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Contrasting neural effects of aging on proactive and reactive response inhibition

Mirjam Bloemendaal [a,*], Bram Zandbelt [a], Joost Wegman [a], Ondine van de Rest [b], Roshan Cools [a,c], Esther Aarts [a]

[a] Centre for Cognitive Neuroimaging, Donders Institute for Brain, Cognition and Behaviour, Radboud University, Nijmegen, The Netherlands
[b] Division of Human Nutrition, Wageningen University, Wageningen, The Netherlands
[c] Department of Psychiatry, Radboud University Medical Center, Nijmegen, The Netherlands

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ABSTRACT

Two distinct forms of response inhibition may underlie observed deficits in response inhibition in aging. We assessed whether age-related neurocognitive impairments in response inhibition reflect deficient reactive inhibition (outright stopping) or also deficient proactive inhibition (anticipatory response slowing), which might be particularly evident with high information load. We used functional magnetic resonance imaging in young (n = 25, age range 18–32) and older adults (n = 23, 61–74) with a stop-signal task. Relative to young adults, older adults exhibited impaired reactive inhibition (i.e., longer stop-signal reaction time) and increased blood oxygen level-dependent (BOLD) signal for successful versus unsuccessful inhibition in the left frontal cortex and cerebellum. Furthermore, older adults also exhibited impaired proactive slowing, but only as a function of information load. This load-dependent behavioral deficit was accompanied by a failure to increase blood oxygen level-dependent (BOLD) signal under high information load in lateral frontal cortex, presupplementary motor area and striatum. Our findings suggest that inhibitory deficits in older adults are caused both by reduced stopping abilities and by diminished preparation capacity during information overload.

1. Introduction

Older adults can have trouble stopping an action. Indeed, relative to young adults, older adults have been shown to exhibit impaired response inhibition in classic stop-signal paradigms; that is they need more time to stop a response when presented with a stop signal (Bedard et al., 2002; Kramer et al., 1994; van de Laar et al., 2011). At the neural level, older adults are known to exhibit attenuated blood oxygen level-dependent (BOLD) signal as well as reduced tract strength between brain regions involved in response inhibition (Coxon et al., 2012, 2014). However, the processes underlying these age-related behavioral and neural deficits in response inhibition are unclear. Two forms of response inhibition have been distinguished: reactive response inhibition is the process of canceling an ongoing response at the moment this is needed (i.e., outright stopping), whereas proactive response inhibition entails the preparation for stopping when this may become necessary. Experimental designs in previous studies on aging did not enable the separate investigation of reactive and proactive response inhibition. Thus, it remains unclear whether the effects of aging on response inhibition, both neurally and behaviorally, reflect deficient reactive or also altered proactive processing. This issue is particularly pertinent given recent proposals that an understanding of cognitive control deficits in aging requires taking into account dual—reactive and proactive—mechanisms of control (Braver et al., 2007) and evidence indicating deficient proactive but intact reactive control with age (Bugg, 2014; Jimura and Braver, 2010; Paxton et al., 2008).

Cautious response slowing in preparation for the possible upcoming need to stop increases the probability of successful stopping. Older adults might lack the cognitive capacity to process preparatory cues during information overload. Indeed, there is clear evidence for (load-dependent) reductions in working memory capacity due to deficits in prefrontal cortex functioning (Gazzaley et al., 2005; Nagel et al., 2009; Nyberg et al., 2010). By analogy, work with patients with schizophrenia has demonstrated an association between poor proactive response inhibition and low working memory capacity as well as reduced BOLD responses in frontal cortex (Zandbelt et al., 2011). Here, we investigated whether

* Corresponding author at: Centre for Cognitive Neuroimaging, Donders Institute for Brain, Behaviour and Cognition, Radboud University, Kapittelweg 29, 6525EN Nijmegen, The Netherlands. Tel.: +31 644 830 194; fax: +31 (0)24 36 10989.
E-mail address: mirjambloemendaal@gmail.com (M. Bloemendaal).

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diminished response inhibition in older adults is accompanied by altered behavioral and neural preparation for inhibition and whether this is particularly evident in situations of information overload.

To address these questions, young and older adults were scanned using event-related functional magnetic resonance imaging (fMRI) during the performance of an adapted version of a stop-signal task that allowed us to disentangle proactive and reactive response inhibition (Zandbelt and Vink., 2010). To assess whether response inhibition in aging varies as a function of information load, we manipulated the information processing demands required for interpreting the stop-signal probability cues.

A simple go task required a button press on every trial, unless a stop signal appeared indicating that the initiated button press had to be canceled. A measure of reactive response inhibition was obtained based on the race model (Logan and Cowan, 1984) by calculating the time needed to cancel an initiated response (i.e., the stop-signal reaction time [SSRT]). In addition, proactive slowing was indexed by the degree of preparatory response slowing of reaction times in response to cues signaling stop-signal probability (Chikazoe et al., 2009; Jahfari et al., 2010; Verbruggen and Logan, 2009c; Vink et al., 2005; Zandbelt and Vink, 2010). This stop-signal probability was manipulated parametrically, so that higher stop-signal likelihood would elicit greater proactive slowing. Critically, we also manipulated the information processing demands for interpreting these stop-signal probability cues, thus allowing us to assess our key hypothesis that besides behavioral and neural impairments during reactive response inhibition (as previously discussed), aging is accompanied also by deficits in proactive inhibition and associated prefrontal cortex signaling. Specifically, the effect of aging on proactive inhibition may vary as a function of information load because increased information load places greater weight on prefrontal resources that are vulnerable to aging.

2. Methods

2.1. Participants

Forty-eight participants were included in the analyses: 25 young (mean age: 22.7 years, range 18–29, 14 men) and 23 older adults (mean age: 67.6 years, range 61–74, 14 men). Participants met the following inclusion criteria: normal or corrected-to-normal vision, right handed, functioning within normal limits of general cognitive function with the mini-mental state examination (Folstein et al., 1975) (cutoff > 27 of 30), estimated verbal intelligence quotient (IQ) >85 (Schmand et al., 1991), no neurological or psychiatric disorders, no contraindications for MRI, and no use of psychotropic medication or medication influencing the BOLD signal, such as blood pressure–normalizing medication. Fifty-six participants were initially tested; 8 participants were excluded, of which 4 young and 4 older adults. Five participants were excluded before statistical data analysis: 2 due to technical problems (1 young and 1 older) and 3 participants (2 young and 1 older) were excluded due to excessive head movement (>4 mm translation). On data analysis of the behavioral effects, 3 participants were excluded due to task noncompliance (see in the following section) (1 young, 2 older). The experiment was approved by the local ethics committee (CMO 2001/095), and all participants gave written informed consent. Participants were matched on verbal IQ, Hospital Anxiety and Depression Scale (HADS) (Bjelland et al., 2002), and gender (Table 1). Participants also completed the Barratt Impulsiveness Scale (BIS-11; Patton et al., 1995), immediate and delayed story recall (Wilson et al., 1985), digit span forward and backward (Wechsler, 1997), Stroop cards (Stroop, 1935), and verbal fluency (Tombaugh et al., 1999).

2.2. Experimental design: load-dependent stop-signal anticipation task

Participants performed a stop-signal anticipation task with blocks differing in information load. The paradigm was based on the stop-signal anticipation task (Zandbelt and Vink, 2010), which involved a modification of the classic stop-signal task (Verbruggen and Logan, 2008).

The paradigm consisted of Go trials and Stop trials. On every trial, a bar moved at a constant speed from a lower horizontal line toward an upper horizontal line, reaching a middle line (flanked by 2 vertical lines) in 800 ms. The horizontal and vertical lines were continuously present throughout the task (Fig. 1). The main Go task was to bring the bar to a halt as close to the middle line as possible, by pressing a button with the right thumb. A minority of trials were Stop trials. On these trials a stop signal appeared: the bar stopped moving automatically before reaching the middle line. This stop signal instructed the participants to withhold the planned Go response. The middle horizontal line and the 2 vertical lines represented cues that indicated stop-signal probability context by varying in color (see caption of Fig. 1). To manipulate information

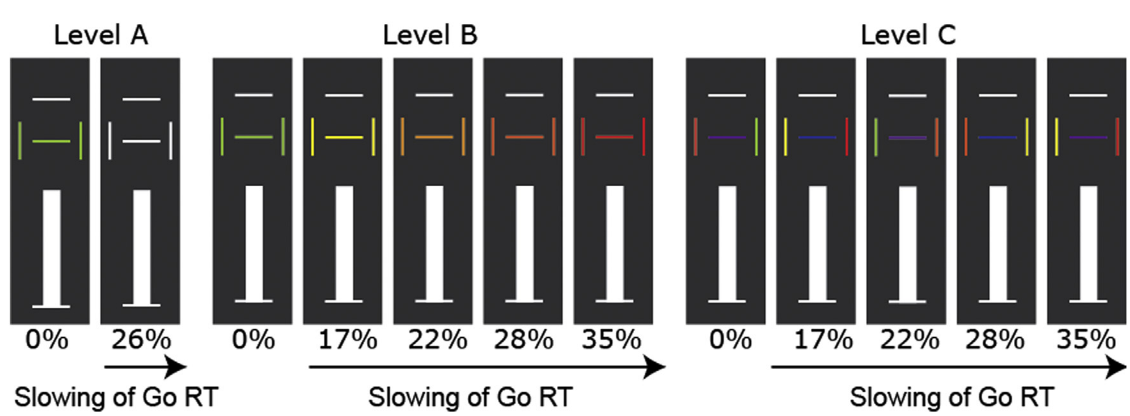

Fig. 1. Load-Dependent Stop-Signal Anticipation Task. Information load increased with level. Percentages reflect the probability a trial will be a Stop trial rather than a Go trial. For level B and C, stop-signal probability increased as a function of cue color. Every level contained 70 trials with 0% (green) and 270 trials with >0% (white) stop-signal probability. Of these 270 >0% trials, 70 were Stop trials, with a mean stop-signal probability of 26%. For Level B and C, each >0% trial type contained 50 Go trials, plus a varying amount of Stop trials per color resulting in varying stop-signal probabilities (in between brackets): 10 yellow (17%), 14 amber (22%), 19 orange (28%), and 27 red (35%). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)