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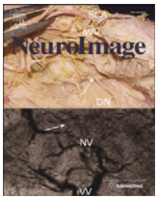

Age-related variability in performance of a motor action selection task is related to differences in brain function and structure among older adults

Jill Campbell Stewart, Xuan Tran, Steven C. Cramer *

Departments of Neurology and Anatomy & Neurobiology, University of California, Irvine, USA

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Task performance for behaviors that engage motor cognitive processes may be particularly sensitive to age-related changes. One well-studied model of cognitive motor function involves engagement of action selection (AS) processes. In young adults, task conditions that add AS demands result in increased preparation times and greater engagement of bilateral dorsal premotor (PMd) and parietal cortices. The current study investigated the behavioral and neural response to a change in motor cognitive demands in older adults through the addition of AS to a movement task. Sixteen older adults made a joystick movement under two conditions during functional magnetic resonance imaging. In the AS condition, participants moved right or left based on an abstract rule; in the execution only (EO) condition, participants moved in the same direction on every trial. Across participants, the AS condition, as compared to the EO condition, was associated with longer reaction time and increased activation of left inferior parietal lobule. Variability in behavioral response to the AS task between participants related to differences in brain function and structure. Overall, individuals with poorer AS task performance showed greater activation in left PMd and dorsolateral prefrontal cortex and decreased structural integrity of white matter tracts that connect sensorimotor, frontal, and parietal regions—key regions for AS task performance. Additionally, two distinct patterns of functional connectivity were found. Participants with a pattern of decreased primary motor–PMd connectivity in response to the AS condition, compared to those with a pattern of increased connectivity, were older and had poorer behavioral performance. These neural changes in response to increased motor cognitive demands may be a marker for age-related changes in the motor system and have an impact on the learning of novel, complex motor skills in older adults.

Introduction

The performance of skilled motor actions declines with age, which has direct implications for the performance of everyday functional activities (Seidler et al., 2010). Older adults tend to move more slowly than younger adults with decreased coordination and less smoothness (Cooke et al., 1989; Ketcham et al., 2002; Poston et al., 2009; Seidler et al., 2002). This decline in motor skill performance with age corresponds to changes in the peripheral and central neural structures that support movement (Seidler et al., 2010; Ward, 2006). Often cited changes in brain activation for the performance of motor skills in older individuals include an overall increase in the magnitude of brain activation compared to young adults and an increase in recruitment of brain regions ipsilateral to the side of movement (Heuninckx et al., 2008; Mattay et al., 2002; Noble et al., 2011; Ward et al., 2008). These changes in brain activation during the performance of motor tasks with age may reflect neural compensation in order to maintain performance level or age-related pathological changes that correspond to performance decline (Cabeza et al., 2002; Cappell et al., 2010; Mattay et al., 2006).

Interaction of the motor and cognitive systems is thought to increase with age (Li and Lindenberger, 2002). Experimental tasks that systematically increase motor cognitive demands may provide insights into the behavioral and neural consequences of aging on the motor system that are not apparent when only simple tasks are performed (Heuninckx et al., 2005; Ward et al., 2008). Therefore, when investigating the effect of aging on the motor system, tasks that are more cognitively demanding offer a unique opportunity to determine age-related changes. One well-studied model of cognitive motor function in young adults involves adding action selection demands to movement. Task conditions that require action selection (AS) based on an abstract, visual-based rule lead to longer preparation time compared with simple motor execution tasks with a corresponding increase in activation of bilateral dorsal premotor (PMd) and bilateral parietal cortices in young adults (Grafton et al., 1998a; Grol et al., 2006; O'Shea et al., 2007a; Toni et al., 2002). Left PMd has been suggested as a key resource for motor AS; when activity in left PMd is disrupted, AS performance degrades (Johansen-Berg et al., 2002; O'Shea et al., 2007a; Rushworth et al., 2003). However, the neural correlates of AS and the role of PMd for AS in older adults have not been reported.

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* Corresponding author at: University of California, Irvine Medical Center, 101 The City Drive South, Building 53, Room 203, Orange, CA 92868-4280, USA. Fax: +1 714 456 8805.
E-mail address: scramer@uci.edu (S.C. Cramer).

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The aging process varies between individuals. It has been proposed that neurophysiological measures of aging may better reflect age-related changes in the motor system than chronological age (Talelli et al., 2008). In young adults, variability in the functional and structural connectivity between PMd and primary motor cortex (M1) has been shown to correlate with motor AS task performance between individuals (Boorman et al., 2007; O'Shea et al., 2007b); greater connectivity between these regions correlated with faster reaction times. Currently, however, it is not known how variability in AS task performance between individuals relates to brain function and structure in older adults. Understanding the neural correlates of age-related changes in AS task performance may provide insight into variability in the aging process, as well as in disease expression for conditions that affect the elderly such as stroke.

The purpose of this study was to determine the behavioral and neural response to a change in motor cognitive demands through the addition of AS to a movement task in older adults. Functional magnetic resonance imaging (fMRI) during task performance was used to quantify brain function, and diffusion tensor imaging (DTI) was used to quantify white matter structure. We hypothesized that individuals would show a significant increase in planning time that corresponded to an increase in bilateral PMd and parietal cortex activation for AS compared to simple movement execution, similar to previous research in young adults (Grafton et al., 1998a; Grol et al., 2006; O'Shea et al., 2007a; Toni et al., 2002). We also hypothesized that variability in AS task performance between individuals would correlate with differences in brain function and structure, specifically within PMd. Since AS task performance could have had a positive or negative correlation with PMd activation, this behavior–brain function hypothesis was two-tailed. Finally, we hypothesized that white matter structure in PMd and motor regions would negatively correlate with AS task performance such that individuals with better task performance would have greater white matter integrity in these regions.

Materials and methods

Participants

Sixteen older adults (mean age ± standard deviation: 65 ± 9 years, range 48–77; 10 females) were recruited from the surrounding community. Participants had to be between the ages of 45 and 80 years of age and right-hand dominant (Oldfield, 1971). Potential participants were excluded if they had a Mini-Mental State Exam (Folstein et al., 1975) score less than 26, history of any neurologic diagnosis that affected movement of the arms, or contraindication to magnetic resonance imaging (MRI) (Kleim et al., 2007). All participants provided informed consent on a form approved by the university institutional review board.

Motor task

All participants performed the motor task with the dominant, right hand. The task involved right or left movement of a standard joystick based on a visual cue in two different conditions. In the action selection (AS) condition, the individual moved right or left based on an abstract rule (Fig. 1). When a small square or large circle was shown, a joystick movement to the right was made; when a large square or small circle was shown, a joystick movement to the left was made. Small cues were 50 × 50 pixels in size while the large cues were 200 × 200 pixels. In the execution only (EO) condition, the visual cues were the same, however, the participant made a joystick movement in the same direction on every trial irrespective of the size/shape of the cue. Movement direction for EO was counterbalanced across participants. In both conditions, a single cue was presented for 2 s in a pseudorandom order such that each cue was presented six times in each block (36 trials per block). The inter-trial interval varied between 2.0 and 3.25 s to minimize anticipatory responses prior to the cue.

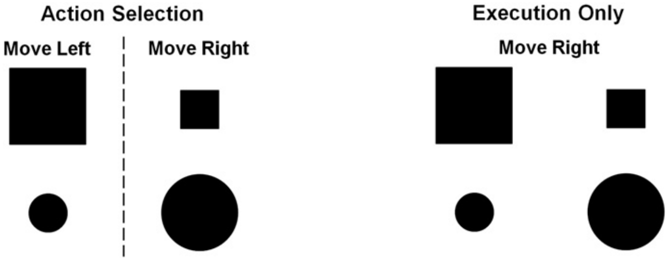

Fig. 1. Participants moved the joystick under two experimental conditions. During *action selection*, movement direction was dictated by an abstract rule (large square or small circle = move left; small square or large circle = move right). During *execution only*, movement direction was the same on every trial regardless of visual cue. Movement direction (right/left) for execution only was counterbalanced across participants.

Prior to MRI, a training session in the laboratory was completed to ensure understanding of both task conditions. First, verbal and visual instruction on the AS condition was provided followed by a practice block of the AS condition. Three blocks of each condition were then completed in alternating order; the condition completed in the first block (AS/EO) was counterbalanced across participants. After completion of the training blocks, the participant practiced the MRI version of the task. This version alternated periods of movement (cues were green) with periods of view only (cues were red) in a block design (see below) and included a total of 10 movement trials (5 trials per movement epoch).

Brain imaging

All brain imaging sessions were performed on a 3 T Achieva MRI scanner (Phillips Medical System, Best, The Netherlands). Functional MRI data were acquired using a block design while the participants performed the AS and EO tasks with an MRI compatible joystick (Current Designs, Philadelphia, PA). Periods of movement (Move, 24 s) alternated with periods of view only (View, 24 s) with a fixation period (red cross, 8 s) between each epoch. Cue duration (2 s) and the inter-trial interval (varied between 2.0 and 3.5 s) were the same as during practice in the laboratory. Just prior to entering the scanner, the movement rule for the AS condition was reviewed; no additional reminders of the rule were provided during scanning. Each participant completed four fMRI runs, two in the AS condition and two in the EO condition in alternating order; the condition completed in the first run (AS/EO) was counterbalanced across participants. Functional runs lasted for 2 min 10 s during which 65 brain volumes were acquired (TR = 2000 ms, TE = 30 ms); each volume included 31 slices that were 4 mm thick with a slice gap of 1 mm (acquisition voxel size 2.5 mm × 2.5 mm × 4 mm). Next, a high resolution structural MPRAGE image was acquired (TR = 8400 ms, TE = 3.9 ms) which included 150, 1 mm thick slices with no interslice gap (acquisition voxel size 1 mm × 1 mm × 1 mm). Finally, DTI images were obtained using echo planar imaging (EPI) (TR = 11,190 ms, TE = 69 ms) and included 60, 2 mm thick slices with no interslice gap (acquisition voxel size 2 mm × 2 mm × 2 mm). Diffusion images included 32 noncollinear directions with a b value of 800 s/mm^2 and a single volume with no diffusion weighting ($b = 0$). Total scan time for each session was approximately 45 min.

Data analysis

Behavioral data

Data from the joystick were used to determine task accuracy, reaction time (RT), and movement time using a custom script in Matlab (Matworks, Inc., Natick, MA). Position data (x,y) were recorded throughout each trial (60 Hz in the laboratory, 30 Hz in