

Failure to Engage Spatial Working Memory Contributes to Age-related Declines in Visuomotor Learning

Joaquin A. Anguera^{1*}, Patricia A. Reuter-Lorenz¹,
Daniel T. Willingham², and Rachael D. Seidler¹

Abstract

■ It is well documented that both cognitive and motor learning abilities decline with normative aging. Given that cognitive processes such as working memory are engaged during the early stages of motor learning [Anguera, J., Reuter-Lorenz, P., Willingham, D., & Seidler, R. Contributions of spatial working memory to visuomotor learning. *Journal of Cognitive Neuroscience*, 22(9), 1917–1930, 2010], age-related declines in motor learning may be due in part to reductions in cognitive ability. The present study examined whether age-related declines in spatial working memory (SWM) contribute to deficits in visuomotor adaptation. Young and older adult participants performed a visuomotor adaptation task that involved adapting manual aiming movements to a 30° rotation of the visual feedback display as well as an SWM task in an fMRI scanner. Young adults showed a steeper learning

curve than older adults during the early adaptation period. The rate of early adaptation was correlated with SWM performance for the young, but not older, adults. Both groups showed similar brain activation patterns for the SWM task, including engagement of the right dorsolateral prefrontal cortex and bilateral inferior parietal lobules. However, when the SWM activation was used as a limiting mask, younger adults showed neural activation that overlapped with the early adaptation period, whereas older adults did not. A partial correlation controlling for age revealed that the rate of early adaptation correlated with the amount of activation at the right dorsolateral prefrontal cortex. These findings suggest that a failure to effectively engage SWM processes during learning contributes to age-related deficits in visuomotor adaptation. ■

INTRODUCTION

Older adults exhibit numerous motor performance declines, including a reduced rate of acquiring new motor skills in comparison with young adults (Seidler, 2006; Rodrigue, Kennedy, & Raz, 2005; Raz, Williamson, Gunning-Dixon, Head, & Acker, 2000). Visuomotor adaptation is one type of motor learning that has been used extensively to examine how humans represent and interact with their environment. Visuomotor adaptation involves the modification of a well-learned sensorimotor transformation and tests the ability to adapt motor performance in response to environmental changes. Studies investigating the effect of age on visuomotor adaptation have reported age-related impairments (Seidler, 2006; Bock, 2005; Teulings, Contreras-Vidal, Stelmach, & Adler, 2002; Fernandez-Ruiz, Hall, Vergara, & Diiiaz, 2000; McNay & Willingham, 1998; alternatively, see Roller, Cohen, Kimball, & Bloomberg, 2002; Canavan et al., 1990). However, the cause of these deficits is unclear because age-related declines in motor (Galea, 1996; Booth, Weeden, & Tseng, 1994; Galganski, Fuglevand, & Enoka,

1993), sensory (Baltes & Lindenberger, 1997; Demer, 1994; Lindenberger & Baltes, 1994), or cognitive functions (Park et al., 2002) could contribute to these differences.

Our recent work (Anguera, Reuter-Lorenz, Willingham, & Seidler, 2010) and that of others (Taylor & Thoroughman, 2007, 2008; Eversheim & Bock, 2001) have documented that cognitive processes play a specific role during the early phase of visuomotor adaptation. With behavioral measures, we found that rate of adaptation in the early learning phase is correlated with spatial working memory (SWM) performance in young adults. With neuroimaging, we found overlapping activation in the right dorsolateral prefrontal cortex (DLPFC) and bilateral inferior parietal lobules (IPL) during SWM performance and the early phase of visuomotor adaptation. We propose that SWM contributes to adaptation—motor error information loaded into SWM may be used to update the mapping between visual and motor space. This proposal suggests that age-related declines in SWM may contribute to deficits in visuomotor adaptation.

Age-related deficits in SWM have been well characterized in the cognitive aging literature (Park et al., 2002; Jenkins, Myerson, Hale, & Fry, 1999; Myerson, Hale, Rhee, & Jenkins, 1999). These and other studies have illustrated an inverse relationship between age and general spatial ability (Kirasic, 2000), including tasks involving mental rotation (Dobson, Kirasic, & Allen, 1995; Salthouse, 1994; Hertzog, Vernon, &

¹University of Michigan, ²University of Virginia

*Present address: Department of Neurology and Keck Center for Integrative Neurosciences, University of California, San Francisco.

Rypma, 1993; Salthouse & Mitchell, 1989). These deficits have been explained in part by neuroimaging studies showing the highest degree of age-related atrophy occurs at the right pFC (Tisserand et al., 2004; Raz et al., 2000), a region engaged during performance of SWM tasks (Milivojevic, Hamm, & Corballis, 2008; Suchan, Botko, Gizewski, Forsting, & Daum, 2006; Walter et al., 2003; Reuter-Lorenz et al., 2000; Courtney, Petit, Maisog, Ungerleider, & Haxby, 1998; Jonides et al., 1993). Given that young adults engage this region during both the early stages of visuomotor adaptation and an SWM task (Anguera et al., 2010), it may be that age differences in functional recruitment of the pFC (D'Esposito, Deouell, & Gazzaley, 2003) provide at least a partial explanation for age-related declines in visuomotor adaptation.

In the present study, the effect of age-related SWM declines on visuomotor adaptation was tested by having young and older adults perform both an SWM task involving mental rotation and a joystick-controlled visuomotor adaptation task while lying prone in an MRI scanner. The visuomotor adaptation task required manual aiming movements to targets under veridical and rotated visual feedback. Participants also performed a battery of neuropsychological and health assessments. We tested the hypothesis that age-related declines in SWM contribute to deficits in visuomotor adaptation for older adults, especially at the early stages of adaptation. Accordingly, we predicted that older adults would lack the behavioral correlations and neural overlap between the SWM and the visuomotor adaptation tasks found in younger adults (Anguera et al., 2010).

METHODS

Participants

Eighteen older (71.4 ± 4.2 years, 9 men) and 18 young adult participants (21.1 ± 2.5 years, 9 men; young adult data were presented in Anguera et al., 2010) were recruited from the community and were paid for their participation. Each participant signed an informed consent document approved by the international review board and filled out a health history questionnaire before their participation. All participants were right-handed as assessed using the 20-item version of the Edinburgh Inventory (Oldfield, 1971; older adult mean handedness score = 0.93 ± 0.05 ; young adult score = 0.83 ± 0.10).

Experimental Setup and Procedures— Neuropsychological Tests

There were two separate days of testing for this experiment. On Day 1, participants completed a series of questionnaires providing an assessment of their cognitive status. Older adults were administered the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh,

1975) and the Mattis dementia rating scale (Mattis, 1988) to potentially exclude participants exhibiting signs of dementia and to confirm that the older adult participants were representative of their age group. A minimum MMSE score of 27 and a Mattis score of 123 were required for participation. Older adults were also given a health history questionnaire as well as the CHAMPS physical activity questionnaire (Stewart et al., 2001) to better quantify each participant's daily activities and general health status. Finally, the DEX questionnaire (dysexecutive syndrome; Wilson, Alderman, Burgess, Emslie, & Evans, 1996) was administered to all participants to determine whether individuals had difficulty with abstract thinking, planning, or other tasks associated with executive functioning.

Participants also performed a battery of neuropsychological tests to assess specific cognitive processes: (1) mental rotation and spatial relation abilities were tested using Thurston's card rotation (two-dimensional) and cube rotation (three-dimensional) tasks (Ekstrom, French, & Harman, 1976); (2) serial short-term visuospatial memory was assessed by the forward Corsi Block tapping test (Corsi, 1972); (3) sensorimotor processing speed was determined by the digit-symbol substitution task from the Wechsler Adult Intelligence Scale—Revised (WAIS-R); (4) short-term verbal memory was evaluated by the forward digit span tasks from WAIS-R (Wechsler, 1997) and the reading span task (Daneman & Carpenter, 1980); and (5) verbal working memory was assessed by the backward digit span task from WAIS-R (Wechsler, 1997), whereas serial visuospatial working memory was assessed through the backward Corsi Block tapping task (Corsi, 1972). By defining SWM here through the involvement of both on-line maintenance and the active manipulation of information (Miyake & Shah, 1999; Baddeley, 1986), SWM resources would only be engaged within the mental rotation tasks and backward Corsi block task. Participants also practiced three blocks of joystick aiming movements made under veridical feedback conditions as well as one block of the SWM control (SWMc) task (detailed below) to familiarize them with basic task requirements before subsequent testing in the fMRI scanner.

The second day of testing was completed within 1 week of the first testing day. During the second testing session, participants performed the visuomotor adaptation task, the SWMc, and the SWM task that involved mental rotation. For these tasks, participants lay supine in a 3.0-T magnet (General Electric, Milwaukee, WI) with their head comfortably restrained to prevent excess head movement. Task presentation and response collection were accomplished with custom Labview 6.1 software (National Instruments, Austin, TX) for the visuomotor adaptation task and E-prime 1.1 software for the SWM tasks (Psychology Software Tools, Pittsburgh, PA). Stimuli were presented through a mirror mounted on a set of specialized goggles, reflecting a video projection screen placed at the rear of the scanner. E-prime recorded participants' responses ("matching" = thumb press, "different" = index finger) via a right-handed button glove.

Experimental Setup and Procedures—SWM Task

The SWM task, modeled after the task employed by Reuter-Lorenz et al. (2000) and recently used by Anguera et al. (2010), required participants to memorize a three-target set (three solid circles) in a 500-msec period (Figure 1). Following presentation of the target set, participants saw a blank screen for 3000 msec (retention interval, RI). During this period, they were instructed to mentally “connect the dots” of the target set and then mentally rotate this shape by 30° clockwise. Following the RI, participants were given 3000 msec to decide whether the subsequently presented probe set of open circles formed the same configuration as the target set that they had mentally rotated. There was a 30-sec visual fixation baseline period before and after each set of 10 trials. Participants performed two runs of this task, with 30 trials within each run. Seventy percent of the trials were “match” trials in which the probe set was rotated 30° clockwise; the remaining “nonmatch” trials had two of the three probe circles displaced by 1.1 cm (hard), 1.5 cm (medium), and 1.9 cm (easy) from the original target dot configuration.

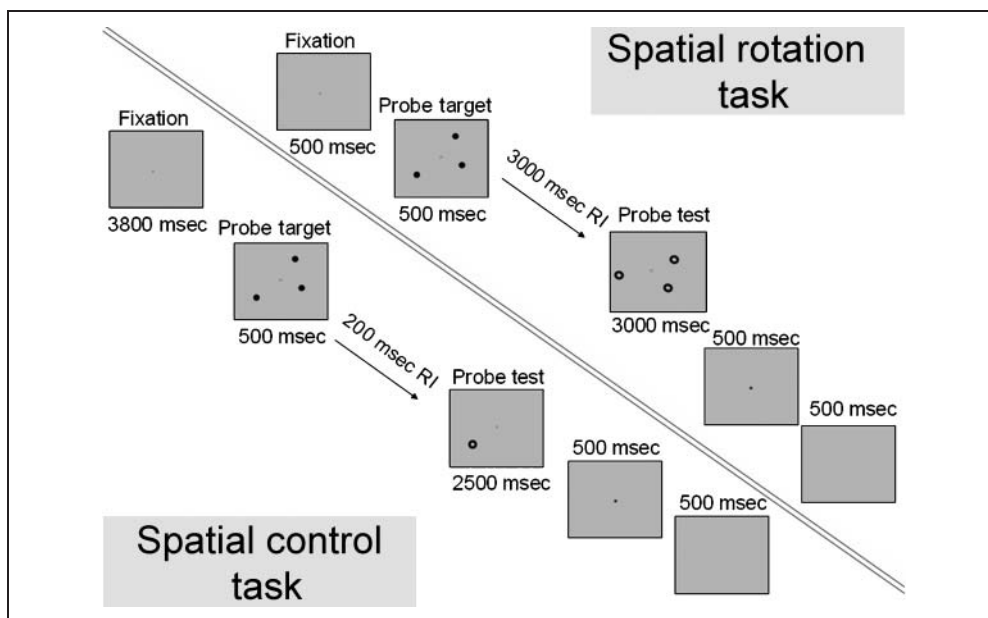
Participants also performed an SWMc task (1 block of 40 trials; see Figure 1) modeled after the control task used by Anguera et al. (2010) and Reuter-Lorenz et al. (2000). In following this methodology, fixation time was 500 msec for the rotation task and 3800 msec for the control task. The differing fixation time and probe periods were used for the working memory and control tasks to maintain the same overall trial duration for both (8000 msec). This is important because having participants make a motor response at a different rate for each task would have confounded the activation patterns. This shortened RI, in theory, requires immediate matching without providing sufficient time to engage working memory processes.

The control task involved the presentation of three solid circles for 500 msec, followed by a 200-msec RI, followed by the presentation of a single circle for 2500 msec. At this point, participants were asked to determine whether its spatial location matched that of a previously observed dot. This control task included all of the cognitive components of the SWM task (e.g., perceptual encoding, response selection, preparation, and initiation) except for the working memory and mental rotation components. Thus, the subtraction of images from the control condition should reveal areas actively involved with SWM and mental rotation (Anguera et al., 2010; Reuter-Lorenz et al., 2000).

Experimental Setup and Procedures—Visuomotor Adaptation Task

For the visuomotor adaptation task, targets (0.8 cm in diameter) appeared for 4 sec in one of four locations: 4.8 cm to the right, left, above, or below the centrally located home position (0.8 cm in diameter). Participants controlled a cursor with a dual potentiometer joystick placed on their lap. Participants held the joystick with their thumb and index finger and made small wrist and finger movements to control the joystick, with real-time feedback displayed as a cursor on the projection screen. Participants were asked to move the cursor into the target circle as quickly and as accurately as possible and to maintain the cursor within the circle until the target disappeared. Participants performed 13 blocks (B) as separate fMRI runs of the task (24 trials per block), with 30-sec visual fixation baseline periods at the beginning and end of each block. An initial practice block (P) performed in the scanner was not included in the analysis. The first experimental

Figure 1. Spatial rotation (SWM) and spatial control (SWMc) tasks schematic. RI = retention interval.



block (B1) was performed under normal visual feedback conditions (control condition), whereas the subsequent 11 blocks (B2–B12; adaptation period) were performed with visual feedback rotated 30° clockwise about the center of the screen.

fMRI Acquisition Parameters

Functional images were acquired using a single-shot gradient-echo reverse spiral pulse sequence (Bornert, Aldefeld, & Eggers, 2000). The field of view was 220 × 220 mm, voxel size was 3.2 × 3.2 × 3.2 mm, repetition time to accomplish a full volume was 2 sec, and echo time was 30 msec. Forty contiguous axial slices were acquired at a slightly oblique angle, encompassing the whole brain, including the cerebellum. Structural images were acquired using a T1-weighted gradient-echo pulse sequence (echo time/repetition time/flip angle = 3 msec/250 msec/25°, with a field of view of 240 × 240 mm, voxel size = 1.4 × 1.4 × 3.2 mm).

Behavioral Data Processing

For both the SWMc and the SWM task, the response time and the percentage of correct responses were calculated. For the adaptation task, the x and y coordinates from the joystick were recorded at a rate of 100 Hz. These data were analyzed off-line using custom Labview 6.1 software (National Instruments) to track behavioral changes with learning. The data were first filtered with a dual low-pass Butterworth digital filter (cf. Winter, 1990), using a cutoff frequency of 10 Hz. The resultant joystick path was calculated by computing the square root of the sum of the squared x and y coordinate data at each time point. The tangential velocity profile was then calculated through differentiation of the resultant position data. Movement onset and offset were computed through the application of Teasdale, Bard, Fleury, Young, and Proteau's (1993) optimal algorithm to the velocity profile for each movement. Learning was assessed by measuring direction error (DE), which is the angle between a straight line from the start to the target position and the position at peak velocity.

The first three and the final three adaptation blocks were designated as the early and late learning periods, respectively (Anguera et al., 2010). A Group × Block × Trial mixed model ANOVA was performed on DE to test for differences across blocks and trials, with significant interactions followed up with simple contrasts. The Huynh-Feldt epsilon (Huynh & Feldt, 1970) was evaluated to determine whether the repeated measures data met the assumption of sphericity ($\Sigma > 0.75$). Pearson correlations were also computed between the rate of learning for each adaptation period with performance on the SWM task, measures of health, and performance on each of the neuropsychological tests.

fMRI Data Processing

The first three volumes of each run were discarded to allow the MRI signal to reach its steady state. Head motion correction was performed using the Automated Image Registration package (Woods, Grafton, Holmes, Cherry, & Mazziotta, 1998). Structural images were skull stripped using FSL's Brain Extraction Tool (<http://www.fmrib.ox.ac.uk/fsl>). fMRI data were processed and analyzed using Statistical Parametric Mapping 2 (SPM2; Wellcome Department of Cognitive Neurology, London, UK). Following the computation of a mean functional image for each participant, their structural image was coregistered to this mean image and then spatially normalized to the Montreal Neurological Institute template (Evans, Kamber, Collins, & Macdonald, 1994). These images were then spatially smoothed with a Gaussian kernel with an FWHM of 8 mm. In addition, head movement parameters were added as covariates of no interest to correct for potential confounding effects induced by head movement.

Boxcar models time locked to the effect of interest were created and convolved with an estimate of the canonical hemodynamic response function. Analyses were performed at the single participant and group levels through SPM2 to determine regions activated in association with task performance. Significant areas of activation were then localized using the automated anatomical atlas (Tzourio-Mazoyer et al., 2002) and confirmed with the Talairach atlas (Talairach & Tournoux, 1988) and visual inspection. Medial motor areas were identified as in Mayka, Corcos, Leurgans, and Vaillancourt (2006) and Picard and Strick (1996) and cerebellar regions as in Schmahmann et al. (1999).

fMRI Contrasts and ROI Analyses

Different contrasts were designed to examine the visuo-motor adaptation task and the SWM task. The SWM contrast searched for regions of statistically greater activation for the two SWM blocks in comparison with the SWMc block. The first adaptation contrast (*early adaptation*) searched for regions of statistically greater activation across the first three adaptation blocks (defined as the early learning phase by the breakpoint analysis) versus the first control block (B1). The second adaptation contrast evaluated the late adaptation period using the final three adaptation blocks (*late adaptation*) versus B1.

We used an uncorrected threshold of p value $\leq .005$ and cluster magnitude ≥ 10 voxels for two reasons: (i) this threshold matches that used by Anguera et al. (2010) and allows for a parallel comparison between the two studies, and (ii) use of this threshold may allow us to avoid excluding activation at the group level as older adults have shown a significantly decreased signal-to-noise ratio (SNR) in the BOLD signal (Huettel, Singerman, & McCarthy, 2001).

To evaluate overlapping regions of SWM activation for each task, an inclusive mask of the SWM contrast was

applied to both the early and the late adaptation activation maps. The threshold for this mask to exclude non-SWM-related voxels was set at a liberal p value of .05 uncorrected; however, all statistical inferences used a more stringent false discovery rate threshold p value of .05 (Genovese, Lazar, & Nichols, 2002).

In addition to the within-group analyses, between-group activation differences were evaluated for the early, late, and SWM scanning runs using a second-level random effects analysis with an uncorrected p value of .001 and cluster size ≥ 10 voxels as a threshold for significance. The rationale for this threshold was also based on avoiding the exclusion of activation at the group level for the older adults because of their diminished BOLD SNR (Huettel et al., 2001).

To better characterize age-related differences in brain activation across the course of the visuomotor adaptation task, we created ROIs using the MARSBAR toolbox (Brett, Anton, Valabregue, & Poline, 2002) for areas that both groups had in common for the SWM > SWMc contrast. These ROIs were based on each age group's separate activation sites to allow for slight differences in localization with age. For regions whose peak activation was within a cluster that spanned multiple anatomical areas, 4-mm spherical ROIs centered at the peak for each cluster were created. Following ROI creation, custom software was used to calculate the percent signal change for each scanning block. The mean magnitude of activation was calculated during the visual fixation baseline period before and after each block of testing. The visual fixation baseline period activation was then subtracted from the mean magnitude of activation during the task period, with this value then divided by the mean control period activation and changed to a percentile for each scanning block to yield percent signal change. Partial Pearson correlations (controlling for age) were computed for the pooled young and older adult data between their ROI percent signal change at early and late adaptation periods with their respective rates of learning.

RESULTS

fMRI data from two young adult participants were excluded because of complications with the collection process. This left 18 young adult participants for the behavioral analysis and 16 for the imaging portion (8 men). The data presented for the older adults include all 18 participants.

Behavioral Dependent Measures—Young and Older Adults

Cognitive and motor learning abilities were characterized by comparing the groups on the neuropsychological tests, CHAMPS measures, SWM tasks, and early and late rates of adaptation (Table 1). Like the young adults, older adults performed more poorly on the SWM task than the

SWMc task, as measured through task accuracy, $t(1, 17) = 8.63, p < .001$. In contrast, the amount of time remaining after a response did not differ between tasks, $t(1, 17) = 1.16, p > .25$, which supports that the relative working memory demands of the tasks, not their timing parameters, dictated performance. Older adults showed reduced performance in comparison with the young adults on a number of the neuropsychological tests: card rotation, $F(1, 34) = 175, p < .001$; cube rotation, $F(1, 34) = 18.80, p < .001$; digit symbol, $F(1, 34) = 32.35, p < .001$; Corsi backward, $F(1, 34) = 124, p < .001$; and reading span task, $F(1, 34) = 4.48, p < .05$. Young adults showed greater accuracy on the SWMc task, $F(1, 34) = 16.78, p < .001$, and the SWM task, $F(1, 34) = 15.67, p < .001$, as well as faster RT: SWMc, $F(1, 34) = 24.57, p < .001$; SWM, $F(1, 34) = 14.28, p < .001$. There was no difference in the amount of calories expended (as estimated by the CHAMPS instrument), $F(1, 34) = 2.04, p > .10$, or bouts of exercise performed each week, $F(1, 34) = 0.18, p > .65$, between the two groups.

Sample spatial trajectories for a single representative young and older adult participant are depicted in Figure 2 at the early stages of adaptation and late in adaptation. Adaptation to the rotated feedback is shown through the less distorted trajectories employed in reaching the targets. Young adults did adapt at a faster rate during the early adaptation period than the older adults, $F(1, 34) = 9.40, p < .005$, but the groups did not differ in their rate of late learning, $F(1, 34) = 0.70, p > .40$ (Figure 2).

Older adults did not show any difference in the rate of learning between the early and the late adaptation periods, $t(1, 17) = 1.85, p > .05$, unlike young adults who showed a steeper rate early versus late in learning, $t(1, 17) = 7.08, p < .0001$. A 2 (Age) \times 12 (Block) \times 24 (Trial) mixed model ANOVA for DE was performed to evaluate group differences on the visuomotor adaptation task. This analysis resulted in a significant Age \times Block interaction, $F(11, 374) = 2.67, p < .01$, with a near significant Age \times Block \times Trial interaction, $F(253, 8602) = 1.25, p = .06$, so follow-up tests were conducted. There was no group main effect at the control condition, $F(1, 34) = 76, p > .05$, across the entire adaptation period, $F(1, 34) = 1.64, p > .20$, across the first three adaptation blocks, $F(1, 34) = 0.176, p > .50$, or the final three adaptation blocks, $F(1, 34) = 3.07, p > .05$. Examination of the adaptation period (11 blocks) resulted in a block main effect, $F(10, 340) = 68.40, p < .001$, a trial main effect, $F(23, 782) = 8.20, p < .001$, and a Block \times Trial interaction, $F(230, 7820) = 6.98, p < .001$. However, there was no Block \times Trial \times Age interaction, $F(230, 7820) = 1.20, p > .05$, indicating equivalent improvement in performance with practice across the adaptation period for both groups.

Behavioral Correlation Analysis

The results of the correlation analysis for each neuropsychological, health, SWM, and adaptation measure for

Table 1. Group Mean and Standard Deviation for Performance on Each Behavioral Measure

<i>Task</i>	<i>Units</i>	<i>Older Adults</i>	<i>Young Adults</i>
<i>Neuropsychological</i>			
Card rotation	No. correct cards (3 min)	32.9 ± 13.0	52.3 ± 20.4**
Cube rotation	No. correct cubes (3 min)	1.6 ± 3.3	8.4 ± 6.4**
Digit symbol	No. correct symbols (2 min)	66.2 ± 8.0	79.6 ± 16.2**
Corsi forward	No. correct trials	7.8 ± 1.5	8.7 ± 1.9
Corsi backward	No. correct trials	6.5 ± 1.2	8.5 ± 1.9**
Digit span forward	No. correct trials	11.3 ± 2.1	11.8 ± 2.6
Digit span backward	No. correct trials	6.8 ± 1.4	7.8 ± 2.5
Reading span	No. words recalled	27.4 ± 4.8	30.2 ± 6.3
Edinburgh Inventory	Handedness	.93 ± .05**	.83 ± .11
Dex	Executive impairment	27.4 ± 4.8*	19.8 ± 8.4
CHAMPS cal/wk	Exercise: calories expended	4825 ± 2442	6802 ± 3996
CHAMPS freq/wk	Bouts of exercise	19 ± 8.3	18 ± 6.3
MMSE		29.3 ± 1.2	–
Mattis		141.3 ± 3.2	–
<i>SWM</i>			
Spatial rotation accuracy	% correct	74 ± 6%	81 ± 7%**
Spatial rotation RT	msec	1580 ± 197**	1257 ± 209
<i>VMA</i>			
DE (early slope)	Linear slope	2.0 ± 2.0	3.4 ± 1.0**
DE (late slope)	Linear slope	1.2 ± .6	1.3 ± 0.9

* $p < .05$, ** $p < .001$ between-group difference, with asterisk location indicating which group had the greater value. 2/3 min = time limit to perform the task; cal/wk = calories expended per week; freq/week = frequency per week of bouts of exercise; VMA = visuomotor adaptation.

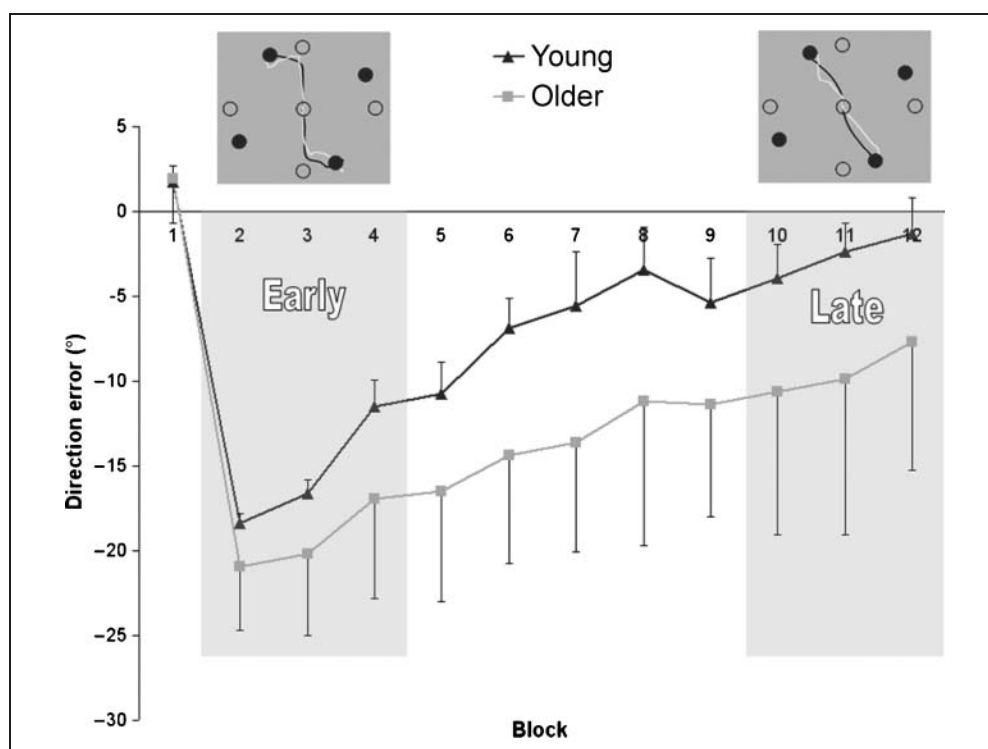
the older adults are presented in Table 2. Unlike the young adults, older adults did not show a correlation between the card rotation task (a visuospatial working memory task) and the rate of early adaptation ($r = .02$, $p > .70$). The young adults' correlation value was statistically greater than that for the older adults ($z = -1.72$, $p < .05$; see Figure 3). However, older adults' Corsi block forward performance (a test of visuospatial STM) correlated with the rate of early adaptation ($r = .51$, $p < .05$). This correlation value was greater for the older adults than the young adults ($z = 1.82$, $p < .05$); however, this significant correlation and between-group difference was driven by one older adult participant who was just within the boundary of being an outlier.¹ Tests of verbal memory (i.e., digit span, reading span) also did not correlate with the rate of early or late adaptation, suggesting that older adults did not use these nonspatial cognitive resources to perform the task at either stage of adaptation. Similarly, no measure of health or mental

status correlated with the rate of early or late adaptation for the older adults.

fMRI Results—Older Adult Visuomotor Adaptation and SWM Activation

Older adult early adaptation activation, with respect to the nonrotated control blocks, was observed in the right medial frontal/cingulate gyrus and middle temporal gyrus (Table 3). Late adaptation activation was in turn observed in the right IPL (Table 3). Older adult SWM > SWMc activation was observed in the bilateral DLPFC and IPL, consistent with a previous investigation using a similar task (Reuter-Lorenz et al., 2000; Table 3) and comparable with what we previously found with the young adults (see Figure 4). Using the SWM > SWMc activation as a limiting mask, there were no overlapping brain regions that reached significance for the older adults when applied to either early or late visuomotor adaptation. This remained

Figure 2. Visuomotor adaptation task (group mean \pm SD). Block numbers correspond with scanning blocks. Block 1 was performed under veridical visual feedback, whereas Blocks 2–12 were performed under 30° clockwise rotation about the center of the screen. Young adults' rate of learning at early adaptation was greater than that of the older adults' rate ($p < .001$), with no difference in the rate of late adaptation ($p > .35$). Examples of young and older adult performance at each stage are shown, with the open circles representing target locations in visual space, whereas the filled circles represent the target locations in joystick space.



true when using a more liberal threshold (uncorrected $p < .25$). It is important to note that in the young adults, the limiting mask analyses revealed activation in the right DLPFC and bilateral IPL (among other regions).

fMRI Results—Between-Group Contrasts and ROI Analyses

Young adults showed more activation than older adults in a number of frontal and motor regions, including the right MFG/DLPFC, during the early adaptation period (Table 4), whereas older adults did not activate any regions more than the young adults. There were no between-group activation differences observed at late adaptation. For the SWM task, older adults engaged a number of regions, including the right MFG/DLPFC, more than the young adults (Table 5a), whereas young adults showed greater activation than older adults only in the right IPL (Table 5B).

In general, the ROI activations followed a similar pattern as the between-group activation contrasts: young adults showed equal or greater activation than the older adults for both early and late adaptation, whereas older adults displayed comparable or greater activation for the SWM task (Figure 5). A 2 (Task, Early Adaptation \times SWM) \times 6 (each ROI) ANOVA resulted in a Task \times Group interaction, $F(1, 32) = 14.25, p < .0001$, as well as an ROI \times Group interaction, $F(5, 160) = 8.00, p < .01$. Follow-up tests of the ROI \times Group interaction revealed a significant Task \times Group effect for each ROI (all greater than), $F(1, 32) = 7.01, p < .01$, except for the R DLPFC, $F(1, 32) = 2.60, p > .10$. Thus, compared with the young adults, older adults showed relatively equivalent activation for the SWM

task but markedly diminished activation during the early adaptation period (Figure 5). ROI activation for each period and their behavioral counterparts (early and late rate of learning) were entered into a pooled group partial correlation controlling for age. One significant correlation emerged: the early rate of learning was significantly correlated with the right DLPFC early activation ($r = .42, p < .05$; see Figure 6).

DISCUSSION

The present study tested the hypothesis that age-related declines in SWM contribute to deficits in visuomotor adaptation for older adults. We found that older adults' rate of early adaptation, which was significantly slower than that of the young adults, did not correlate with any SWM measures² nor did their activation during this period overlap with that exhibited during SWM. This is particularly striking given that older adults showed an overall pattern of activation during SWM similar to that of young adults, albeit with regions of higher activation. The presence of these relationships in young adults and their absence in the older group are consistent with our hypothesis that a failure to effectively engage SWM during early learning contributes to age-related deficits in visuomotor adaptation.

Relationship between Behavioral Measures of SWM and Visuomotor Adaptation

In agreement with previous age-related studies of motor learning (Seidler, 2006; Rodrigue et al., 2005; Raz et al., 2000; Brown, 1996), older adults' rate of early adaptation

Table 2. Older Adult Performance Correlations

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. Card rotation	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2. Cube rotation	0.27	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
3. Digit Symbol	–0.37	–0.17	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
4. Corsi forward	0.01	–0.03	0.02	–	–	–	–	–	–	–	–	–	–	–	–	–	–
5. Corsi backward	0.03	–0.15	0.12	0.23	–	–	–	–	–	–	–	–	–	–	–	–	–
6. Digit span forward	0.16	0.35	–0.56*	0.25	0.15	–	–	–	–	–	–	–	–	–	–	–	–
7. Digit span backward	0.09	0.24	–0.54*	0.10	–0.16	0.56**	–	–	–	–	–	–	–	–	–	–	–
8. Reading span	0.04	0.50*	–0.17	–0.01	–0.47	0.18	0.25	–	–	–	–	–	–	–	–	–	–
9. Edinburgh inventory	–0.18	–0.19	–0.17	–0.01	0.23	0.12	–0.07	0.12	–	–	–	–	–	–	–	–	–
10. Dex	0.09	0.43	–0.33	0.34	0.11	0.28	0.01	–0.11	–0.03	–	–	–	–	–	–	–	–
11. Spatial Rotation Accuracy	0.18	0.48*	–0.38	0.10	0.03	0.34	0.15	0.41	–0.13	0.45	–	–	–	–	–	–	–
12. Spatial Rotation RT	–0.32	0.14	–0.18	0.08	0.25	0.26	0.11	–0.12	0.32	0.26	0.08	–	–	–	–	–	–
13. DE early slope	0.02	0.30	0.25	0.51*	0.16	0.35	–0.04	0.27	–0.10	0.17	–0.07	–0.05	–	–	–	–	–
14. DE late slope	0.14	0.06	–0.27	–0.11	0.25	0.01	–0.10	–0.06	0.04	0.00	–0.02	–0.14	–0.05	–	–	–	–
15. MMSE	0.02	0.24	0.12	0.04	–0.25	–0.30	–0.29	0.27	–0.06	–0.01	–0.12	0.08	0.13	–0.09	–	–	–
16. Mattis	0.04	0.07	0.10	–0.04	0.19	–0.08	0.15	0.33	–0.18	–0.32	0.06	–0.43	0.12	0.18	0.08	–	–
17. Cal/wk. exercise-related	0.49*	0.02	–0.05	–0.06	0.32	0.24	0.20	–0.08	0.05	–0.34	–0.07	–0.33	–0.06	–0.34	–0.35	0.37	–
18. Freq exercise-related	0.17	–0.02	0.12	0.16	0.35	0.23	0.29	–0.19	0.00	–0.27	–0.22	–0.26	0.01	–0.10	–0.19	0.48*	0.84**

Cal/wk. = calories per week.

*Correlation is significant at the .05 level (two-tailed).

**Correlation is significant at the .01 level (two-tailed).

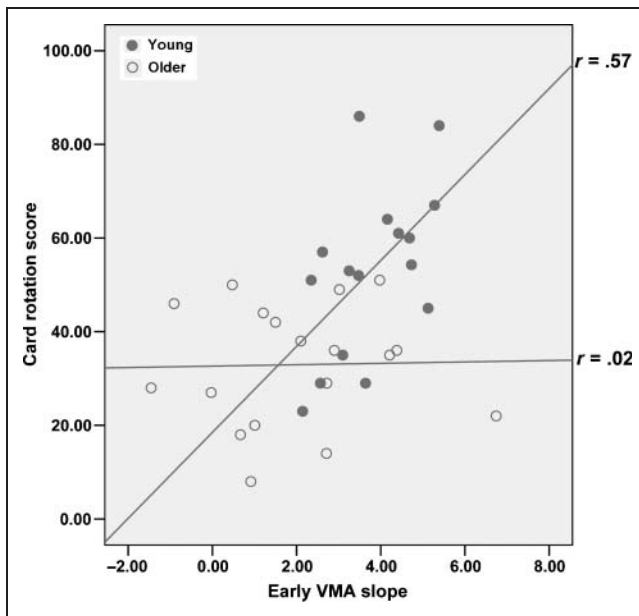


Figure 3. Correlations between early rate of learning and card rotation task for young and older adults. * $p < .05$.

was slower than that of the young adults. Moreover, older adults' card rotation, cube rotation, and SWM accuracy were significantly poorer compared with the young adults, in line with previous age-related studies of SWM (Park et al., 2002; Jenkins et al., 1999; Myerson et al., 1999) and mental rotation (Dobson et al., 1995; Salthouse, 1994; Hertzog et al., 1993; Salthouse & Mitchell, 1989). Unlike the young adults, however, older adults did not exhibit a correlation between the rate of early adaptation and any test of SWM. Importantly, older adults' deficits in these SWM measures did not explain their reduced early rate of adaptation, given the absence of correlation between measures. Rather, these findings suggest that SWM resources are used ineffectively during the early adaptation period for older adults compared with young adults.

These results highlight the importance of targeting specific cognitive processes when evaluating correlations between cognitive capacity and sensorimotor adaptation. Our previous work suggests that the specificity of the correlations tested underlies the observation of distinct cognitive operations contributing to motor learning (Anguera et al., 2010; see also Bock, 2005). For example, Bock (2005) reported a lack of correlation between the magnitude of visuomotor adaptation and the performance on the trail-making test, which measures multiple cognitive domains including spatial organization and visual pursuit. Similarly, Bock and Girgenrath (2006) did not observe a correlation between motor inhibition and mental flexibility. These null correlations suggest that these specific cognitive processes may not contribute to sensorimotor adaptation.

We have proposed that motor error information is passed into SWM and used to update one's visuomotor mapping (Anguera et al., 2010), with deficits in visuomotor adaptation

potentially being associated with age-related impairments in SWM. Although older adults showed poorer performance on the SWM measures compared with the young adults, they were able to complete these tasks at a level well above chance. This behavioral result suggests that although the older adults' SWM faculties showed age-related impairments, the recruitment of these resources during the SWM tasks was successful. With regard to the visuomotor adaptation task, the present findings suggest that older adults' inability to effectively use their SWM resources at this period appears to have resulted in the slower rate of adaptation as well as the greater performance variability during early adaptation.

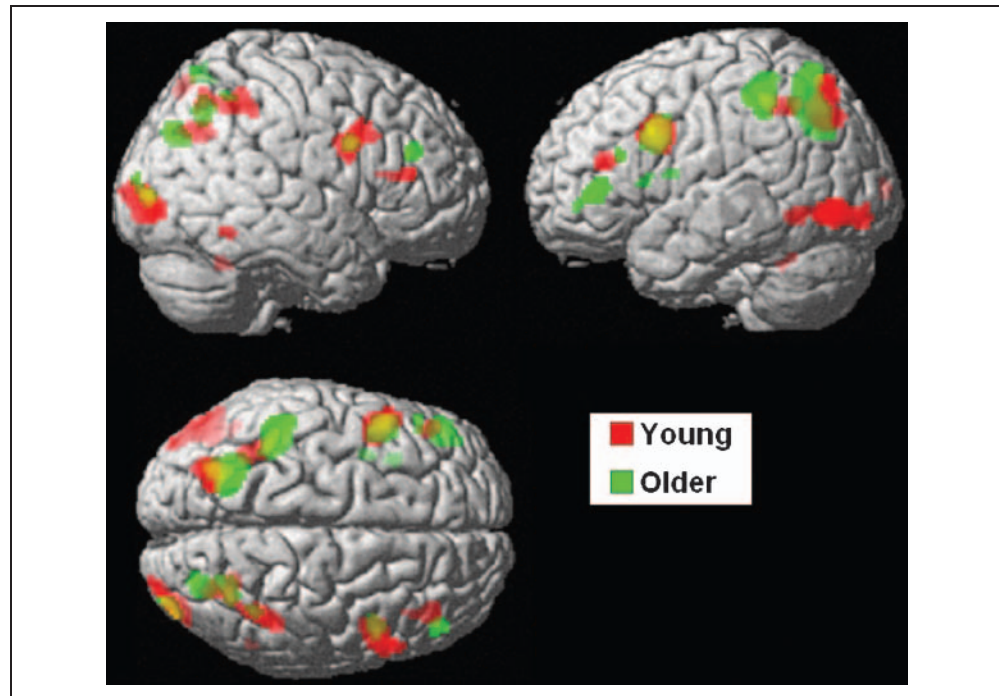
One may question whether these findings extend to other tests of motor learning. Bo and Seidler (2009) recently observed a correlation between visuospatial working mem-

Table 3. Older Adult SWM, Early, and Late Activation

Anatomic Location	BA	Coordinates of Peak	Z Score
<i>SWM—Frontal</i>			
R IFG	44	46, 6, 28	3.0
L IFG	44	-48, 8, 30	3.3
L IFG	45	-52, 28, 20	2.7
L DLPFC	46	-44, 40, 4	3.5
R DLPFC	46	48, 36, 26	3.5
<i>SWM—Parietal</i>			
R IPL	40	40, -50, 50	2.6
L IPL	40	-46, -42, 50	4.0
L Prec	7	-22, -64, 60	3.6
<i>SWM—Others</i>			
R Cuneus	19	26, -78, 34	3.3
L Insula	22	-34, 2, 12	2.7
R MOG	19	42, -88, 4	3.0
R MOG	18	34, -95, 12	2.7
L Caudate		-32, 16, 8	2.8
<i>Early Adaptation</i>			
R MeFG/CG	11/25	12, 22, -12	3.9
R MTG	21	66, -30, -8	3.2
<i>Late Adaptation</i>			
R IPL	40	40, -66, 28	2.7

BA = Brodmann's area; R = right; L = left; IFG = inferior frontal gyrus; MeFG = medial frontal gyrus; CG = cingulate gyrus; DLPFC = dorsolateral prefrontal cortex; IPL = inferior parietal lobule; Prec = precuneus; MOG = middle occipital gyrus; MTG = middle temporal gyrus.

Figure 4. Young (red) and older (green) adults SWM > SWMc rendered brain activation profiles.



ory capacity and motor sequence chunk length for young adults performing another form of motor learning, sequence learning. In addition, older adults exhibited reductions in both working memory capacity and rate of sequence learning (Bo, Borza, & Seidler, 2009). This result suggests that working memory declines with age at least partially explain

Table 4. Young Adults > Older Adults at Early Adaptation

Anatomic Location	BA	Coordinates of Peak	Z Score
<i>Frontal/Motor</i>			
R MeFG	8	6, 32, 46	3.6
R MFG/DLPFC	9	46, 10, 40	3.4
L CG	23	-8, -28, 26	3.9
R S1	1, 2, 3	54, -26, 42	3.3
R S2	5	12, -32, 52	3.2
<i>Others</i>			
R MOG	37	40, -66, 4	3.5
L Insula	22	-36, -20, 8	3.9
L STG	22	-48, -4, 4	3.4
R Caudate		10, 12, 8	3.7
L Pulvinar		-20, -30, 4	3.3
R Thalamus (DM)		6, -14, 14	3.3

BA = Brodmann's area; R = right; L = left; DLPFC = dorsolateral prefrontal cortex; MFG = middle frontal gyrus; MeFG = medial frontal gyrus; CG = cingulate gyrus; S1 = primary somatosensory cortex; S2 = secondary somatosensory cortex; MOG = middle occipital gyrus; STG = superior temporal gyrus; DM = dorsal medial.

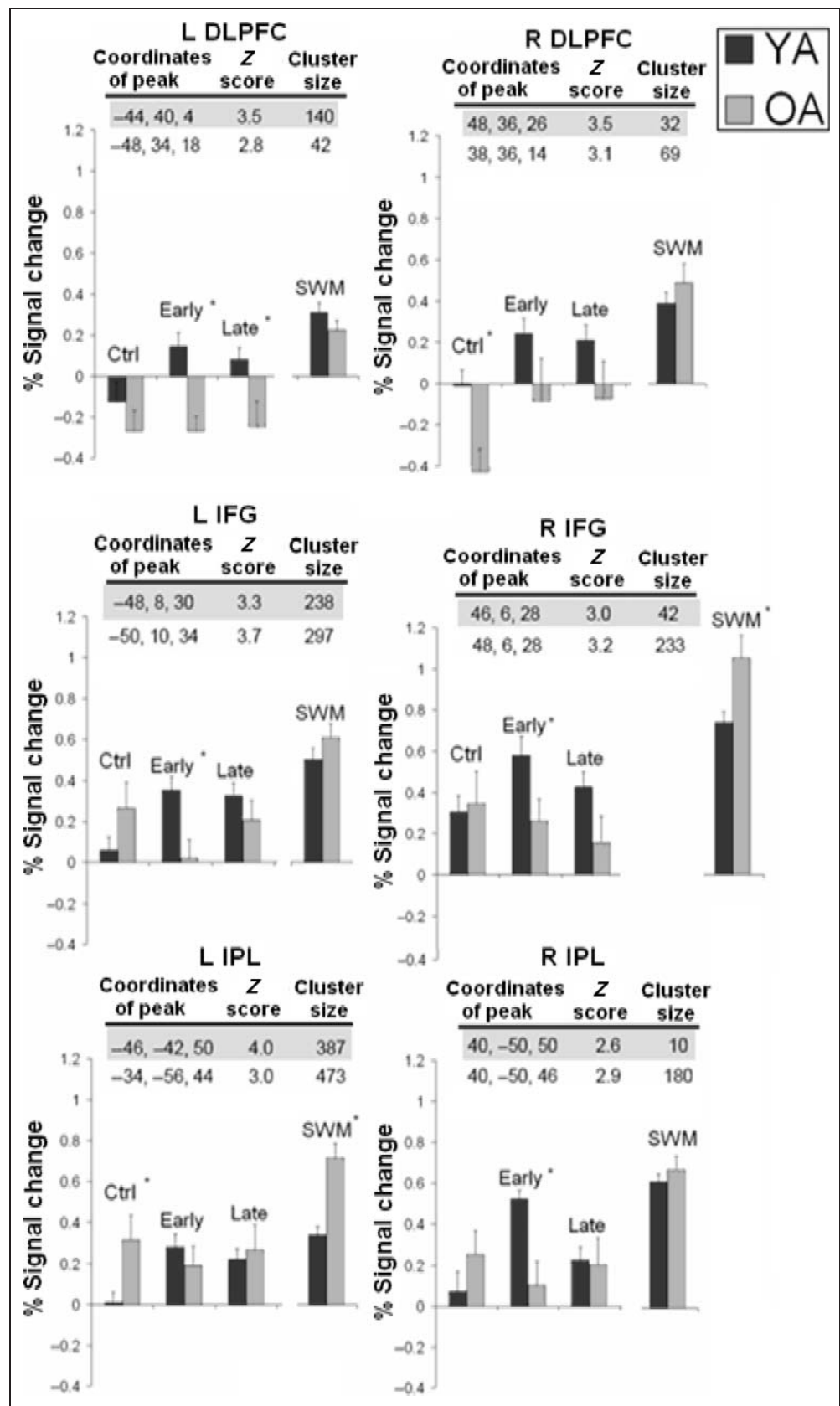
age-related differences in explicit motor sequence learning. However, individual variations in visuospatial working memory capacity did not correlate with the rate of learning in older adults, similar to the null correlation found here with

Table 5. Older versus Young Adults SWM Activation

Anatomic Location	BA	Coordinates of Peak	Z Score
<i>A. Older Adults > Young Adults SWM Activation</i>			
Frontal/motor			
R DLPFC/MFG	46	38, 44, 28	3.7
L MFG	8	-42, 32, 38	3.4
R SMA	6	6, -8, 64	4.6
Parietal			
R IPL	40	56, -42, 38	3.5
L Precuneus	7	-6, -52, 70	5.0
Other			
L Cuneus	31	-10, -66, 8	3.2
R Lingual gyrus	18	6, -78, 0	3.2
L Cerebellum (HV)		-20, -52, -12	3.2
L SN		-54, -36, 28	4.2
L GP		-20, -10, 4	4.2
<i>B. Young Adults > Older Adults SWM Activation</i>			
R IPL	40	44, -38, 56	3.3

BA = Brodmann's area; R = right; L = left; DLPFC = dorsolateral prefrontal cortex; MFG = middle frontal gyrus; IPL = inferior parietal lobule; SN = substantia nigra; GP = globus pallidus.

Figure 5. ROI activation from regions defined by the SWM > SWMc contrasts for young and older adults. Mean activation and standard error for each adaptation period (control [ctrl], early, late, and SWM task). * $p < .05$ reflects activation differences between groups for each period. Gray shading = older adult SWM region; white = young adults SWM region; BA = Brodmann's area; R = right; L = left; IFG = inferior frontal gyrus; DLPFC = dorsolateral prefrontal cortex; IPL = inferior parietal lobule.



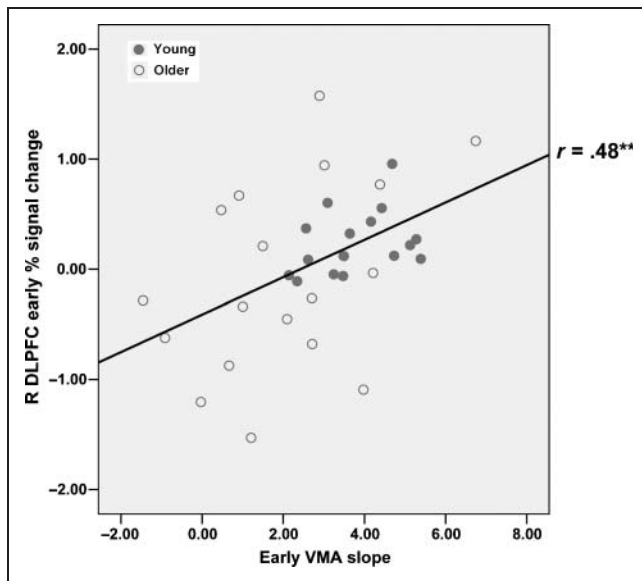


Figure 6. Right DLPFC cortex activation correlation with early rate of adaptation. VMA = visuomotor adaptation. The fit line/Pearson score reflects the pooled scores for both groups; a partial correlation controlling for age also resulted in a significant effect here ($r = .42$, $p < .05$). $**p < .01$.

the early rate of adaptation and SWM performance. It is important to note that each of the young and older adult correlations would fail to reach significance had we corrected for multiple comparisons (resulting in $p < .0005$) for each test, although the correction would not be appropriate for correlations examining some of the more specific predictions. Thus, although the individual strength of these correlations is modest, the significant group difference between the rate of early adaptation and the card rotation correlations supports our interpretations.

Neural Relationship between SWM and Visuomotor Adaptation Activation

For the SWM task, older adults showed bilateral activation in the DLPFC and IPL, comparable with what we observed in young adults. However, a between-group contrast of this activation revealed that older adults engaged a number of regions, including the right DLPFC, to a greater extent than the young adults. In particular, the right DLPFC and the bilateral IPL, regions which have previously been associated with mental rotation in SWM tasks (Suchan et al., 2006; Jordan, Heinze, Lutz, Kanowski, & Jancke, 2001; Gill, O'Boyle, & Hathaway, 1998), were engaged. Thus, older adults were able to appropriately engage several regions associated with SWM, although this increased activation did not lead to equal or greater levels of performance. These results are in agreement with what has been previously reported for older adults performing this SWM task (Reuter-Lorenz et al., 2000), with more pronounced bilateral activation than young adults (Table 5A). This pattern of activation is also in line with cognitive aging research describing a

compensatory effect of bilateral activation in older adults (Cabeza, Anderson, Locantore, & McIntosh, 2002; Reuter-Lorenz et al., 2000), although the differences here were evaluated in a qualitative fashion.

During the early adaptation period, young adults engaged a number of motor and frontal regions to a greater extent than older adults. These findings are in contrast to several imaging studies showing that older adults exhibit stronger and/or more widespread brain activation patterns than young adults during the execution of a tapping (Mattay et al., 2002; Calautti, Serrati, & Baron, 2001), gripping (Ward & Frackowiak, 2003), or a complex interlimb coordination task (Heuninckx, Wenderoth, & Swinnen, 2008a, 2008b; Heuninckx, Wenderoth, Debaere, Peeters, & Swinnen, 2005; Ward & Frackowiak, 2003). However, these studies differ from the current investigation in that they focused on stable motor performance rather than on motor learning. The use of a very simple motor task (Mattay et al., 2002) or the implementation of prescanning practice until a specified level of performance was reached (Heuninckx et al., 2005, 2008a, 2008b; Ward & Frackowiak, 2003; Calautti et al., 2001) essentially removed learning-related activation. Given young adults' faster rate of early adaptation, the greater activation likely reflects areas involved with both the adaptation and the performance processes.

Older adults show a greater reliance on cognitive processes than young adults for the control of relatively simple actions such as maintaining standing balance and walking (Huxhold, Li, Schmiedek, & Lindenberger, 2006). The present findings show, however, that older adults were unable to effectively engage the relevant cognitive processes during visuomotor adaptation. It was also not the case that older adults recruited these regions later than the young adults, as no overlap was observed between the SWM activation and the late adaptation activation. When older adults' early adaptation period was masked with this SWM activation, there was no significant overlap (unlike young adults). Even when a much more liberal threshold for significance was used (uncorrected $p < .25$), no regions reached significance, suggesting that these results were not simply due to a lower SNR in the older adults (Huettel et al., 2001; D'Esposito, Zarahn, Aguirre, & Rypma, 1999).

The ROI activation suggested that older adults were able to successfully engage several regions of the SWM network but failed to recruit these areas appropriately during the early visuomotor adaptation period. These interpretations are supported by the ROI analyses showing a Task \times Group interaction between the SWM and the early adaptation activation as well as the partial correlation (controlling for age) between the early rate of adaptation and the activation at the right DLPFC. Thus, young adults' more effective engagement of SWM resources during early adaptation resulted in a between-group rate of learning difference.

A potential concern is that the early and late adaptation activations may also contain neural activity related to processing movement errors and their associated emotional responses. We have recently demonstrated that larger

movement errors correspond with a greater amount of error-related neural activity (Anguera, Seidler, & Gehring, 2009). It is reasonable to assume that participants would have feelings of frustration during the early adaptation period. It may be that young and older adults process error information differently and vary in their affective responses to errors as well. This is an interesting topic for future study. However, in the current study, we focused specifically on activation related to SWM by using activation from this task as a limiting mask. Thus, we are confident that the frontal and parietal activation we report for early learning are associated with SWM processes.

Conclusions

Unlike younger adults, older adults did not effectively engage SWM resources during the early period of visuomotor adaptation. This was evidenced by a lack of neural overlap between the early adaptation period and the SWM task performance as well as the partial correlation with early adaptation rate of learning with the right DLPFC ROI activation. These findings suggest that specific cognitive factors contribute to age-related differences in the rate of visuomotor adaptation, with the ineffective engagement of SWM resources as a source of these declines.

Acknowledgments

The authors thank B. L. Benson, H. Cheema, K. Haydar, and T. Mitchell for assistance with data analyses, K. Newnham with data collection, and S. H. Brown, W. J. Gehring, and C. Lustig for their feedback in the development of this project. This work was supported by the National Institutes of Health [AG024106 (RS)] and the UM NIH Claude D. Pepper Center Human Subjects and Assessment Core (NIH AG024824).

Reprint requests should be sent to Rachael D. Seidler, 401 Washtenaw Ave., Ann Arbor, MI 48109-2214, or via e-mail: rseidler@umich.edu.

Notes

1. This participant scored 10 on Corsi forward, whereas 7.8 ± 1.5 was the group mean and standard deviation. With this participant removed, the group r value was .384 ($p > .125$).
2. Although Corsi forward performance did show a correlation with the rate of early adaptation, this correlation was driven by one participant. Furthermore, although a relationship between SWM and STM has been established (Miyake & Shah, 1999), this task, like other STM tasks, does not require the mental manipulation of information, which we operationally define as being an integral part of SWM.

REFERENCES

- Anguera, J., Reuter-Lorenz, P., Willingham, D., & Seidler, R. (2010). Contributions of spatial working memory to visuomotor learning. *Journal of Cognitive Neuroscience*, *22*, 1917–1930.
- Anguera, J., Seidler, R., & Gehring, W. (2009). Changes in performance monitoring during sensorimotor adaptation. *Journal of Neurophysiology*, *102*, 1868–1879.
- Baddeley, A. (1986). *Working memory*. Oxford: Oxford University Press.
- Baltes, P. B., & Lindenberger, U. (1997). Emergence of a powerful connection between sensory and cognitive functions across the adult life span: A new window to the study of cognitive aging? *Psychology and Aging*, *12*, 12–21.
- Bo, J., Borza, V., & Seidler, R. D. (2009). Age-related declines in visuospatial working memory correlate with deficits in explicit motor sequence learning. *Journal of Neurophysiology*, *102*, 2744–2754.
- Bo, J., & Seidler, R. D. (2009). Visuospatial working memory capacity predicts the organization of acquired explicit motor sequences. *Journal of Neurophysiology*, *101*, 3118–3125.
- Bock, O. (2005). Components of sensorimotor adaptation in young and elderly subjects. *Experimental Brain Research*, *160*, 259–263.
- Bock, O., & Girgenrath, M. (2006). Relationship between sensorimotor adaptation and cognitive functions in younger and older subjects. *Experimental Brain Research*, *169*, 400–406.
- Booth, F. W., Weeden, S. H., & Tseng, B. S. (1994). Effect of aging on human skeletal muscle and motor function. *Medicine and Science in Sports and Exercise*, *26*, 556–560.
- Bornert, P., Aldefeld, B., & Eggers, H. (2000). Reversed spiral MR imaging. *Magnetic Resonance in Medicine*, *44*, 479–484.
- Brett, M., Anton, J., Valabregue, R., & Poline, J. (2002). *Region of interest analysis using an SPM toolbox*. Paper presented at the 8th International Conference on Functional Mapping of the Human Brain, June 2–6, 2002, Sendai, Japan, and is available on CD-ROM in *Neuroimage*, *16*(2).
- Brown, S. (1996). Control of simple arm movements in the elderly. In A. Ferrandez & N. Teasdale (Eds.), *Changes in sensory motor behavior in aging* (pp. 27–52). New York: Elsevier.
- Cabeza, R., Anderson, N. D., Locantore, J. K., & McIntosh, A. R. (2002). Aging gracefully: Compensatory brain activity in high-performing older adults. *Neuroimage*, *17*, 1394–1402.
- Calautti, C., Serrati, C., & Baron, J. C. (2001). Effects of age on brain activation during auditory-cued thumb-to-index opposition: A positron emission tomography study. *Stroke*, *32*, 139–146.
- Canavan, A. G., Passingham, R. E., Marsden, C. D., Quinn, N., Wyke, M., & Polkey, C. E. (1990). Prism adaptation and other tasks involving spatial abilities in patients with Parkinson's disease, patients with frontal lobe lesions and patients with unilateral temporal lobectomies. *Neuropsychologia*, *28*, 969–984.
- Corsi, P. (1972). Human memory and the medial temporal region of the brain. *Dissertation Abstracts International*, *34*(02), 819B. (University Microfilms No. AAI05-77717).
- Courtney, S. M., Petit, L., Maisog, J. M., Ungerleider, L. G., & Haxby, J. V. (1998). An area specialized for spatial working memory in human frontal cortex. *Science*, *279*, 1347–1351.
- Daneman, M., & Carpenter, P. (1980). Individual differences in working memory and reading. *Journal of Verbal Learning and Verbal Behavior*, *19*, 450–466.
- Demer, J. L. (1994). Effect of aging on vertical visual tracking and visual-vestibular interaction. *Journal of Vestibular Research*, *4*, 355–370.
- D'Esposito, M., Deouell, L. Y., & Gazzaley, A. (2003). Alterations in the BOLD fMRI signal with ageing and disease: A challenge for neuroimaging. *Nature Reviews Neuroscience*, *4*, 863–872.

- D'Esposito, M., Zarahn, E., Aguirre, G. K., & Rypma, B. (1999). The effect of normal aging on the coupling of neural activity to the bold hemodynamic response. *Neuroimage*, *10*, 6–14.
- Dobson, S., Kirasic, K., & Allen, G. (1995). Age-related differences in adults spatial task-performance—Influences of task complexity and perceptual speed. *Aging and Cognition*, *2*, 19–38.
- Ekstrom, R., French, J., & Harman, H. (1976). *Manual for kit of factor referenced cognitive tests*. Princeton, NJ: Educational Testing Service.
- Evans, A., Kamber, M., Collins, D., & Macdonald, D. (1994). An MRI-based probabilistic atlas of neuroanatomy. In S. Shorvon, D. Fish, F. Andermann, G. Bydder, & H. Stefan (Eds.), *Magnetic resonance scanning and epilepsy. NATO ASI Series A, Life Sciences* (Vol. 264, pp. 263–274). New York: Plenum Press.
- Eversheim, U., & Bock, O. (2001). Evidence for processing stages in skill acquisition: A dual-task study. *Learning and Memory*, *8*, 183–189.
- Fernandez-Ruiz, J., Hall, C., Vergara, P., & Diaz, R. (2000). Prism adaptation in normal aging: Slower adaptation rate and larger aftereffect. *Brain Research, Cognitive Brain Research*, *9*, 223–226.
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). “Mini-mental state.” A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, *12*, 189–198.
- Galea, V. (1996). Changes in motor unit estimates with aging. *J Clinical Neurophysiology*, *13*, 253–260.
- Galganski, M. E., Fuglevand, A. J., & Enoka, R. M. (1993). Reduced control of motor output in a human hand muscle of elderly subjects during submaximal contractions. *Journal of Neurophysiology*, *69*, 2108–2115.
- Genovese, C. R., Lazar, N. A., & Nichols, T. (2002). Thresholding of statistical maps in functional neuroimaging using the false discovery rate. *Neuroimage*, *15*, 870–878.
- Gill, H. S., O'Boyle, M. W., & Hathaway, J. (1998). Cortical distribution of EEG activity for component processes during mental rotation. *Cortex*, *34*, 707–718.
- Hertzog, C., Vernon, M. C., & Rypma, B. (1993). Age differences in mental rotation task performance: The influence of speed/accuracy tradeoffs. *Journal of Gerontology*, *48*, P150–P156.
- Heuninckx, S., Wenderoth, N., Debaere, F., Peeters, R., & Swinnen, S. P. (2005). Neural basis of aging: The penetration of cognition into action control. *Journal of Neuroscience*, *25*, 6787–6796.
- Heuninckx, S., Wenderoth, N., & Swinnen, S. P. (2008a). Age-related reduction in the differential pathways involved in internal and external movement generation. *Neurobiology of Aging*.
- Heuninckx, S., Wenderoth, N., & Swinnen, S. P. (2008b). Systems neuroplasticity in the aging brain: Recruiting additional neural resources for successful motor performance in elderly persons. *Journal of Neuroscience*, *28*, 91–99.
- Huettel, S. A., Singerman, J. D., & McCarthy, G. (2001). The effects of aging upon the hemodynamic response measured by functional MRI. *Neuroimage*, *13*, 161–175.
- Huxhold, O., Li, S. C., Schmiedek, F., & Lindenberger, U. (2006). Dual-tasking postural control: Aging and the effects of cognitive demand in conjunction with focus of attention. *Brain Research Bulletin*, *69*, 294–305.
- Huynh, H., & Feldt, L. (1970). Conditions under which the mean square ratios in repeated measures designs have exact *F*-distributions. *Journal of the American Statistical Association*, *65*, 1582–1589.
- Jenkins, L., Myerson, J., Hale, S., & Fry, A. F. (1999). Individual and developmental differences in working memory across the life span. *Psychonomic Bulletin & Review*, *6*, 28–40.
- Jonides, J., Smith, E. E., Koeppe, R. A., Awh, E., Minoshima, S., & Mintun, M. A. (1993). Spatial working memory in humans as revealed by PET. *Nature*, *363*, 623–625.
- Jordan, K., Heinze, H. J., Lutz, K., Kanowski, M., & Jancke, L. (2001). Cortical activations during the mental rotation of different visual objects. *Neuroimage*, *13*, 143–152.
- Kirasic, K. (2000). Age differences in adults' spatial abilities, learning environmental layout, and wayfinding behavior. *Spatial Cognition and Computation*, *2*, 117–134.
- Lindenberger, U., & Baltes, P. B. (1994). Sensory functioning and intelligence in old age: A strong connection. *Psychology and Aging*, *9*, 339–355.
- Mattay, V. S., Fera, F., Tessitore, A., Hariri, A. R., Das, S., Callicott, J. H., et al. (2002). Neurophysiological correlates of age-related changes in human motor function. *Neurology*, *58*, 630–635.
- Mattis, S. (1988). *Dementia rating scale: Professional manual*. Odessa, FL: Psychological Assessment Resources.
- Mayka, M. A., Corcos, D. M., Leurgans, S. E., & Vaillancourt, D. E. (2006). Three-dimensional locations and boundaries of motor and premotor cortices as defined by functional brain imaging: A meta-analysis. *Neuroimage*, *31*, 1453–1474.
- McNay, E. C., & Willingham, D. B. (1998). Deficit in learning of a motor skill requiring strategy, but not of perceptuomotor recalibration, with aging. *Learning and Memory*, *4*, 411–420.
- Milivojevic, B., Hamm, J. P., & Corballis, M. C. (2008). Functional neuroanatomy of mental rotation. *Journal of Cognitive Neuroscience*, *21*, 945–959.
- Miyake, A., & Shah, P. (Eds.) (1999). *Models of working memory: Mechanisms of active maintenance and executive control*. New York: Cambridge University Press.
- Myerson, J., Hale, S., Rhee, S. H., & Jenkins, L. (1999). Selective interference with verbal and spatial working memory in young and older adults. *Journals of Gerontology, Series B, Psychological Sciences and Social Sciences*, *54*, P161–P164.
- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*, *9*, 97–113.
- Park, D. C., Lautenschlager, G., Hedden, T., Davidson, N. S., Smith, A. D., & Smith, P. K. (2002). Models of visuospatial and verbal memory across the adult life span. *Psychology and Aging*, *17*, 299–320.
- Picard, N., & Strick, P. L. (1996). Motor areas of the medial wall: A review of their location and functional activation. *Cerebral Cortex*, *6*, 342–353.
- Raz, N., Williamson, A., Gunning-Dixon, F., Head, D., & Acker, J. D. (2000). Neuroanatomical and cognitive correlates of adult age differences in acquisition of a perceptual-motor skill. *Microscopy Research and Technique*, *51*, 85–93.
- Reuter-Lorenz, P. A., Jonides, J., Smith, E. E., Hartley, A., Miller, A., Marshuetz, C., et al. (2000). Age differences in the frontal lateralization of verbal and spatial working memory revealed by PET. *Journal of Cognitive Neuroscience*, *12*, 174–187.
- Rodrigue, K., Kennedy, K., & Raz, N. (2005). Aging and longitudinal change in perceptual-motor skill acquisition in healthy adults. *Journals of Gerontology, Series B, Psychological Sciences and Social Sciences*, *60*, 174–181.
- Roller, C. A., Cohen, H. S., Kimball, K. T., & Bloomberg, J. J. (2002). Effects of normal aging on visuo-motor plasticity. *Neurobiology of Aging*, *23*, 117–123.
- Salthouse, T. A. (1994). Aging associations: Influence of speed on adult age differences in associative learning. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *20*, 1486–1503.

- Salthouse, T. A., & Mitchell, D. R. (1989). Structural and operational capacities in integrative spatial ability. *Psychology and Aging, 4*, 18–25.
- Schmahmann, J. D., Doyon, J., McDonald, D., Holmes, C., Lavoie, K., Hurwitz, A. S., et al. (1999). Three-dimensional MRI atlas of the human cerebellum in proportional stereotaxic space. *Neuroimage, 10*, 233–260.
- Seidler, R. D. (2006). Differential effects of age on sequence learning and sensorimotor adaptation. *Brain Research Bulletin, 70*, 337–346.
- Stewart, A. L., Mills, K. M., King, A. C., Haskell, W. L., Gillis, D., & Ritter, P. L. (2001). CHAMPS physical activity questionnaire for older adults: Outcomes for interventions. *Medicine and Science in Sports and Exercise, 33*, 1126–1141.
- Suchan, B., Botko, R., Gizewski, E., Forsting, M., & Daum, I. (2006). Neural substrates of manipulation in visuospatial working memory. *Neuroscience, 139*, 351–357.
- Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain. 3-Dimensional proportional system, an approach to cerebral imaging* (M. Rayport, Trans.). New York: Thieme.
- Taylor, J. A., & Thoroughman, K. A. (2007). Divided attention impairs human motor adaptation but not feedback control. *Journal of Neurophysiology, 98*, 317–326.
- Taylor, J. A., & Thoroughman, K. A. (2008). Motor adaptation scaled by the difficulty of a secondary cognitive task. *PLoS ONE, 3*, e2485.
- Teasdale, N., Bard, C., Fleury, M., Young, D. E., & Proteau, L. (1993). Determining movement onsets from temporal series. *Journal of Motor Behavior, 25*, 97–106.
- Teulings, H. L., Contreras-Vidal, J. L., Stelmach, G. E., & Adler, C. H. (2002). Adaptation of handwriting size under distorted visual feedback in patients with Parkinson's disease and elderly and young controls. *Journal of Neurology, Neurosurgery and Psychiatry, 72*, 315–324.
- Tisserand, D. J., van Boxtel, M. P., Pruessner, J. C., Hofman, P., Evans, A. C., & Jolles, J. (2004). A voxel-based morphometric study to determine individual differences in gray matter density associated with age and cognitive change over time. *Cerebral Cortex, 14*, 966–973.
- Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., et al. (2002). Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage, 15*, 273–289.
- Walter, H., Bretschneider, V., Gron, G., Zurowski, B., Wunderlich, A. P., Tomczak, R., et al. (2003). Evidence for quantitative domain dominance for verbal and spatial working memory in frontal and parietal cortex. *Cortex, 39*, 897–911.
- Ward, N. S., & Frackowiak, R. S. (2003). Age-related changes in the neural correlates of motor performance. *Brain, 126*, 873–888.
- Wechsler, D. (1997). *Wechsler Adult Intelligence Scale* (3rd ed.). San Antonio, TX: Psychological Corporation.
- Wilson, B., Alderman, N., Burgess, P., Emslie, H., & Evans, J. (Eds.) (1996). *Behavioural assessment of the dysexecutive syndrome*. Bury St. Edmunds, UK: Thames Valley Test Company.
- Winter, D. (1990). *Biomechanics and motor control of human movement* (2nd ed.). New York: Wiley.
- Woods, R. P., Grafton, S. T., Holmes, C. J., Cherry, S. R., & Mazziotta, J. C. (1998). Automated image registration: I. General methods and intrasubject, intramodality validation. *Journal of Computer Assisted Tomography, 22*, 139–152.