Differential effects of age on subcomponents of response inhibition

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ABSTRACT

Inhibitory deficits contribute to cognitive decline in the aging brain. Separating subcomponents of response inhibition may help to resolve contradictions in the existing literature. A total of 49 healthy participants underwent functional magnetic resonance imaging (fMRI) while performing a Go/no-go-, a Simon-, and a Stop-signal task. Regression analyses were conducted to identify correlations of age and activation patterns. Imaging results revealed a differential effect of age on subcomponents of response inhibition. In a simple Go/no-go task (no spatial discrimination), aging was associated with increased activation of the core inhibitory network and parietal areas. In the Simon task, which required spatial discrimination, increased activation in additional inhibitory control regions was present. However, in the Stop-signal task, the most demanding of the three tasks, aging was associated with decreased activation. This suggests that older adults increasingly recruit the inhibitory network and, with increasing load, additional inhibitory regions. However, if inhibitory load exceeds compensatory capacity, performance declines in concert with decreasing activation. Thus, the present findings may refine current theories of cognitive aging.

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1. Introduction

Inhibitory deficit is thought to be one essential cause of cognitive decline in the aging brain by impairing working memory and the ability to restrain impulses (Hasher and Zacks, 1988; Zacks et al., 2000). The decline of inhibitory control in older adults has been shown for several inhibitory tasks, for example the Simon task (Kubo-Kawai and Kawai, 2010; Maylor et al., 2011; van der Lubbe and Verleger, 2002; West and Alain, 2000) or the Stop-signal task (Andrés et al., 2008; Hu et al., 2012; Williams et al., 1999), whereas studies using Go/no-go tasks report both impaired and equal performance, depending on the complexity of the task (e.g. Grandjean and Collette, 2011; Rush et al., 2006; Vallesi and Stuss, 2010). These three tasks may well reflect subcomponents of response inhibition (Barkley, 1997; Eagle et al., 2008; Nigg, 2000; Schachar et al., 2007; Sebastian et al., 2013), that is interference inhibition, withholding of prepotent actions (action withholding), and stopping of already initiated actions (action cancellation) (Fig. 1).

Interference inhibition can be captured by stimulus–response–incompatibility tasks such as the Simon task (Simon, 1969). The Simon task is thought to involve a conflict of response selection by involuntarily co-activating response tendencies due to incompatible stimulus dimensions. This results in longer reaction times (RT) in incompatible trials, as opposed to compatible trials ("interference inhibition"; Simon and Berbaum, 1990). A measure of interference inhibition is thus the difference in RT in incompatible as compared to compatible trials. The ability to withhold a motor response ("action withholding"; Schachar et al., 2007) is usually assessed using a Go/no-go task in which rare no-go-stimuli instead of frequent go-stimuli are presented, requiring inhibition of a prepotent response tendency. A measure of action withholding is the proportion of correctly withheld responses as compared to incorrectly performed reactions in case of a no-go stimulus (commission errors). In a Go/no-go task as well as implicitly in a Simon task the signal to inhibit a reaction is given contiguous with the go-signal. In a Stop-signal task, however, rare stop signals occur at some delay after the go stimuli, thus requiring inhibition of an already ongoing motor response ("action cancelation"; Schachar et al., 2007). Usually, an adaptive paradigm is employed varying the onset of the Stop-signal (Stop-signal delay, SSD) and resulting in a commission error rate of approximately 50%. Hence, commission
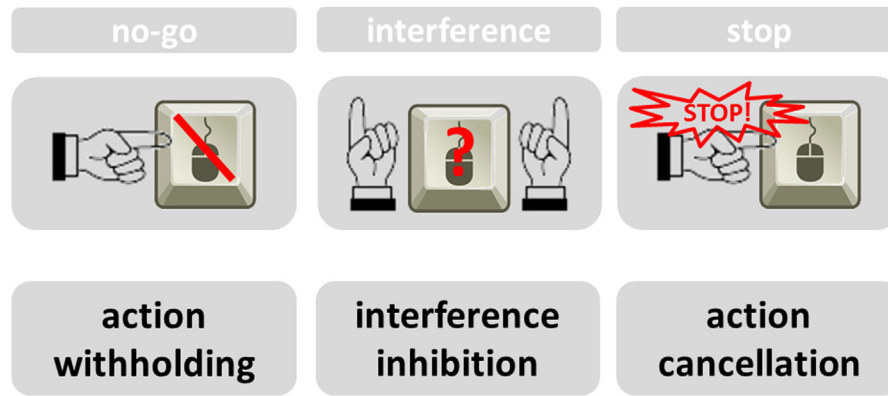
Fig. 1. Schematic display of three subcomponents of response inhibition. Action withholding refers to inhibiting prepotent response tendencies; interference inhibition comprises the suppression of interfering response tendencies, for instance, when being presented with incompatible stimulus dimensions; and action cancellation refers to stopping an ongoing action or response.

error rate cannot be used as a measure of action cancellation. Instead, the Stop-signal reaction time (SSRT) is used, reflecting the latency of the inhibition process. Inhibition latency can be indirectly estimated by subtracting the mean SSD for correctly canceled responses from the RT, according to the race model (Logan et al., 1984).

Simon-, Go/no-go-, and Stop-signal tasks qualitatively differ from each other. Whereas the emphasis of inhibition in the Stop-signal task is motor/response related, the other two tasks involve more sensory/stimulus-related neural activity (Sebastian et al., 2013). Furthermore, the tasks differ in terms of response related complexity. A simple Go/no-go task usually requires a unimanual reaction. However, Simon- and Stop-signal tasks entail two response alternatives and hence usually require bimanual responses. Stimulus/response-related qualitative differences across the tasks may also contribute quantitatively to inhibitory demand. However, increasing the number of choices also increases task demand and thereby inhibitory load. If only one possibility of responding is present, as is the case in a simple Go/no-go task, the participant can prepare the unimanual response more easily than in tasks that require a choice between two or more alternatives. Canceling an ongoing motor program, as is the case in the Stop-signal task, might further increase the inhibitory demand as compared to suppressing motor response tendencies.

Inhibitory control is thought to be executed by a distributed neural core network including the inferior frontal gyrus (IFG), right middle frontal gyrus (MFG), pre-supplementary motor area (pre-SMA), and basal ganglia (e.g., Aron, 2011; Jahfari et al., 2011; Swick et al., 2011; Sebastian et al., 2013). Although this neural core inhibition network should be commonly recruited during response inhibition, cortical regions seem to be differentially activated during the above-mentioned subcomponents.

In a meta-analysis of Go/no-go (action withholding) and Stop-signal tasks (action cancellation) in young healthy participants, Swick et al. (2011) reported a stronger activation of a right-sided fronto-parietal network for Go/no-go tasks compared to a stronger cingulo-opercular activity in Stop-signal tasks. However, Simmonds et al. (2008) could show that fronto-parietal hyperactivation is present in Go/no-go tasks with relatively high working memory demand. Stimulus response interference control as captured, for instance, by the Simon task, is instead associated with contributions to the left prefrontal cortex (PFC) (Nee et al., 2007). Results of Rubia et al. (2006) also pointed toward a stronger activation of the cingulo-opercular network in a Simon task compared to a Go/no-go task. Another study by McNab et al. (2008) also compared a Go/no-go and a Stop-signal task that resulted in stronger bilateral prefrontal activation for the latter. Similarly,

when action cancellation (Stop-signal condition) was directly compared to action withholding (Go/no-go condition) and interference inhibition (Simon condition) within one paradigm, increased bilateral fronto-striatal activation was revealed (Sebastian et al., 2013). These hyperactivations and activations of additional prefrontal, parietal, and insular networks might already be regarded as expanded inhibitory networks that help to achieve better performances by the use of additional inhibitory regions (left PFC), attentional circuits (fronto-parietal network), or regions that control for higher task-set maintenance (cingulo-opercular network) (Dosenbach et al., 2007; Swick et al., 2011). Studying the neural basis of age-related changes in inhibitory circuitries, Dennis and Cabeza (2008) postulated an "expanded inhibition deficit theory" based on Hasher and Zacks (1988). They suggested that a primary deficit in the core inhibition network itself, and thus neuronal activation measured using functional magnetic resonance imaging (fMRI), declines with age, whereas activity in formerly inhibited regions should increase. At the same time, hyperactivation, especially in the contralateral PFC in older adults, may represent compensational recruitment of additional circuits to form an expanded inhibition network. Another approach to explain simultaneous hyper- and hypoactivation in aging is made by the compensation-related utilization of neural circuits hypothesis (CRUNCH) (Reuter-Lorenz and Cappell, 2008) and the scaffolding theory of aging and cognition (STAC) (Park and Reuter-Lorenz, 2009). These theories suggest that, with increased task demands, older adults engage additional brain regions, (e.g. bilateral prefrontal recruitment), whereas younger adults recruit unilateral regions, to compensate for declining neural structures and functions. However, as demands increase, such compensatory effects may break down, leading to deactivation in those regions and declining performance.

A recent meta-analysis by Turner and Spreng (2012) could not support these views concerning the neural dysfunction of inhibitory systems. By using activation likelihood estimation meta-analytic methods across several inhibitory tasks, the authors found age-related hyperactivation during successful inhibition in regions that are particularly associated with inhibitory control, such as right IFG and the pre-SMA, whereas a decline in activation was found in visual cortical areas. Thus, contrary to the prediction of the expanded inhibition deficit theory (Dennis and Cabeza, 2008), these investigators reported increased activation of brain regions correspondingly recruited by young adults and termed it a "young plus" pattern.

Notably, the above-mentioned approaches have not differentiated between subcomponents of response inhibition. However, there is a need of a more precise differentiation (Dalley et al., 2011;