Neurobiology of Aging 46 (2016) 149–159

Contents lists available at ScienceDirect

Neurobiology of Aging

journal homepage: www.elsevier.com/locate/neuaging

Neuronal mechanisms of motor learning are age dependent

Kelly M.M. Berghuis [a,*], Veerle De Rond [a], Inge Zijdewind [b], Giacomo Koch [c], Menno P. Veldman [a], Tibor Hortobágyi [a]

[a] Center for Human Movement Sciences, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands
[b] Department of Neuroscience, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands
[c] Laboratorio di Neurologia Clinica e Comportamentale, Fondazione Santa Lucia IRCCS, Rome, Italy

ARTICLE INFO

Article history:
Received 2 February 2016
Received in revised form 21 June 2016
Accepted 22 June 2016
Available online 29 June 2016

Keywords:
Motor skill
Retention
Transcranial magnetic stimulation
Corticospinal excitability
Short-interval intracortical inhibition
Aging

ABSTRACT

There is controversy whether age-related neuroanatomical and neurophysiological changes in the central nervous system affect healthy old adults' abilities to acquire and retain motor skills. We examined the effects of age on motor skill acquisition and retention and potential underlying mechanisms by measuring corticospinal and intracortical excitability, using transcranial magnetic stimulation. Healthy young (n = 24, 22 years) and old (n = 22, 71 years) adults practiced a wrist flexion-extention visuomotor task or only watched the templates as an attentional control for 20 minutes. Old compared with young adults performed less well at baseline. Although the absolute magnitude of skill acquisition and retention was similar in the 2 age groups (age × intervention × time, $p = 0.425$), a comparison of baseline-similar age sub-groups revealed impaired skill acquisition but not retention in old versus young. Furthermore, the neuronal mechanisms differed as revealed by an opposite direction of associations in the age-groups between relative skill acquisition and intracortical facilitation during the task, and opposite changes during skill retention in corticospinal excitability at rest and during the task and intracortical inhibition during the task.

1. Introduction

For an enjoyable daily life, children, adults, and seniors need to acquire new motor skills and retain previously acquired abilities. Motor skill acquisition and the need to be able to perform previously learned skills relatively free of error are particularly relevant for the increasing number of old adults (World Health Organization, 2015). Beyond gross motor skills, old adults must also cope with new technologies that require manipulative motor challenges, such as operating computer keyboards and portable electronic devices that are reconfigured with each upgrade.

It is expected that old adults' abilities to acquire unfamiliar motor skills would decline based on the numerous and predominantly unfavorable age-related neuroanatomical and neurophysiological changes (Cabeza et al., 2002; Seidler, 2010; Seidler et al., 2010). However, it is actually unclear whether and to what extent advancing age impairs skill acquisition. Although some studies suggest that motor skill acquisition is impaired (Cirillo et al., 2010; Coats et al., 2014; Swinnen, 1998; Zimerman et al., 2013), other studies show similar (Cirillo et al., 2011) or even superior (Brown et al., 2009) capacity to acquire new motor skills in old as compared to young adults. One of the reasons for these inconsistencies is that baseline motor performance levels are similar (Rogasch et al., 2009) or different (Brown et al., 2009) between age groups.

In addition to motor skill acquisition, it is equally unclear to what extent age affects motor skill retention. One study reported that old adults only stabilize motor performance after a 24-hour offline period of no training, whereas young adults are able to further increase skill performance beyond levels of stabilization (Brown et al., 2009). In other experiments, the improvements in performance after the 12-hour offline period are smaller in old adults compared with young adults, and young adults further increase performance until a week after training, whereas old adults did not (Nemeth and Janacsek, 2011).

With much inconsistency concerning the effects of age on the magnitude of motor skill acquisition and retention, it is not unexpected that there is also disagreement on the possible mechanisms underlying these processes. For example, diffusion tensor imaging and functional magnetic resonance imaging (fMRI) studies showed contradictory results regarding neuronal mechanisms of motor skill acquisition in aging (Aizenstein et al., 2006; Bennett et al., 2011; Daselaar et al., 2003; Schulz et al., 2014). On the other hand, transcranial magnetic stimulation (TMS) studies revealed consistently no effects of age but inconsistent results regarding the effect

* Corresponding author at: Center for Human Movement Sciences, University Medical Center Groningen, A. Deusinglaan 1, 9700 AD Groningen, The Netherlands. Tel.: +31503616024.
E-mail address: k.m.m.berghuis@umcg.nl (K.M.M. Berghuis).

0197-4580/$ – see front matter © 2016 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.neurobiolaging.2016.06.013

of motor practice on TMS variables. Regardless of age, corticospinal excitability (CSE), measured as the peak-to-peak amplitude of the motor evoked potential (MEP), increased during motor skill acquisition (Cirillo et al., 2010 [left thumb], 2011) or did not change (Cirillo et al., 2010 [right thumb]). In contrast, 1 study showed age-related differences in CSE after 10 minutes of motor practice (Rogasch et al., 2009). CSE increased in young but remained unchanged in old adults. In addition to CSE, age did not either affect changes in short-interval intracortical inhibition (SICI) during motor skill acquisition, although the directions of change are different between studies, showing decreases (Cirillo et al., 2011) or no changes (Cirillo et al., 2010; Rogasch et al., 2009).

The underlying neuronal mechanisms of motor skill retention in aging remain unclear. Only 1 fMRI study has examined age-related changes in neuronal networks during skill retention, showing clear age-related differences in brain connectivity (Lin et al., 2012). Three days after interleaved practice of a motor sequence, functional connectivity increased in old adults between the right and left dorsolateral prefrontal cortex (DLPFC) and between the dorsal premotor cortex and inferior parietal cortex. However, the functional connectivity in young adults increased between DLPFC and the supplementary motor area and inferior frontal gyrus. To the best of our knowledge, no study has yet examined changes in potential neuronal mechanisms of motor skill retention in young and old adults using TMS.

In an effort to address the many inconsistencies, we examined the effects of age on motor skill acquisition and retention as well as potential underlying mechanisms by measuring corticospinal and motor cortical excitability using TMS in both young and old adults. We paid particular attention to baseline differences in motor skills between the 2 age groups (Vallence and Goldsworthy, 2014) by using multilevel analyses. Based on previous studies, we expected that (1) old adults compared with young adults would perform less well at baseline on the visuomotor task (Cirillo et al., 2011); (2) both age groups would improve motor performance similarly relative to baseline (Cirillo et al., 2011); (3) old adults would improve their motor performance less than young adults during the 24-hour offline period; and (4) there would be no age-related differences in practice-related changes in motor cortical and corticospinal function. Furthermore, as attentional resources are known to be involved in motor learning (Dayan and Cohen, 2011; McNevin et al., 2000), we controlled for attentional load of the motor practice. Because attention activates brain areas similar to those used in motor skill acquisition (Dayan and Cohen, 2011; Lin et al., 2012; Niendam et al., 2012) and aging is associated with a decline in attention (Li et al., 2015), we expected that (5) old versus young adults in the attentional control group would improve motor performance to a lesser extent.

2. Methods

2.1. Participants

Twenty-four young adults (18–30 years, 12 male) participated in the main experiment, and the data of these young adults are compared with the data of the 22 old adults (≥65 years, 14 male) who participated in our previous study (Berghuis et al., 2015). In addition to the main experiment, 12 young and 5 old adults participated in a control experiment. All participants were right-handed (Oldfield, 1971). All participants signed an informed consent document before participating in a study protocol that was approved by the Medical Ethical Committee of the University Medical Center Groningen.

2.2. General organization of the study

The young adults performed the same testing procedures and training protocol as the old adults did and as described detailed previously (Berghuis et al., 2015), with the only exception that the Mini Mental State Examination and Groningen Activity Restriction Scale questionnaires were not assessed in young adults. Fig. 1 shows the study design. In summary, participants practiced a wrist flexion-extension visuomotor task, in which they had to match a preprogrammed template as accurately as possible (motor practice group; MP) or only watched the templates for 20 minutes to control for attentional demands (attentional control group; AC). TMS was

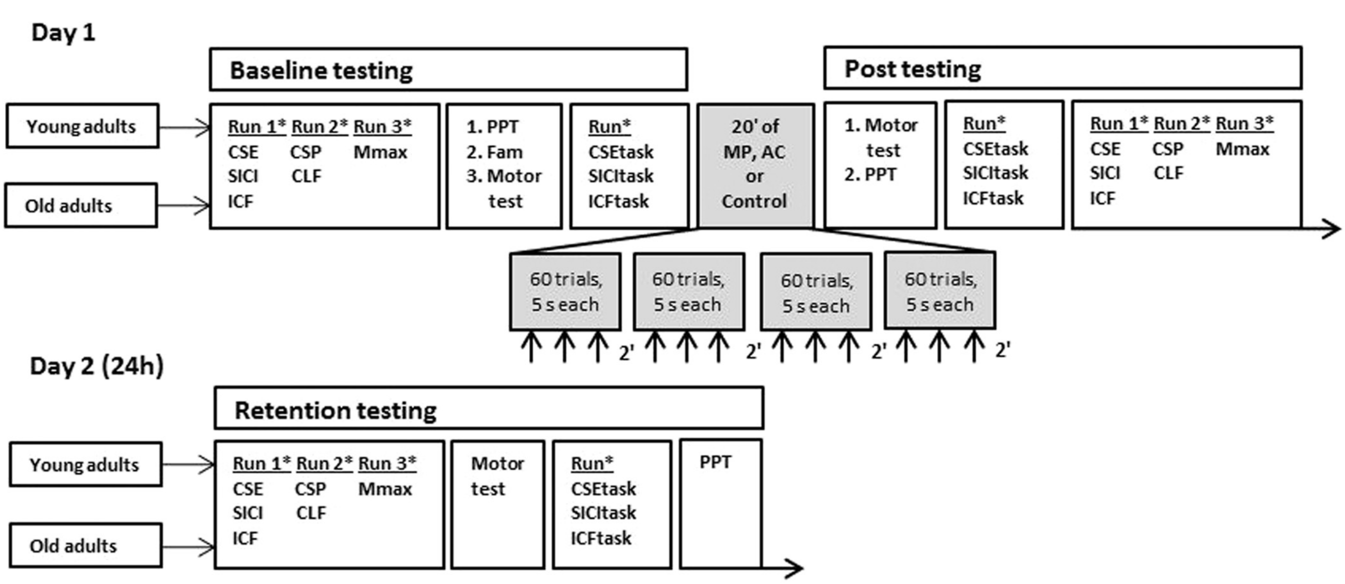

Fig. 1. Young and old adults followed the same experimental design. Day 1 consisted of a baseline test, an intervention, and posttest, and day 2 consisted of a retention test. Upward directed arrows indicate the time when participants performed a counting task to control for attentional drift. The order of the runs within a block and the order of the pulses within a block were randomized (asterisk). Abbreviations: AC, attentional control; CLF, contralateral facilitation; CSE, corticospinal excitability; CSE_{task}, corticospinal excitability during task; CSP, cortical silent period; Fam, familiarization; ICF, intracortical facilitation; ICF_{task}, intracortical facilitation during task; M_{max}, maximal compound action potential; MP, motor practice; PPT, Purdue Pegboard test; SICI, short-interval intracortical inhibition; $SICI_{task}$, short-interval intracortical inhibition during task.