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Associations between age, motor function, and resting state sensorimotor network connectivity in healthy older adults

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ABSTRACT

Aging is associated with impaired motor performance across a range of tasks. Both primary neural representations of movement and potential compensatory cognitive mechanisms appear to be disrupted in older age. Here we determined how age is associated with resting state sensorimotor functional connectivity, and whether connectivity strength is associated with motor performance. We investigated the association between age and resting state functional connectivity of several sensorimotor networks in 191 healthy older, right-handed individuals. Regions of interest were defined in the left motor cortex, left putamen, and right cerebellar lobules V and VIII. Analyses were adjusted for head motion, gray matter volume, diastolic blood pressure, and smoker status; we then evaluated whether connectivity is associated with participants' manual motor performance. We found both increased and decreased connectivity within portions of the motor cortical and cerebellar networks after adjusting for covariates. We observed that connectivity increased with age for the motor cortex and cerebellar lobule VIII with the putamen, providing evidence of greater interactivity across networks with age. Higher tapping frequency and greater grip force were associated with stronger connectivity between the motor cortex during resting state, putamen, cerebellar lobule VIII and the insular cortex, suggesting that greater network interactivity may protect against age declines in performance.

Introduction

Aging is associated with degeneration of the central nervous system and decreases in motor performance (Seidler et al., 2010). Although task-based fMRI studies have provided important knowledge regarding the aging brain and sensorimotor control (Mattay et al., 2002; Noble et al., 2011; Ward and Frackowiak, 2003; Ward et al., 2008), examining resting state functional connectivity strength also has the potential to provide key insights into motor declines in healthy aging. Resting state functional connectivity MRI (rs-fcMRI) involves acquiring functional images across several minutes while participants are not performing a task (Biswal et al., 1995). Resting state activity can be seen as a kind of starting or reference point from which task-related activation emerges. Since its first application, rs-fcMRI has been used to investigate age differences in a variety of brain networks, including sensorimotor networks (Bernard et al., 2012; Bernard et al., 2013; Biswal et al., 1995; Fling et al., 2011; Fling et al., 2012; Langan et al., 2010). Several studies have reported altered resting state connectivity in both healthy aging (Andrews-Hanna et al., 2007; Damoiseaux et al., 2008) and disease (Greicius et al., 2004; Sorg et al., 2007; Wang et al, 2007), but most have studied the default mode network. Far fewer have examined sensorimotor network connectivity in healthy older adults (Roski et al., 2013; Wu et al., 2007), and whether sensorimotor network connectivity strength is associated with motor performance (Bernard et al., 2013; Fling et al., 2012; Langan et al., 2010). Our work and that of others suggests that age is associated with both increased and decreased connectivity strength within several sensorimotor networks, including the motor cortical network, the corticostriatal and the corticocerebellar networks (Bernard et al., 2013; Langan et al., 2010; Roski et al., 2013; Tomasi and Volkow, 2012; Wu et al., 2007), with greater resting state connectivity between the two motor cortices in older versus young adults (Langan et al., 2010), and decreased cortico-cerebellar connectivity (Bernard et al., 2013).

Several previous studies have found connectivity strength to be positively associated with motor performance in older adults,

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suggesting that it may serve as a biomarker of brain health and functional performance (Langan et al., 2010). However, the studies that have related connectivity strength to motor performance in older adults have used small sample sizes, ranging from 10 – 30 participants. In the current study, we applied rs-fcMRI to investigate connectivity strength in several sensorimotor networks in a large sample (nearly 200 participants) of healthy older adults. We investigated motor cortical connectivity, motor corticostriatal connectivity, and motor corticocerebellar connectivity. Based on the existing literature, we hypothesized that: 1. Participants with advanced age would demonstrate reduced sensorimotor network connectivity, similar to what has been observed with default mode network connectivity in older adults (cf. Andrews-Hanna et al., 2007). Further, we hypothesized that: 2. When controlling for age and other confounding variables, better motor performance would be associated with stronger sensorimotor network connectivity, supporting the notion that maintained brain functional connectivity with age is important for sensorimotor function.

Methods

Participants

We included 193 subjects from the first time point of the longitudinal Healthy Aging Brain (LHAB) database study, an ongoing longitudinal project at the International Normal Aging and Plasticity Imaging Center (INAPIC) at the University of Zurich (Zollig et al., 2011) who had complete data for rs-fcMRI and all covariates (i.e., head motion, gray matter volume, smoker status and electronic measurement of diastolic blood pressure (Omron, Model: M6 HEM-7211-E)). Participants were older than 64 years old, right handed, native German speakers, had a mini-mental status examination (MMSE) score >26 (Folstein et al., 1975) and passed the MRI safety standards (e.g., no metallic implants). In addition, participants had no history of neurological diseases (e.g., Parkinson Disease, Alzheimer's Diesease), mental disorders (e.g., depression), diseases of the hematopoietic system (e.g., Anemia, Leukemia), traumatic brain injuries in the last 2 years, and did not suffer from diabetes or tinnitus. After preprocessing, two participants were excluded because of excessive head motion inside the scanner (>2 mm), thus leading to a final sample size of N = 191 (89 males and 102 females, mean age 70.3 $\pm$ sd 4.8).

Sensorimotor Assessments

We used a sensory-motor test battery that includes tests of right and left hand motor tapping (Schatz, 2010), right and left hand maximum grip force (Podell, 2010), bimanual visual-motor control (Schufried, 2011) and right and left hand grooved pegboard performance (Merker and Podell, 2010), yielding the following outcome measures: a) maximum grip force, b) taping frequency, c) bimanual visuo-motor coordination (duration in seconds to finish the track, duration off track and duration off track as percentage of the total duration), and d) manual dexterity (duration in seconds). Scores on sensorimotor tests were compared mutually by means of their significance of correlation with age and with each other (see, Table 1). Due to high correlation between several of the motor measures, we chose to include only right hand maximum grip force and right hand motor tapping measures in our fMRI analyses. Tapping speed has been linked primarily to the motor cortex and cerebellum (Lutz et al., 2005), while control of grip force has been linked to these regions as well as the supplementary motor cortex and basal ganglia nuclei (cf., Spraker et al., 2007). Thus we ended up with two tasks that rely on partially overlapping yet distinct motor circuits.

Grip force was measured using a hand dynamometer (Hydraulic Hand Dynamometer, Model: SH5001, Saehan Corporation, Korea). Participants were instructed to sit upright, feet positioned flat on the ground, shoulder in a neutral position, elbow in a 90° flexion, the forearm in a neutral position and the wrist in 0°–30° of extension. Data were collected alternately for the right and left hand with a break of 30 s between measurements. Participants were asked to keep the force stable for 4 s for each trial. Three trials per hand were executed. If the third measurement was the highest, data collection continued until performance dropped below that of a previous measurement. In

Table 1
Correlation between age and motor measures. Abbreviations: R: right hand, L: left hand, Pegtime: pegboard completion time, Tap: # taps, VMC: visual motor control task, Errdur: error duration, Errperc: error percentage, GF: grip force.

Correlations	Age	PegTime_R	PegTime_L	Tap_R	Tap_L	VMC_duration	VMC_errdur	GF_Max_R	GF_Max_L
Age	1								
p value	<0.001								
Number of subjects	191								
PegTime_R	.354**	1							
p value	<0.001								
Number of subjects	190	190							
PegTime_L	.334**	.675**	1						
p value	<0.001	<0.001							
Number of subjects	189	189	189						
Tap_R	−.254**	−.251**	−.203**	1					
p value	<0.001	<0.001	0.005						
Number of subjects	187	187	187	188					
Tap_L	−.134	−.246**	−.291**	.718**	1				
p value	0.066	0.001	<0.001	<0.001					
Number of subjects	188	187	187	188	188				
VMC_duration	.279**	.200**	.252**	−.268**	−.261**	1			
p value	<0.001	0.007	<0.001	<0.001	<0.001				
Number of subjects	178	177	177	178	178	178			
VMC_errdur	.145	.175*	.188*	−.295**	−.270**	.531**	1		
p value	0.054	0.02	0.012	<0.001	<0.001	<0.001			
Number of subjects	178	177	177	178	178	178	178		
GF_Max_R	−.196**	−.128	−.07	.337**	.323**	−.446**	−.339**	1	
p value	0.008	0.086	0.353	<0.001	<0.001	<0.001	<0.001		
Number of subjects	182	181	180	180	180	170	170	182	
GF_Max_L	−.217**	−0.118	−0.092	.335**	.334**	−.442**	−.344**	.953**	1
p value	0.003	0.113	0.218	<0.001	<0.001	<0.001	<0.001	<0.001	
Number of subjects	181	180	180	180	180	170	170	181	181

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).