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Executive functions and neurocognitive aging: dissociable patterns of brain activity

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Abstract

Studies of neurocognitive aging report altered patterns of brain activity in older versus younger adults performing executive function tasks. We review the extant literature, using activation likelihood estimation meta-analytic methods, to compare age-related differences in the pattern of brain activity across studies examining 2 categories of tasks associated with executive control processing: working memory and inhibition. In a direct contrast of young and older adult activations, older adults engaged bilateral regions of dorsolateral prefrontal cortex as well as supplementary motor cortex and left inferior parietal lobule during working memory. In contrast, age-related changes during inhibitory control were observed in right inferior frontal gyrus and presupplementary motor area. Additionally, when we examined task-related differences within each age group we observed the predicted pattern of differentiated neural response in the younger subjects: lateral prefrontal cortex activity associated with working memory versus right anterior insula/frontal opercular activity associated with inhibition. This separation was largely maintained in older subjects. These data provide the first quantitative meta-analytic evidence that age-related patterns of functional brain change during executive functioning depend on the specific control process being challenged.

Keywords: Aging; Neuroimaging; Activation likelihood estimation; Executive function; Working memory; Inhibition; Meta-analysis

1. Introduction

Neurocognitive changes in healthy aging have now been reported for almost 2 decades. Early work from Grady and colleagues (1994) first reported age-related differences in patterns of functional brain activity during a perceptual matching task using positron emission tomography. With the advent of functional magnetic resonance imaging, the number of investigations of neurocognitive aging has expanded exponentially and now include studies of numerous cognitive domains (see Spreng et al., 2010). Of these, executive functions have received the most attention. Functional brain imaging studies of executive control processes report robust differences in brain activity between older and younger subjects, particularly under conditions of high executive control demand (e.g., Grady et al., 1998; Jonides et al., 2000; Milham et al., 2002; Nielson et al., 2002; Postle et al., 1999; Reuter-Lorenz et al., 2000). These differences have been replicated across studies (see Park and Reuter-Lorenz, 2009; Reuter-Lorenz and Cappell, 2008 for reviews) and have generated several theoretical accounts of neurocognitive aging in the domain of executive functions.

The most commonly reported age-related pattern of brain activity during executive function tasks (e.g., working memory, inhibition, and task-switching) is increased recruitment of lateral aspects of the prefrontal cortex (PFC) bilaterally (Rypma and D'Esposito, 2000; Jonides et al., 2000; Townsend et al., 2006). These changes may reflect increased PFC modulation of processing operations in posterior cortices in response to noisier (i.e., reduced processing specificity) signaling in these regions (Persson et al.,

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2006). Increased lateral PFC activity may also reflect greater demands for executive control as cognitive operations become less automated with age, resulting in a general "posterior to anterior shift" (PASA) in functional brain activity (Davis et al., 2008) or as neural circuits become increasingly inefficient (compensation-related utilization of neural circuits hypothesis; CRUNCH; Reuter-Lorenz and Cappell, 2008). Recently, this increased demand for frontally-mediated control processes has been characterized as "neural scaffolding" (Park and Reuter-Lorenz, 2009). As age-related structural and functional brain changes, including cortical thinning, white matter changes, and reductions in hippocampal activation, lead to inefficient and/or noisy processing, demands for controlled processing operations are increased. In response, lateral prefrontal brain regions are recruited to provide a "neural scaffold" in support of new learning and sustained behavioral performance, particularly in the context of novel or complex tasks. A similar pattern has been observed in young adults as task challenge is increased requiring new strategy learning (Erickson et al., 2007a and see Hillary et al., 2006 for a review of functional brain changes in healthy young, aging, and neurological populations). While each of these theories argue that functional brain changes, particularly engagement of lateral PFC regions, occurs in normal aging they differ somewhat with respect to the mechanism underlying these changes. The work of Persson and colleagues (Persson et al., 2006) or the PASA account (Davis et al., 2008) suggest that lateral PFC recruitment may represent additional demands for frontally-mediated neuromodulation of posterior neural processing operations. In contrast, the CRUNCH (Reuter-Lorenz and Cappell, 2008) and neural scaffolding hypotheses (Park and Reuter-Lorenz, 2009) suggest that as brain circuits become less efficient with age, additional or alternate neural resources are engaged to compensate for degraded processing operations in both frontal and posterior brain regions. Further discussion of these mechanistic accounts is beyond the scope of the current study (but see Turner and D'Esposito, 2010, for a review). However, it is interesting to note that while each of these accounts converge around the notion of increased recruitment of lateral PFC to support controlled (i.e., executive) processing, to our knowledge, there has been no direct examination of how age-related changes are manifest for specific executive control processes.

It is now well understood that executive functions can be fractionated into dissociable processes both behaviorally (e.g., Miyake et al., 2000; Salthouse et al., 2003; Stuss et al., 1995) and neurally (e.g., Chikazoe, 2010; McNab et al., 2008; Wager and Smith, 2003). This raises the question of whether the age-related patterns of functional brain change described above are similarly dissociable depending upon the executive control process being challenged. The goal of the current report is to review the extant literature, using quantitative meta-analytic methods, to compare age-related differences in the pattern of brain activity between 2 executive processes that have been most frequently studied in the cognitive neuroscience literature: working memory and inhibition (Cabeza and Nyberg, 2000; Wager and Smith, 2003). Neurocognitive aging of task switching, the third executive control process identified by Miyake et al. (2000), remains an understudied domain of executive function and was not included in the current analysis (for exceptions, see: DiGirolamo et al., 2001; Esposito et al., 1999; Townsend et al., 2006). Specifically, we investigate whether age-related patterns of functional brain changes are similar across executive processes or whether changes with aging are specific to the executive process being challenged.

Working memory is a system for actively maintaining and manipulating information that is no longer present in the environment, yet must be organized and retained in the service of current and future goals (Wager and Smith, 2003). In younger subjects, working memory is associated with activation of lateral prefrontal cortical regions, typically left-lateralized (Smith and Jonides, 1998; Wager and Smith, 2003). In older adults, working memory tasks also engage PFC regions, however, neural response is greater and more bilateral at lower levels of task demand than in younger adults (Emery et al., 2008; Jonides et al., 2000; Reuter-Lorenz and Cappell, 2008). This pattern has been hypothesized to reflect poor modulation of prefrontal brain activity in response to increasing working memory demands (Reuter-Lorenz and Cappell, 2008; Schneider-Garces et al., 2010). Cappell and colleagues (Cappell et al., 2010) recently tested this hypothesis in a study of verbal working memory in older and younger adults under high and low load conditions. Consistent with their predictions, older adults overrecruited regions of right lateral PFC at lower working memory loads relative to younger subjects and underrecruited lateral prefrontal cortex regions bilaterally at higher memory loads. Thus age-related increases in lateral PFC during working memory may reflect reduced capacity to modulate this region in response to shifting executive control demands. Here we examine whether this account of age-related functional brain changes generalizes beyond working memory to other domains of executive function such as inhibitory control. To our knowledge this has not been investigated.

Inhibitory control is generally defined as intentional control over dominant, automatic, or prepotent responses and has also been widely studied using brain imaging methods (Chikazoe, 2010). As with working memory, the functional neural correlates of inhibitory control in younger adults have been well characterized for both cognitive and motor inhibition tasks (see Buchsbaum et al., 2005). Critical regions include ventral PFC (Chambers et al., 2009; Leung and Cai, 2007; Swann et al., 2009), presupplementary motor areas (Chen et al., 2009; Floden and Stuss, 2006; Li et al., 2006), as well as posterior parietal cortices, subthalamic nuclei, and cerebellar regions (see Chambers et al., 2009; Chikazoe, 2010 for recent reviews). However, the neural