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The significance of caudate volume for age-related associative memory decline

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ABSTRACT

Aging comes along with reduced gray matter (GM) volume in several cerebral areas and with cognitive performance decline in different cognitive domains. Moreover, regional GM volume is linked to specific cognitive sub processes in older adults. However, it remains unclear which regional changes in older individuals are directly associated with decreased cognitive performance. Moreover, most of the studies on this topic focused on hippocampal and prefrontal brain regions and their relation to memory and executive functioning. Interestingly, there are only a few studies that reported an association between striatal brain volume and cognitive performance. This is insofar surprising that striatal structures are (1) highly affected by age and (2) involved in different neural circuits that serve intact cognition. To address these issues, voxel-based morphometry (VBM) was used to analyze GM volume in 18 younger and 18 older adults. Moreover, several neuropsychological tests from different neuropsychological test batteries were applied to assess a broad range of cognitive domains. Older adults showed less GM volume than younger adults within frontal, striatal, and cerebellar brain regions. In the group of older adults, significant correlations were found between striatal GM volume and memory performance and between prefrontal/temporal GM volume and executive functioning. The only direct overlap between brain regions associated with regional atrophy and cognitive performance in older adults was found for the right caudate: older adults showed reduced caudate volume relative to younger adults. Moreover, caudate volume was positively correlated with associative memory accuracy in older adults and older adults showed poorer performances than younger adults in the respective associative memory task. Taken together, the current findings indicate the relevance of the caudate for associative memory decline in the aging brain.

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1. Introduction

Aging comes along with various structural and functional changes in the brain, like for example changes in brain structure (Kalpouzos et al., 2012; Kennedy and Raz, 2009; Langenecker et al., 2007; Taki et al., 2011) and in neurotransmission (Bäckman et al., 2011; Castner and Goldman-Rakic, 2004; Sarter and Bruno, 2004). Besides, age-related decline in cognitive performance is reported for various cognitive domains (e.g. Park and Reuter-Lorenz, 2009). With regard to structural changes, particularly the loss of gray matter (GM) has been observed in aging individuals (Good et al., 2001). This GM loss is closely associated with cognitive function (He and Wong, 2012). However, the specific relationship between GM volume loss and cognitive decline with advancing age is not truly understood yet. In a recent review examining the brain structure correlates of successful cognitive aging, it is concluded that the findings regarding the structure-cognition relationship are 'inconsistent at best' (Kaup et al., 2011) which implies the claim for further studies on this topic.

1.1. *Structural changes with advancing age*

GM volume loss with advancing age is well supported by previous research. Analyzing the results of 22 voxel-based morphometry (VBM) studies using activation likelihood estimation, for example, revealed age-related GM reductions in several cortical and subcortical brain structures as the prefrontal cortex, the bilateral insula, pre- and post-central gyri, the thalamus, and the caudate (Di et al., 2014). Shrinkage in frontal and striatal areas with age is also supported by other findings (Chee et al., 2009; Raz et al., 2003, 2005; Resnick et al., 2003; Tisserand et al., 2004; Van Petten et al., 2004). Longitudinal results, for example, revealed a very high average shrinkage rate of 0.83% per year for the caudate nucleus, 0.73% for the putamen, and 0.51% for the globus pallidus (Raz et al., 2003). Other studies consistently reported a specific vulnerability of the frontal cortex and showed that frontal GM volume loss particularly manifests in lateral prefrontal and orbitofrontal areas (Chee et al., 2009; Raz et al., 2005; Resnick et al., 2003; Tisserand et al., 2004). For other brain regions, the findings are less consistent. The meta-analysis by Di et al. (2014), for example, suggests relative GM preservation in the bilateral parahippocampal gyrus, the amygdala, specific thalamus nuclei, and the cingulate gyrus, whereas other studies showed a shrinkage of the cingulate gyrus and the hippocampal area with advancing age (Good et al., 2001; Raji et al., 2012; Resnick et al., 2003; Tisserand et al., 2004). Moreover, there are sporadic reports about GM volume loss in the cerebellum, in temporal and parietal areas, as well as in the primary visual cortex (Chee et al., 2009; Good et al., 2001; Raz et al., 2005; Resnick et al., 2003; Van Petten et al., 2004). Taken together, aging particularly seems to be associated with GM volume loss in frontal and subcortical brain regions, whereas other cerebral areas appear to be less affected by age-related structural decline.

1.2. *GM volume and neuropsychological performance in older adults*

Besides structural cerebral changes, aging goes along with alterations in cognitive performance. Different aspects of information-processing, working memory capacity, inhibition, and long-term-memory were found to decline with advancing age, whereas other cognitive domains like implicit or semantic memory are relatively preserved from age-related change (Park and Reuter-Lorenz, 2009). However, the exact relationship between GM volume in older individuals and performance accuracy is not fully understood yet. Reviewing the literature on this relationship resulted in inconsistent findings (Kaup et al., 2011). However, most of the reviewed studies reported positive correlations between regional brain volume and performance accuracy in older adults. Thereby, the clearest associations between GM volume and cognitive performance were found for the frontal cortex and for the hippocampal formation (Kaup et al., 2011).

Lateral frontal and prefrontal cortical GM volume were most frequently examined in relation to executive functioning. Mostly positive correlations were found, but results are not consistent across studies either. For the relationship between orbitofrontal cortex (OFC) volume and attention or working memory performance, the findings are even more heterogeneous and the same applies to the association between frontal brain volume and memory (Kaup et al., 2011), although it is common sense that prefrontal brain areas play an important role for memory retrieval, for example (Fletcher and Henson, 2001). For hippocampal areas, there is much evidence for a positive relation between GM volume and memory performance in older adults (Kaup et al., 2011). Cardenas et al. (2011), for example, reported positive correlations between hippocampal and entorhinal cortex volume and performance accuracy in a delayed verbal recall task, whereas Paul et al. (2011) found a positive correlation between hippocampal volume and semantic memory performance. Moreover, hippocampal volume was attributed to global cognition (Hackert et al., 2002; Tisserand et al., 2004). Longitudinal results even suggest that medial temporal GM is relevant for maintaining overall cognitive function in late life (Rosano et al., 2012). Noteworthy, a positive correlation between hippocampal volume and memory performance was not found in all studies (Sullivan et al., 1995). Interestingly, the review of Kaup et al. (2011) neither revealed an association between lateral temporal GM volume and memory. However, there are a few studies reporting positive correlations between GM volume of bilateral anterior and left superior temporal cortices and semantic memory performance (Cardenas et al., 2011; Taki et al., 2011). Valid assumptions about the relation between regional brain volume and cognitive performance in other brain regions cannot be made since conclusions are based on only a few studies. However, posterior parietal cortex volume was found to be associated with global cognition (Tisserand et al., 2004; Zimmerman et al., 2006).

1.3. *Objectives*

Taken together, the results described above indicate that the current scientific knowledge about the association between GM volume and cognitive performance in older adults is far from complete. Besides quite consistent findings regarding positive correlations between hippocampal GM volume and memory performance and between frontal GM volume and