.014	-0.073**	-0.050*	-0.042*	-0.084**	-0.028	-0.011	-				
12. BMI	-0.02	-0.047*	-0.14**	0.057**	0.061**	0.039*	-0.071**	-0.067**	-0.27**	-0.21**	0.067**	-			
13. SOC	0.018	-0.093**	0.14**	-0.13**	-0.24**	-0.13**	0.12**	0.059**	0.040*	0.042*	-0.067**	-0.071**	-		
14. GAD T2	-0.063**	0.084**	-0.056**	0.45**	0.23**	0.16**	-0.044*	0.026	0.013	-0.018	-0.022	0.023	-0.12**	-	
15. GAD Diagnosis T2	-0.059**	0.076**	-0.042*	0.383**	0.218**	0.174**	-0.050*	0.033	0.018	-0.006	-0.023	0.02	-0.119**	0.934**	-
Mean	55.20	-	7.56	0.11	0.57	0.30	0.16	0.12	-	-	4.59	27.83	5.61	0.11	-
s.d.	11.41	-	2.51	0.78	1.68	0.97	0.93	0.96	-	-	1.02	5.71	0.96	0.81	-
Min	33	-	1	0	0	0	-4.80	-2.42	-	-	1	14.23	1.08	0	-
Max	84	-	12	10	7	6	3.39	3.83	-	-	5	82.31	7	10	-
n	-	1467	-	45	252	154	-	-	719	214	-	-	-	-	42
%	-	56.31	-	1.73	9.67	5.91	-	-	27.60	8.21	-	-	-	-	1.61
Skewness	0.19	-0.26	0.08	8.36	2.79	3.53	-0.07	0.60	-1.00	-3.05	-2.47	1.45	-0.74	8.56	7.69

GAD, generalized anxiety disorder; MDD, major depressive disorder; PD, panic disorder; EF, executive function; EM, episodic memory; HTN, hypertension; DM, diabetes mellitus; BMI, body mass index; SOC, sense of control; GC, global cognition; Min, minimum; Max, maximum

Note: Gender was coded as 1 = male and 2 = female. EF and EM reflect composite z-scores. Education level ranged from 1 = no school/ some grade school to 12 = medical, law, or doctoral degree. HTN and DM medication use were coded as 1 = yes and 2 = no. Exercise status was coded as 1 = yes and 2 = no. Sense of control was coded from 1 = strongly disagree to 7 = strongly agree. * $p < 0.05$; ** $p < 0.01$.

within a minute (Rey, 1964). Verbal WM [Digit Span (Wechsler, 1997)] required participants to correctly reiterate increasingly lengthy digit strings backwards. For verbal fluency (semantic), participants named as many unique animals/foods within 1 min (Tombaugh *et al.* 1999). Inductive reasoning required responding with the correct final number in a series by inferring a pattern (Number Series; Salthouse & Prill, 1987). Processing speed (novel 30-Seconds-and-Counting-Task) required counting backwards from 100 rapidly and accurately within 30 s.

Inhibition, set-shifting, and WM updating were assessed using the Stop-and-Go Switch Task (Tun & Lachman, 2006) and indexed by accuracy and latencies. Baseline, Single-Task blocks comprised two conditions: Normal and Reverse. In the Normal condition, respondents had to answer 'STOP' or 'GO' in response to cues 'RED' and 'GREEN', respectively. The Reverse condition entailed stating the diametrically opposite answer (i.e. 'STOP' for 'GREEN' and 'GO' for 'RED'). In the *Mixed-Task* block, respondents *alternated* between Normal and Reverse conditions at *random* periods of two to six trials following cues of 'NORMAL' or 'REVERSE.' Latencies were recorded in milliseconds (ms) i.e. time between cue and accurate response. In Switch trials, respondents had to alternate from one condition to another. Non-Switch/Repeat trials referred to blocks with virtually no change in cues. Respondents first received 20 Normal and 20 Reverse trials (Single-Task block). Next, the Mixed-Task block included 32 trials. Lower latency denoted faster response times. Good associations were observed between the telephone-administered Brief Test of Adult Cognition and a face-to-face interview with good 6-month retest reliability (Tun & Lachman, 2008). Inhibition was assessed by Single-Task block reverse trials. Set-shifting was indexed by Mixed-Task block trials and *local* switch costs. WM updating was indicated by *general* switch costs. Switch costs capture ability to swiftly change between distinct WM representations and update responses accordingly (Rogers & Monsell, 1995). General switch costs (WM updating) were computed as the distinction between latency on the Mixed-Task and Single-Task trials (Ryff & Lachman, 2017). Local switch costs (set-shifting) refer to the latency difference between Mixed-Task Switch and Repeat trials. *Absolute* costs [score difference between the simple and complex condition (A–B)] and *relative* costs [proportional reduction in performance from the simple to complex condition to adjust for baseline performances (i.e. (A–B)/A)] were computed. Larger switch costs indicated greater impairment.

Global cognition and episodic memory composites

Following Lachman *et al.* (2014), scores on the Backward Digit Span, Categorical Verbal Fluency, Number Series, 30-Seconds-And-Counting-Task, and Stop-and-Go Switch Task–Mixed Task Trials were standardized and averaged to obtain a global cognition *z*-score. A composite EM score was derived by standardizing and averaging Immediate and Delayed Word List Recall. Exploratory and confirmatory factor analyses revealed a two-factor solution offering the most parsimonious model fit of the Brief Test of Adult Cognition by Telephone with factors comprising the stated subtests within each composite (see Fig. 1 in Lachman *et al.* 2014). All tests showed strong convergent and discriminant validity.

*Composite international diagnostic interview – short form (CIDI-SF; Kessler *et al.* 1998)*

GAD diagnosis was based on the Diagnostic and Statistical Manual for Mental Disorders–Third Version–Revised criteria using the CIDI-SF. GAD severity was also based on the CIDI-SF and DSM-III-R (Wittchen *et al.* 1994; Kessler *et al.*

1998). Respondents who experienced a period of a month or more of worry and anxiety rated on a 4-point Likert-type scale (1 = *most days* to 4 = *never*) their level of worry-linked cognitive, somatic, or behavioral symptoms in the past 12 months (e.g. restlessness). Diagnosis required participants to report that they worry 'a lot more' than most people, worried almost every day, and endorsed at least 3 out of 10 symptoms on most days. The CIDI-SF showed adequate retest (agreement = 0.89; κ = 0.69) and inter-rater reliability (agreement = 0.98; κ = 0.96) with psychiatric diagnoses. Internal consistency of the 10-item GAD severity scale was good at Time 1 (α = 0.86) and Time 2 (α = 0.89).

Lifestyle factors and perceived control

Participants answered whether or not they regularly exercised, and were managing chronic diabetes/hypertension during the past 12 months on a binary scale (1 = *yes*; 2 = *no*). Perceived control was measured with 12 items on a 7-point Likert scale (1 = strongly agree to 7 = strongly disagree; α = 0.67; Lachman & Weaver, 1998). Scores were reverse coded i.e. higher scores reflected greater control.

Data analytic plan

Given the count nature of GAD severity and diagnosis, assumptions of normality, homogeneity of error variance, and linearity of the association were not met. Conducting ordinary least squares regression analyses were thus inappropriate, as various transformation methods failed to normalize the GAD outcome variable. We thus used Poisson and negative binomial regressions to predict GAD severity and diagnosis respectively (Agresti, 2002; Vives *et al.* 2006; Atkins & Gallop, 2007; Karazsia & van Dulmen, 2008). In Poisson regression models, computing the exponential of the regression coefficient generates an incident rate ratio i.e. a multiplicative degree that the predicted symptom count would be expected to rise or fall with each unit increase in the predictor. Negative binomial regression models yield an OR i.e. the probability of meeting GAD criteria increases/reduces with each unit change in the predictor. Whereas an OR greater than 1 denoted higher likelihood for GAD, an OR below 1 reflected a lower probability. All multivariate Poisson and negative binomial regression models offered the best fit to the data (all *p* values for the χ^2 goodness-of-fit tests were >0.05). No over-dispersion was detected. Importantly, we removed individuals with GAD at baseline and focused on new onsets to determine whether cognitive deficits predated GAD across 9 years. We included the following covariates to test if each cognitive construct *independently* predicted GAD. First, we included age (Ramsawh *et al.* 2009), gender (Craske, 2003), and education (Rhebergen *et al.* 2017) as these have been associated with GAD. Second, as GAD, panic disorder, and major depressive disorder are linked sequentially (e.g. Moffitt *et al.* 2007), we controlled for their baseline severity. Also, as perceived uncontrollability (Gallagher *et al.* 2014), low exercise frequency (Gonçalves & Byrne, 2012; Zschucke *et al.* 2013), body mass index (Hasler *et al.* 2004), as well as diabetes mellitus and hypertension were associated with GAD in the MIDUS and other culturally diverse samples (Barger & Sydeman, 2005; Culpepper, 2009; Grimsrud *et al.* 2009; Carroll *et al.* 2010), we adjusted for those variables. The pattern of correlations among the predictors of GAD suggested no multicollinearity (all of *r*s were <0.39; see Table 1). Last, as set-shifting builds on inhibition, we controlled for inhibition when examining set-shifting as a predictor. Multicollinearity was absent (small correlations; all *r*s < 0.23). We followed up significant effects

with comparisons using the Simes Bonferroni correction procedure to protect for Type I error (Simes, 1986). Normal and reverse trials of the Stop-and-Go Switch Task were each run in *separate* models in terms of either accuracy *or* latency predicting for GAD, as with absolute *or* relative switch costs.

Results

Primary analyses of EF constructs predicting for GAD

Tables 2 and 3 summarize results for cognitive constructs as predictors of GAD. For inhibition (Stop-and-Go Switch Task; Single-Task Reverse condition), Time 1 accuracy was negatively associated with Time 2 GAD severity and diagnosis. Time 1 inhibition latency, however, was not substantively related to Time 2 GAD. Set-shifting (latency scores on the Stop-and-Go Switch Task; Mixed-Task Repeat Trials) was positively longitudinally associated with Time 2 heightened GAD. As predicted, verbal WM (backward digit span) did not significantly forecast GAD. However, WM updating (general switch costs) positively forecasted GAD. Last, local switch costs were not significantly linked to Time 2 GAD.

Secondary analyses of non-EF cognitive constructs predicting for GAD

Lower Time 1 global cognition *z*-score was independently significantly linked to higher Time 2 GAD severity and diagnosis. Consistent with predictions, for inductive reasoning (number series), accuracy was negatively linked to Time 2 GAD severity and diagnosis. On the other hand, processing speed (30-Seconds-and-Counting), verbal fluency (semantic category), and global/immediate/delayed EM (word list) were not significantly associated with Time 2 GAD.

Discussion

This is the first study to show that poor global cognition, as well as specific EF and non-EF facets, were precursors of heightened GAD 9 years later. Multivariate analyses revealed that inhibition, set-shifting, WM updating, inductive reasoning, and global cognition deficits independently predicted future elevated GAD after controlling multiple covariates and removing those who met criteria for GAD at baseline. This study thus presents original evidence that EF and other cognitive deficits function as distal risk factors of GAD in mid-adulthood.

The novel finding that inhibition deficits contributed to GAD validates the proposition that processing deficits engender worry (Eysenck & Derakshan, 2011). Accuracy on the Reverse, but not Normal, condition of the Stop-and-Go Switch Task Single-Task trials predicted GAD arguably because there is an incongruity between top-down/volitional and bottom-up/stimulus-driven inhibition processes in the former, but not latter condition. Deficient top-down voluntary cognitive control processing thus may be instrumental in producing excessive worry (Hirsch *et al.* 2009). Accordingly, high- (*v.* low-anxious) persons showed longer accurate *anti*-, but not pro-saccade latencies (Derakshan & Eysenck, 2009). Further, a meta-analysis showed that GAD persons displayed above normative levels of inappropriately abstaining responses ($z = 2.14$) on other inhibition measures (Wright *et al.* 2014). Moreover, anxiety induction (Fox & Knight, 2005) and GAD status (Hallion *et al.* 2017) uniquely predicted lower Stroop paradigm accuracy. Inhibition issues may also reflect

abnormalities in neural coupling between the ventromedial PFC and dorsal raphe nucleus that regulates anxiety (Munakata *et al.* 2011) and cerebral blood flow patterns (Andresescu *et al.* 2011). Prospective neuroimaging studies should test these proposals.

Accompanying inhibition, higher general switch costs and latencies on the Stop-and-Go Switch Task Mixed-Task Repeat Trials suggested that WM updating and set-shifting predicted future GAD. These results concur with studies that used other set-shifting measures. GAD persons (*v.* controls) insisted on applying the same rule despite negative feedback (Mantella *et al.* 2007; Tempesta *et al.* 2013). General switch costs reflect problems in sustaining and improving selection among two or more distinct possible response sets *between* trial blocks (Reimers & Maylor, 2005) and thus includes basic WM maintenance and updating. Our results are largely aligned with recent findings of higher general switch costs among high (*v.* low) worriers towards emotional (Beckwé *et al.* 2014) and non-emotional (Gustavson & Miyake, 2016; Gustavson *et al.* 2017) material. Furthermore, we observed medium-to-large effect sizes implying that WM updating deficits were potent antecedents of late-life GAD (average OR estimates were 6.05–6.31 herein) (Chen *et al.* 2010). Of note, is that verbal WM did not portend future GAD. This observation is congruent with studies on elderly reported by Wetherell *et al.* (2002) (high *v.* low trait anxious) and Price & Mohlman (2007) (GAD *v.* non-GAD) who performed similarly on the digit span. WM (digit span) did not predict GAD perhaps because it taps into *verbal* (*v.* visuospatial) WM (Shackman *et al.* 2006). Verbal WM requires primarily left pre-frontal and posterior cortical activities which remain largely intact among anxiety patients. Also, the digit span did not require overriding a prepotent schema.

Several justifications may account for why inductive reasoning deficits predicted GAD. Persistent failure to examine, weigh, or draw valid conclusions from available data may lead to the habit of generating inaccurate hypotheses without sufficient forethought. Persons with GAD and high trait anxiety were impulsively faster than controls at proposing explanations for arbitrary statements (Pélissier & O'Connor, 2002) and probabilistic decision-making (Bensi *et al.* 2010). Also, inductive reasoning deficits may interfere with effective problem-solving (e.g. Kail, 2007), prevent insight into self-defeating patterns, and prepare for recurring difficulties (Overholser, 1993). Further, GAD persons showed a proclivity to generate threat-linked, instead of benign, words on a homophone task (e.g. 'die/pain' instead of 'dye/pane'; Mathews *et al.* 1989; Mogg *et al.* 2004). These issues, if not remedied, understandably generate anxious apprehension by overestimating threats and underestimating ones' coping abilities. Subsequent studies could test these ideas by including other inductive reasoning paradigms.

The observation that global cognition predicted GAD in our study aligns with the aging study conducted in France (Zhang *et al.* 2015) but not the Netherlands (De Beurs *et al.* 2000; Schoevers *et al.* 2005). These prior studies used the Mini Mental State Examination (Folstein *et al.* 1975) to measure global cognition. Variable findings may thus be due to distinctive assessments (Brief Test of Adult Cognition by Telephone *v.* Mini Mental State Examination) and sample characteristics (e.g., age ranged from 55 to 88 years in De Beurs *et al.* (2000) compared with the wider age range herein). Continued longitudinal work is clearly needed to better understand the global cognition-GAD relationship.

Findings concerning verbal fluency and processing speed concur with current evidence. Verbal fluency necessitates initiating new cognitive tasks. That verbal fluency was not a risk factor for GAD accords with former cross-sectional studies showing

Table 2. Longitudinal and multivariate Poisson and negative binomial regression analyses of Time 1 factors predicting novel cases of Time 2 GAD severity and diagnosis by removing participants at Time 1 who met clinical GAD ($n = 2605$)

Time 1 Predictors	Time 2 GAD Severity					Time 2 GAD Diagnosis				
	β	IRR	95% CI		p	β	OR	95% CI		p
			Lower	Upper				Lower	Upper	
Intercept	-4.73					-4.72				
General cognitive ability z-score	-0.57	0.57	0.36	0.88	0.012	-0.55	0.58	0.37	0.90	0.015
Age	-0.03	0.97	0.93	1.02	0.210	-0.03	0.97	0.93	1.02	0.232
Female gender	0.57	1.77	0.68	4.66	0.245	0.56	1.74	0.65	4.64	0.266
Level of education	0.02	1.02	0.85	1.22	0.841	0.01	1.01	0.85	1.21	0.895
GAD severity	1.51	4.53	1.72	11.92	0.002	1.64	5.13	1.75	15.03	0.003
Major depression severity	0.17	1.19	1.02	1.39	0.031	0.18	1.19	1.02	1.40	0.032
Panic disorder severity	0.34	1.40	1.13	1.74	0.002	0.35	1.42	1.13	1.78	0.002
Hypertension medication use	0.35	1.41	0.53	3.80	0.495	0.38	1.47	0.52	4.11	0.468
Diabetes mellitus medication use	0.89	2.43	0.31	19.00	0.397	0.88	2.42	0.30	19.49	0.406
Exercise status	-0.10	0.90	0.65	1.26	0.543	-0.12	0.89	0.63	1.24	0.490
Body mass index	-0.01	0.99	0.93	1.06	0.853	0.00	1.00	0.93	1.07	0.942
Sense of control	-0.33	0.72	0.51	1.03	0.074	-0.34	0.72	0.49	1.04	0.076

GAD, generalized anxiety disorder; IRR, incidence risk ratio

Note: Gender was coded as 1 = male and 2 = female. Education level ranged from 1 = no school/ some grade school to 12 = medical, law, or doctoral degree. Hypertension and diabetes mellitus medication use were coded as 1 = yes and 2 = no. Exercise status was coded from 1 = yes and 2 = no. Overall model statistic were $\chi^2(13) = 50.24$, $p < 0.0001$ (GAD severity) and $\chi^2(13) = 49.36$, $p < 0.0001$ (GAD diagnosis). Text in bold denote findings which are statistically significant.

no link between anxiety severity and verbal fluency in clinical (Airaksinen *et al.* 2005; Smitherman *et al.* 2007) and community samples (Beaudreau & O'Hara, 2009; Yochim *et al.* 2013). To our knowledge, this is the first study to use a backward counting task (Lachman *et al.* 2014) to investigate processing speed in future GAD. Beaudreau & O'Hara (2009) who used the symbol digit modality test (Smith, 1982) found a negative processing speed-trait anxiety correlation ($r = -0.35$). The symbol digit modality test is a more complex processing speed test than the counting task, and subsequent studies may test whether task complexity determines the sequential processing speed-GAD association.

With regard to EM, our findings were largely concordant with the literature but discrepant from two prior studies which showed weaker EM in GAD patients (*v.* controls) (Mantella *et al.* 2007; Butters *et al.* 2011). Perhaps this is because the EM indices used in Butters *et al.* (2011) were an aggregate score of the list, story, and figure recall that vastly differed from the singular 15-word list recall used herein. Similarly, Mantella *et al.* (2007) used more sensitive 16-item word list and dementia measures. Also, lack of concordance in the EM-GAD relationship across studies may be partly due to age differences (e.g. older adults above 65-years-old in the two prior studies compared with the middle-aged sample of MIDUS project who was a year short of meeting the definition of 'older adults' at follow-up). Last, although EM deficits may not precede and predict GAD, worry itself may negatively affect recollection capacities and impair EM ahead of time. Slightly heightened worry severity (*v.* minimal worry) compromised visual memory and learning as well as delayed verbal recall 2 years later among community-dwelling middle-aged adults (Pietrzak *et al.* 2012). A similar pattern may hold true for processing speed and verbal fluency, which may emerge several years after the onset of GAD, but are not by themselves predictive of GAD.

Noteworthy is that GAD itself may be a predictor of future general and specific EF impairments. For instance, acute anxiety induction compromised set-shifting capacities (Shields *et al.* 2016). Moreover, verbal (*v.* imagery) worry induction diminished WM abilities (Leigh & Hirsch, 2011) and increased undesirable intrusive thoughts were associated with impaired inhibition (Stokes & Hirsch, 2010). Further, trait worry was considerably related to deficits in WM ability to filter out threat distractors (Stout *et al.* 2015). Worry induction also led to enhanced electrophysiology in WM-linked areas (Moran *et al.* 2015) reflective of diminished error-monitoring WM updating capacities. Collectively, the EF-GAD link may be bi-directional. For instance, greater initial worry severity was associated with larger reductions in WM, and lower baseline WM was related to sharper increases in worry (Trezise & Reeve, 2016). The same iterative pattern may apply to WM updating, set-shifting, and inhibition in predicting GAD, and vice versa (White *et al.* 2011).

Strengths, limitations, and future directions

Several limitations of the study deserve mention. First, this sample lacked ethnic and economic diversity, thereby limiting generalizability. Future research should thus investigate this phenomenon in a more heterogeneous sample. Second, few participants met criteria for DSM-III-R-defined GAD at both time points, which is common in community-dwelling samples (Schoevers *et al.* 2005). Large, well-characterized at-risk or clinical samples are recommended moving forward. Also, replication is required to corroborate these initial observations. The limitations notwithstanding, this study presented with strong statistical power, used psychometrically strong measures, and has important mental health implications. A fruitful line of research would involve testing whether improving

Table 3. Longitudinal and multivariate Poisson and negative binomial regression analyses of Time 1 factors predicting Time 2 GAD severity and binary GAD diagnosis using distinct facets of executive function predicting for GAD in separate models ($n = 2605$)

Time 1 Predictors	Time 2 GAD Severity					Time 2 GAD Diagnosis				
	β	IRR	95% CI		p	β	OR	95% CI		p
			Lower	Upper				Lower	Upper	
Primary Analyses with Executive Function Facets as Predictors										
Verbal WM – Digit backwards	–0.08	0.93	0.70	1.22	0.592	–0.07	0.93	0.70	1.23	0.603
WM Updating – General switch costs ^a										
Absolute	1.70	5.44	1.37	21.70	0.016	1.80	6.05	1.27	28.78	0.024
Relative	1.71	5.54	1.71	18.02	0.004	1.84	6.31	1.60	24.90	0.009
Inhibition – Stop and Go Switch Task Single-Task Trials										
Reverse condition (# correct)	–0.20	0.82	0.69	0.97	0.022	–0.21	0.81	0.67	0.98	0.031
Latency	–0.89	0.41	0.02	10.26	0.587	–0.86	0.42	0.02	11.29	0.608
Set-Shifting – Stop and Go Switch Task Mixed-Task Repeat Trials										
Reverse condition (# correct)	0.05	1.06	0.67	1.67	0.819	0.05	1.05	0.66	1.65	0.847
Latency	1.57	4.82	1.27	18.30	0.021	1.49	4.42	1.06	18.44	0.042
Set-Shifting – Stop and Go Switch Task Mixed-Task Switch Trials										
Reverse condition (# correct)	–0.15	0.87	0.37	2.01	0.735	–0.14	0.87	0.37	2.05	0.746
Latency	–0.57	0.57	0.19	1.68	0.303	–0.54	0.59	0.19	1.77	0.343
Set-Shifting – Local switch costs ^a										
Absolute	–0.17	0.84	0.13	5.52	0.859	–0.14	0.87	0.13	5.77	0.882
Relative	–0.24	0.79	0.11	5.77	0.817	–0.22	0.80	0.11	6.06	0.83
Secondary Analyses of Non-EF Cognition Facets as Predictors										
Inductive Reasoning – Number series (# correct)	–0.34	0.71	0.52	0.98	0.036	–0.34	0.71	0.51	0.99	0.041
Verbal Fluency – Category fluency	0.003	1.00	0.93	1.08	0.928	0.003	1.00	0.93	1.08	0.942
Processing Speed – 30-Seconds And Counting Task (# correct)	–0.03	0.97	0.93	1.01	0.186	–0.03	0.97	0.93	1.02	0.203
Episodic Memory – Word list delayed	0.07	1.07	0.91	1.27	0.400	0.07	1.07	0.90	1.27	0.421
Episodic Memory – Word list immediate	0.001	1.00	0.83	1.21	0.994	–0.002	1.00	0.82	1.21	0.987
Stop and Go Switch Task Accuracy (# correct) on the Normal conditions										
Single-Task Trials	–0.07	0.93	0.69	1.25	0.626	–0.07	0.93	0.68	1.27	0.654
Mixed-Task Repeat Trials	–0.16	0.85	0.66	1.09	0.203	–0.16	0.85	0.66	1.10	0.224
Mixed-Task Switch Trials	–0.13	0.88	0.26	2.93	0.835	–0.13	0.88	0.26	3.01	0.838

ms, milliseconds; 30-SACT, 30 s and counting task.

Note: Latency is measured as Score Difference on the trials (Reverse – Normal) [in milliseconds (ms)]; Each cognitive construct predicting for GAD severity or diagnosis were run in separate models. The following covariates were entered simultaneously into each model: age, gender, education level, generalized anxiety disorder severity, major depressive disorder severity, panic disorder severity, hypertension and/or diabetes mellitus medication use, exercise status, body mass index, and sense of control. Text in bold denote findings which are statistically significant. ^aAbsolute costs [score difference between the simple and complex condition (A–B)] and relative costs [proportional reduction in performance from the simple to complex condition to adjust for baseline performances (i.e. (A–B)/A)] were computed. Larger switch costs indicated greater impairment.

EF, inductive reasoning, and global cognition are effective as *preventative* measures against the development of GAD.

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