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Age-related alterations in functional connectivity patterns during working memory encoding of emotional items

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ABSTRACT

Previous findings indicate age-related differences in frontal-amygdala connectivity during emotional processing. However, direct evidence for age differences in brain functional activation and connectivity during emotional processing and concomitant behavioral implications is lacking. In the present study, we examined the impact of aging on the neural signature of selective attention to emotional information during working memory (WM) encoding. Participants completed an emotional WM task in which they were asked to attend to emotional targets and ignore irrelevant distractors. Despite an overall reduction in accuracy for older relative to younger adults, no behavioral age effect was observed as a function of emotional valence. The functional connectivity patterns of left ventrolateral prefrontal cortex showed that younger adults recruited one network for encoding of both positive and negative emotional targets and this network contributed to higher memory accuracy in this cohort. Older adults, on the other hand, engaged two distinct networks for encoding of positive and negative targets. The functional connectivity analysis using left amygdala further demonstrated that older adults recruited one single network during encoding of positive as well as negative targets whereas younger adults recruited this network only for encoding of negative items. The engagement of amygdala functional network also contributed to higher memory performance and faster response times in older adults. Our findings provide novel insights into the differential roles of functional brain networks connected to the medial PFC and amygdala during encoding of emotionally-valenced items with advancing age.

1. Introduction

Aging is characterized by an overall decline in several cognitive domains, including working memory (WM) and episodic memory. Behavioral and neural evidence has suggested that attentional deficits in suppressing task-irrelevant information underlie decline in WM performance with advancing age (Gazzaley and D'Esposito, 2007). However, despite overall age-related cognitive impairment in inhibiting task-irrelevant information, emotional processing is typically well preserved in aging (Reuter-Lorenz and Lustig, 2005). According to one dominant theory, the socioemotional selectivity theory (SST), limited time perception in late adulthood leads to a motivational shift, and subsequent changes in processing of emotional information (Carstensen et al., 1999). Consistent with this account, a number of behavioral studies have demonstrated that older adults show a processing bias for positive, compared to negative information in attention (Allard and Isaacowitz, 2008; Mather and Carstensen, 2003, 2005; Samanez-Larkin et al., 2009), decision making (Lockenhoff and Carstensen, 2007; Löckenhoff and Carstensen, 2004), and memory (Charles et al., 2003; Mather and Knight, 2005; Ziaei et al., 2015). This processing bias is often referred to as the positivity effect (For a review see Reed et al. (2014), Ziaei & Fischer (2016)). It has been argued that the positivity effect relies on top-down attentional control subserved by the prefrontal cortex (Mather, 2012). However, there is limited understanding of the underlying neural correlates involved in the positivity effect.

In addition to behavioral support for the positivity effect in aging, neuroimaging studies have reported changes in activity patterns of regions involved in emotional processing, such as the amygdala and lateral PFC. More specifically, age-related increased recruitment of PFC, along with decreased amygdala activity is the most consistent finding across studies (for reviews see Mather (2012); Nashiro et al.

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(2012)). In addition to regional activation differences, age-related alterations in the functional connectivity between amygdala and PFC regions have been reported. For instance, St Jacques et al. (2010) showed that the functional connectivity between the amygdala and ventral anterior cingulate cortex was greater during evaluation of negative items in older compared to younger adults. Moreover, during the processing of positive relative to negative stimuli, older adults showed a stronger connectivity between medial PFC and retrosplenial cortex when engaged in deep processing (semantic elaboration), whereas younger adults demonstrated the opposite pattern (Ritchey et al., 2011a). The findings of prefrontal - amygdala functional connectivity during processing of emotional items suggest that older adults, more so than their younger counterparts, may engage in regulatory mechanisms, particularly during processing of negative emotions. Given that emotional processes are widely distributed over multiple functionally interacting brain regions (Pessoa, 2008), it is reasonable to suggest that the process of encoding emotional items are supported by large-scale brain networks rather than isolated brain areas. Therefore, understanding the functional brain networks of such highly complex processes will provide insights into how emotional and cognitive operations are affected by increasing age in both healthy and clinical populations. Only a few studies, however, have investigated age-related changes in functional brain connectivity during emotional processing and the results have been inconclusive. The primary aim of this study is to investigate the impact of aging on functional brain network connectivity between PFC and amygdala and the rest of the brain during WM encoding of emotional items.

In order to identify age-related differences in neural activation and functional connectivity patterns associated with selective attention during encoding of emotional items in WM, both univariate and multivariate (spatial-temporal partial-least-squares, PLS) analyses were applied. First, we aimed to investigate age-related differences in behavior and brain activation by instructed attention to emotional targets during WM encoding; second, to examine the functional connectivity pattern between *lateral PFC* and the rest of the brain in response to task-relevant emotional items, and third, to explore the functional connectivity pattern between the *amygdala* and the rest of the brain during instructed attention to task-relevant emotional items.

In order to achieve these aims, we first identified activity patterns associated with instructed attention to emotional target items across age groups using whole-brain univariate statistics. Key regions implicated in selective attention during WM encoding were subsequently used for seed-behavioral PLS to examine whether functional connectivity patterns involved in WM encoding were modulated by emotional valence, if functional connectivity differed between age groups, and whether functional connectivity was related to task performance. Given previous evidence for a positivity effect in older adults, we hypothesized that younger and older adults would show differential recruitment of brain networks in response to positive and negative target items. If younger and older adults show age-invariant functional network engagement from each of the seed regions, results from the seed PLS analysis should reveal a common circuitry with a possibility for quantitative differences. Alternatively, if younger and older adults engage distinct networks that support emotional processing, then results from the seed PLS analysis should reveal separate networks that are differentially connected to the seed regions as a function of emotional valence.

2. Methods and materials

2.1. Participants

Sixteen healthy younger adults and 15 healthy older adults participated in this study. Three younger and two older participants were excluded from the analysis due to extensive movement in the scanner and brain signal losses. Therefore, analyses were conducted on the data from 13 younger adults (9 females; M=22.6, SD=1.69; range=23–26 years) and 13 older adults (9 females; M=68.23, SD=3.7 years; age range=64–74). Younger participants were undergraduate students recruited from Stockholm University and older adults were community volunteers. All participants were right-handed, Swedish speakers, with no history of neurological or psychiatric problems, and had normal or corrected-to-normal vision using MRI compatible glasses. All participants were screened for claustrophobia, neurological and psychiatric medications, and MRI compatibility. Additionally, older adults were screened for cognitive impairments using Mini Mental State Examination (MMSE; Folstein et al. (1975)). All participants took part in two separate test sessions; one for behavioral assessments, and one for the fMRI scanning. Informed consents were obtained from all participants. The investigation was approved by the Ethical Review Board in Stockholm. Participants were paid 800 SEK (~$95 USD) for their participation and were debriefed after they completed the second session.

2.2. Materials

Stimuli consisted of seven hundred eighty six pictures that were drawn from the International Affective Pictures Systems (IAPS; Lang et al., 2008). Based on the IAPS rating system, 312 were rated as negative (valence: M=2.83, SD=1.7, arousal: M=5.54, SD=2.17), 312 as positive (valence: M=6.79, SD=1.73; arousal: M=4.83, SD=2.3), and 162 as neutral (valence: M=4.87, SD=1.26; arousal: M=2.79, SD=2.0). No significant differences were found between the arousal levels of positive and negative pictures ($p > 0.05$). Pictures were presented against a black background using E-prime 2.0 (Psychology Software Tools, Pittsburgh, PA, USA), and were presented at a 600×800-pixel resolution.

2.3. Procedure

The study consisted of two sessions; first a behavioral testing session which took place at the Department of Psychology at Stockholm University, and second, an fMRI session which took place at the MRI facility at the Karolinska hospital on a separate day. Both sessions were conducted within a week. During the behavioral testing session, participants completed the color-word Stroop test (Jensen and Rohwer, 1966), a complex short-term memory tests (operation span; Unsworth et al. (2005), and an emotion regulation questionnaire (Gross and John, 2003). Older adults also completed the MMSE. In addition, practice runs of the emotional WM tasks were performed in preparation for the scanning session. During the second session, and prior to MR scanning, participants were verbally instructed on how to perform the task, and also performed a practice run until they were familiarized with the task.

2.4. Experimental design

2.4.1. Emotional working memory task

A modified version of a visual WM task developed by Gazzaley et al. (2005a) was used to investigate age-related changes in brain networks involved in selective attention to emotional items. Participants first received an instruction to either attend to negative or positive pictures (5 s), while ignoring irrelevant distractors. Then, three sequential screens, each composed of a pair of pictures were presented (2.5 s for each pair separated by a 0.5 s fixation cross). Presentation of all three screens were followed by a fixation cross (maintenance phase; 4 s), and finally a WM probe (retrieval phase; 2 s). Trials were separated by an intertrial interval (ITI) with a variable length (42% ITIs of 1.5 s, 28% ITIs of 3 s, 14% ITIs of 4.5 s, 12% ITIs of 6 s, and 4% ITIs of 7.5 s), allowing for an independent estimation of the BOLD response on a trial-by-trail basis (Huettel et al., 2014).

A full description of the task is provided elsewhere (Ziaei et al.,