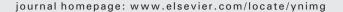
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## NeuroImage





### Does variability in cognitive performance correlate with frontal brain volume?

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#### ABSTRACT

Little is known about the neural correlates of within-person variability in cognitive performance. We investigated associations between regional brain volumes and trial-to-trial, block-to-block, and day-to-day variability in choice-reaction time, and episodic and working memory accuracy. Healthy younger (n=25) and older (n=18) adults underwent 101 daily assessments of cognitive performance, and their regional brain volumes were measured manually on magnetic resonance images. Results showed that smaller prefrontal white matter volumes were associated with higher block-to-block variability in choice-reaction time performance, with a stronger association observed among older adults. Smaller volumes of the dorsolateral prefrontal cortex covaried with higher block-to-block variability in episodic memory (number-word pair) performance. This association was stronger for younger adults. The observed associations between variability and brain volume were not due to individual differences in mean performance. Trial-to-trial and day-to-day variability in cognitive performance were unrelated to regional brain volume. We thus report novel findings demonstrating that block-by-block variability in cognitive performance is associated with integrity of the prefrontal regions and that between-person differences in different measures of variability of cognitive performance reflect different age-related constellations of behavioral and neural antecedents.

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#### Introduction

Much attention has been paid to individual differences in cognitive performance and age-related differences therein (Craik and Salthouse, 2008). However, less is known about intra-individual variability in cognitive performance, which is defined as lawful but transient within-person changes in behavior within a defined period (Nesselroade, 1991) and which can be observed across a wide range of tasks (Hultsch et al., 2008; MacDonald et al., 2006; Rabbitt et al., 2001). Our ignorance is even greater when it comes to the neural underpinnings of intra-individual variability in cognitive performance (MacDonald et al., 2006, 2009b).

For all its apparent simplicity, the concept of intra-individual variability in cognitive performance can be approached in many meaningful ways. Speed and accuracy characteristics of performance may fluctuate on a yearly, monthly, daily, hourly, or momentary basis, thus demanding examination on various scales, with a wide range of

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resolution (Boker et al., 2009). Moreover, selection of scale is not just a decision about measurement as, depending on the time scale, variability may reflect different behavioral and neural antecedents (Boker et al., 2009: Lindenberger and von Oertzen, 2006: MacDonald et al., 2009b; Rabbitt et al., 2001). For example, trial-to-trial variability in performance on simple reaction time (RT) tasks may reflect lapses of attention (Bunce et al., 1993; West et al., 2002; Williams et al., 2005) and admixture of neural noise to task-related processes (Bäckman et al., 2006; Li et al., 2001; MacDonald et al., 2009a). Such factors may also induce variability in performance across blocks of trials, but block-to-block variability may additionally reflect influences such as search and selection of optimal strategies (Allaire and Marsiske, 2005; Li et al., 2004; Shing et al., 2012; Siegler, 1994). Day-to-day variability in cognitive performance may stem from fluctuations in non-cognitive factors, such as stress (Sliwinski et al., 2006) or motivation (Brose et al., 2010). Tasks may also vary in the degree to which they tap different antecedents of variability in cognitive performance. Simple RT tasks present relatively little opportunity for exploration of strategies. In contrast, working memory (e.g., Shing et al., 2012) and episodic memory (e.g., Kirchhoff, 2009) tasks provide ample room for within-subject differences in strategies, which may contribute to performance variability.



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In sum, intra-individual variability in cognitive performance is not a unitary construct (Allaire and Marsiske, 2005; Boker et al., 2009; Lindenberger and von Oertzen, 2006; MacDonald et al., 2009b), and its heterogeneity should inform the search for neural correlates of intra-individual variability. However, extant studies on brain correlates of variability in cognitive performance have focused almost exclusively on fluctuations in response latency across trials of simple and choice RT tasks. These studies report that higher trial-to-trial variability in RT is associated with smaller volume (Anstey et al., 2007; Walhovd and Fjell, 2007) and lower integrity of white matter in frontal, parietal, temporal, and central brain regions (Bunce et al., 2007; Fjell et al., 2011; Moy et al., 2011; Tamnes et al., 2012). In a related vein, variability in finger tapping is associated with white matter integrity (Ullén et al., 2008). Although at least two studies (Moy et al., 2011; Ullén et al., 2008) failed to observe significant associations between gray matter volume and variability, other research suggests that trial-to-trial variability may be linked to prefrontal cortex integrity. For example, individuals with lesions in the dorsolateral prefrontal cortices (DLPFC) display greater variability in performance on simple and complex RT tasks than patients with orbitofrontal or non-frontal lesions and healthy controls (Stuss et al., 2003). In primates, direct pharmacological manipulations of the DLPFC affect trial-to-trial variability in saccade response time (Pouget et al., 2009). In addition, individual differences in cognitive variability have been linked to activation in the attentional control network, including the prefrontal cortices, in a number of functional imaging studies (Bellgrove et al., 2004; Prado et al., 2011; Simmonds et al., 2007).

The extant literature contains no studies of neural correlates of block-to-block variability in the accuracy of performing complex tasks geared to assess working memory and episodic memory. It is therefore unknown whether the association between white matter integrity and variability is unique for RT tasks and to the time-scale of trial-to-trial measurements, or whether the observed associations generalize to other measures of variability extracted over different time scales and with indices unrelated to speed of response. We also note that slower performance fluctuations, similar to block-to-block variability, are confounding many measures of trial-to-trial variability used in previous reports. Hence, there is a need for a more systematic and nuanced investigation of the neural underpinnings of variability in cognitive performance.

In this study, we address the outlined lacunae in knowledge by taking advantage of a unique data set from the COGITO study (Schmiedek et al., 2010b), an investigation of younger and older adults who underwent 101 daily assessments of cognitive performance. The COGITO study presents an opportunity to follow methodological recommendations (e.g., Boker et al., 2009), and simultaneously examine and directly compare intra-individual and inter-individual variability on three nested time scales: trial-to-trial, block-to-block, and day-today. In the COGITO study, we assessed cognitive performance at various levels of complexity, ranging from choice-reaction time (CRT) to working and episodic memory accuracy. The CRT task allowed for estimation of all three levels of variability, while the accuracy tasks allow for estimation of block-to-block and day-to-day variability. To examine neural substrates of cognitive variability, we measured volumes in several brain regions that differed in their putative relevance to the cognitive tasks.

We based our prediction on the empirical review as well as the theoretical link between prefrontal cortex function and transient failures of cognitive control (Miller and Cohen, 2001; Weissman et al., 2006), which have been related to trial-to-trial variability (e.g., West et al., 2002; Williams et al., 2005). In addition to the reviewed evidence, findings link white matter integrity to speeded performance (e.g., Bender and Raz, 2012; Bucur et al., 2008; Espeseth et al., 2006; Kennedy and Raz, 2009) suggesting that white rather than gray matter of the PFC would be relevant to variations in speed. We thus hypothesized that trial-to-trial and block-to-block variability in speed-based indices of CRT performance would be associated specifically with the prefrontal white matter volume. In addition, we predicted that greater trial-totrial and block-to-block variability in accuracy of cognitive performance would be associated with smaller frontal gray matter volumes, but that no associations between day-to-day variability in cognitive performance and brain volume would emerge. As the association between trial-to-trial variability in RT and white matter integrity has been reported to increase in old age (Fjell et al., 2011), this association may emerge only in old age due to correlated individual differences in decline of variability and white matter integrity. Thus, we predicted such an increase with age group for trial-to-trial and block-to-block variability of CRT performance. We assumed that block-to-block variability in working and episodic memory accuracy might contain larger influence from search and selection of optimal strategies. We expected that such adaptive influences on variability of cognitive performance might mask the predicted age-related increase in the association between variability of cognitive performance and brain volume.

#### Material and methods

#### Participants

Participants were recruited through newspaper advertisements, word-of-mouth recommendations, and fliers circulated in Berlin, Germany (see Schmiedek et al., 2010b for details). The main COGITO study involved 101 younger (aged 20-31 years) and 103 older adults (aged 65-80 years). Out of these participants, 30 younger and 27 older individuals volunteered and were eligible for magnetic resonance imaging (MRI). To be eligible, participants had to report being right-handed, have normal or corrected-to-normal vision, and report no cardiovascular disease (except treated hypertension, recorded in seven older adults), diabetes, neurological or psychiatric conditions, use of anti-seizure or antidepressant drugs, or drug or alcohol abuse. Scores on the Mini-Mental State Examination (Folstein et al., 1975) were all above 25. Based on evaluations of the anatomical images by a clinical neurologist, one younger and six older adults were excluded due to various brain abnormalities, and one older participant was excluded from this study because of significant movement artifacts. Four younger and two older participants dropped out during the course of the study.

Thus, the sample with complete data consisted of 25 younger (13 women/12 men) and 18 older (9 women/9 men) adults. Descriptive statistics at pretest (see Table 1) showed that the sample displayed the typical age-related differences: lower perceptual speed (Digit-symbol substitution; Wechsler, 1981) and higher vocabulary (Spot-a-word; Lindenberger et al., 1993) scores in the older participants. The age groups were comparable on self-reported years of education. Relative to the mean Digit-symbol scores reported in a meta-analysis (Hoyer et al., 2004), the sample was less positively selected (about 1.1 *SD* for the younger and 0.6 *SD* for the older group) than typical samples in cognitive aging research.

Table 1			
Participant	characteristics	at	pretest.

Measure	Younger		Older		F(1,42)	р
	М	SD	М	SD		
Age	25.0	3.2	70.1	3.8	1793.8	<.001
Digit-symbol	59.8	9.3	44.6	6.9	34.3	<.001
Spot-a-word	0.66	0.11	0.82	0.07	32.5	<.001
Years of education	16.9	3.1	16.3	3.9	0.3	.572
Daily sessions	101.8	3.1	100.0	3.8	3.0	.089

The *F*- and *p*-values correspond to the age effect in a one-way ANOVA. Digit-symbol — Digit-Symbol Substitution Test (Wechsler, 1981); Spot-a-word — a German vocabulary test (Lindenberger et al., 1993); daily sessions — the number of sessions completed during the longitudinal phase of the study.

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