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Research Report

An evaluation of distinct volumetric and functional MRI contributions toward understanding age and task performance: A study in the basal ganglia

Scott A. Langenecker[a,b,*], Emily M. Briceno[b], Najat M. Hamid[b], Kristy A. Nielson[a,c]

[a]Department of Psychology and the Integrative Neuroscience Research Center, Marquette University, Milwaukee WI, USA
[b]Department of Psychiatry, Section of Neuropsychology, University of Michigan Medical Center, Ann Arbor MI, USA
[c]Functional Imaging Research Center, Foley Center for Aging and Development, and the Department of Psychiatry and Behavioral Medicine, Medical College of Wisconsin, Milwaukee WI, USA

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ABSTRACT

Prior work by our group and others has implicated the basal ganglia as important in age-related differences in tasks involving motor response control. The present study used structural and functional MRI approaches to analyze this region of interest (ROI) toward better understanding the contributions of structural and functional MRI measures to understanding age-related and task performance-related cognitive differences. Eleven healthy elders were compared with 11 healthy younger adults while they completed the "go" portion of a complex Go/No-go task. Separate ROI's in the bilateral caudate (C) and putamen/globus pallidus (PGp) were studied based upon previous findings of age-related functional MRI differences in basal ganglia for this portion of the task. Structural volumes and functional activation (in percent area under the curve during correct responses) were independently extracted for these ROI's. Results showed that age correlated with ROI volume in bilateral PGp and C, while multiple task performance measures correlated with functional activation in the left PGp. The Go/No-go task measures were also significantly correlated with traditional attention and executive functioning measures. Importantly, fMRI activation and volumes from each ROI were not significantly inter-correlated. These findings suggest that structural and functional MRI make unique contributions to the study of performance changes in aging.

1. Introduction

Healthy aging is associated with some well characterized cognitive changes, but their etiology is not well understood. The development of in vivo neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), and MRI techniques examining structural volumes (volumetric MRI—vMRI), are contributing to a better understanding of the physiological processes underlying cognitive tasks and the foundations of cognitive

* *Corresponding author*. Department of Psychiatry, University of Michigan Medical Center, 1500 E. Medical Center Drive, Ann Arbor, MI 48109, USA. Fax: +1 734 936 9262.
E-mail address: slangen@umich.edu (S.A. Langenecker).

Abbreviations: C, Caudate; PGp, Putamen/Globus Pallidus; PCTT, Percent Correct Target Trials; PCIT, Percent Correct Inhibition Trials; RTT, Response Time to Targets; BV, Brain Volume in the Anterior–Posterior Commissure Plane

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changes in both normal and abnormal aging. There are now various studies examining the structural integrity of the brain in aging, as well as studies examining its functional integrity. While age-related changes are evident using both approaches, few studies have concurrently examined both structural and functional integrity. Such studies are needed because some of these cognitive changes, which affect basic processes such as processing time (Salthouse, 1996), as well as more complex functions such as working memory and behavioral inhibition (Kramer et al., 1994; Langenecker et al., 2004; Park et al., 2002), might be better understood by the concurrent or differential use of these strategies.

Volume-behavior and volume-age relationships have been explored over the past two decades using vMRI. There is a body of literature indicating global volumetric decreases in elders (Mueller et al., 1998; Resnick et al., 2003); and more region-specific age-related volume reductions, most commonly involving fronto-striatal and hippocampal structures (Golomb et al., 1993; Head et al., 2002; Lupien et al., 1998; Raz et al., 1997, 2000; Tisserand et al., 2000; Van Petten, 2004). Volume reductions are related to severe general cognitive decline in pathological aging and are used diagnostically for Alzheimer's disease (Kantarci and Jack, 2003). However, when evaluating the relationship between volumetric measurements and cognitive ability in healthy elders and across the age range, effect sizes have been weak to modest at best, with only weak relationships with subcortical, basal ganglia and hippocampal regions and weak to more moderate relationships with total volume and cortical regions, particularly dorsolateral prefrontal cortex (Andreasen et al., 1993; Egan et al., 1994, 1995; Flashman et al., 1997; MacLullich et al., 2002; Raz et al., 1993; Walhovd et al., 2005; Wickett et al., 1994; Yeo et al., 1987). Moreover, comparisons between basal ganglia volume and executive function and motor planning tasks (such as the Wisconsin Card Sorting Test) indicate only weak, yet significant relationships (Head et al., 2002). Thus, the volume-behavior literature overall suggests that other factors and more performance-specific techniques might be fruitfully pursued towards understanding the interface between brain and behavior in aging. One of these techniques might be functional brain activity, as measured by fMRI, because functional activity may be affected by different factors than is brain volume.

fMRI, developed in the 1990s, measures the hemodynamic changes within the brain areas supporting cognitive tasks. Functional neuroimaging research (i.e., fMRI and PET) with elders suggests that the specialized neural networks tend to be recruited differently with age (Cabeza, 2002). Specifically, older adults have been shown to recruit neural regions to a lesser extent than younger adults in some studies (Rypma and D'Esposito, 2000; Stebbins et al., 2002). Other studies report recruitment in some task-related regions to a comparable or lesser degree accompanied by increased activation of other regions (Cabeza et al., 2004; DiGirolamo et al., 2001; Langenecker et al., 2004; Madden et al., 2004). These areas of increased activation are frequently in homologous areas contralateral to the regions activated in younger adults, typically in the frontal lobes and basal ganglia (Nielson et al., 2002; Reuter-Lorenz, 2002; Rosen et al., 2002). Additionally, some evidence suggests that age-related increases in activation are related to better task performance (Nielson et al., 2002; Rosen et al., 2002), while other studies have found age-related activation increases related to poorer performance (Dickerson et al., 2004). Increased activation related to better performance supports a functional compensation view (see Cabeza, 2002), which is also consistent with a prominent view in the stroke literature (Cao et al., 1998, 1999; Cramer et al., 1997). Increased activation related to poor performance may suggest activation foci that interfere with optimal performance, or foci that are compensatory, but do not provide sufficient compensation to attain optimal performance levels (Langenecker and Nielson, 2003).

Only a few studies have employed functional and volumetric MRI concurrently to assess their distinct contributions to understanding cognitive performance, in aging, only one of which was in normal aging. The study that pursued vMRI and fMRI in normal aging indicated that elders had decreased activation relative to young adults in a left middle and inferior frontal gyrus cluster during a dichotic listening, working memory task and reduced volume in an overlapping anatomical area. This activation was interpreted as decreased interference resolution (e.g., decreased recruitment) between the prepotent right ear advantage and the desired left ear instruction (Thomsen et al., 2004). A second study combining functional and volumetric measurements of mild cognitive impairment demonstrated a significant difference in activation in the right parahippocampal gyrus between those who later did and did not decline in cognitive ability, but no volumetric differences between these groups (Dickerson et al., 2004). A third study comparing AD patients to healthy adults reported that AD patients had decreased activation in the left inferior frontal gyrus during semantic decision-making that was correlated with decreased volume in the region (Johnson et al., 2000). In these studies, although relationships between vMRI and fMRI were discussed, there was no exploration of the relationships between performance and volume or performance and activation. Explorations of this type may have clarified the nature of age-related differences in light of recruitment or interference interpretations.

The present study was designed to address functional and volumetric contributions to age- and performance-related differences in response control on a specific type of Go/No-go (GNG) task, focusing on the "Go" response execution activation. GNG tasks can vary greatly in the types of stimuli, the timing of stimuli, similarity of target and non-target stimuli, or proportion of "go" and "no-go" items. In fact, many use "static" or constant target and distractor stimuli throughout the task (e.g., green = go, red = stop) and these are virtually indistinguishable from continuous performance tasks. In contrast, "context-based" GNG tasks include a rule for changing or shifting the target and distractor stimuli during the test. Thus, the to-be-inhibited distracter is dependent upon the context, or previous performance and stimuli presented. Performance on context-based GNG tasks has been shown to correlate with performance on traditional executive functioning measures (e.g., Langenecker and Nielson, 2003; Nielson et al., 2002). Thus, these tasks have been purported to require attention, set-shifting, processing speed and inhibitory control (Langenecker and Nielson, 2003; Nielson et al., 2002; Langenecker et al., in press; Garavan et al., 1999).

For the present study, healthy older and younger adults performed a context-based GNG task in order to evaluate