Motor Sequence Learning in Older Adults

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MOTOR SEQUENCE LEARNING IN OLDER ADULTS

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GENERAL INTRODUCTION

In 2017, 18% of the people living in The Netherlands are aged 65 or older, the current Dutch retirement age. In 2060, this age group will account for 26% of the population. In the same period, the proportion of Dutch citizens in the working age range, 20 to 65, drops from 59% to 53% (Centraal Bureau voor de Statistiek, 2016). This means that we have an incredible challenge on our hand if we want to increase or even maintain our current standard of living. One important way to help making sure the aging society will thrive, is by increasing our understanding of the aging process. What happens when people age? Why do even healthy older adults (OA) seem to have difficulties learning new skills, and how can we support them in this respect? The re-LOAD project, a collaboration of universities from the USA, Germany and The Netherlands, addressed these questions by investigating the effect of age on the basic capacity to develop new motor skills. In this project, we first focused on characterizing age differences, and later investigated behavioral and neurophysiological interventions to enhance motor learning. This dissertation describes the studies conducted in The Netherlands.

The tasks used in this research were all centered on motor sequence learning, a flexible paradigm that has been used extensively in previous research on the cognitive underpinnings of motor learning (e.g., Rhodes, Bullock, Verwey, Averbeck, & Page, 2004). This is a highly relevant paradigm since our daily movements consist for a large part of sequences of motor actions. Furthermore, motor sequence tasks are usually implemented in such a way that they require relatively little time to learn, making them suitable for studying automatic processes in lab environments. Literature on cognitive psychology and motor learning has developed many perspectives on automaticity, focusing mainly on inflexibility and resistance to dual-task interference as markers of automaticity (Ashby & Crossley, 2012). In line with this perspective, we here consider performance of sequences automatic when they are performed with limited effort or attentional monitoring (Abrahamse, Ruitenberg, de Kleine, & Verwey, 2013). Young adults (YA) usually reach this level of performance within reasonable time frames. However, OA seem to have more difficulty developing efficient representations of motor sequences and approaching automaticity (Verwey, 2010; Verwey, Abrahamse, Ruitenberg, Jiménez, & De Kleine, 2011). Note that the concept of a representation is essential to the research presented here. In essence, this concept describes how information is represented in memory. A representation of a motor sequence includes information in a particular format or code, which may be verbal, spatial, or motoric (Verwey, Shea, & Wright, 2015). The aim of this dissertation is to answer the questions: how do the representations that OA develop differ from those that YA develop, and how can we support OA in learning new motor skills in an optimal manner?

In this Chapter, the general cognitive and neural changes taking place during aging are considered first. Then, the motor sequence learning paradigm will be described in more detail along with the motor tasks that have been used in this research. The cognitive processes underlying motor sequence performance are then discussed, together with a small overview of the associated neural processes. Finally, a current overview of the literature concerning motor learning deficits and opportunities for improvement in OA is presented.

General age effects on cognitive and neural functioning in healthy OA

One of the most evident age-related changes in cognitive functioning is a declining processing speed (Harada, Natelson Love, & Triebel, 2013; Salthouse, 2000). Surprising to some, this decline already starts in early adulthood. Besides processing speed, mental reasoning capacity and memory decline (Salthouse, 2010). Conversely, the store of factual knowledge usually increases, this is why OA often have a large vocabulary, although, as many OA experience, retrieving information sometimes takes a little more time (Salthouse, 2010).

With advancing age, the healthy brain changes at a structural, biochemical and functional level. A common finding is gray matter atrophy, accompanied by increasing ventricular and cerebrospinal fluid volume. White matter deteriorates too, both in terms of volume and quality (Seidler, 2010). These structural changes are accompanied by biochemical changes like reduced dopamine and serotonin concentrations. Interestingly, neural degradation does not develop uniformly over the brain but some areas are affected earlier than others, the prefrontal cortex being the prime example. Functional brain recruitment patterns change with advancing age, these changes have been hypothesized to be a mechanism to compensate for neural degradation. Hemispheric asymmetry reduction in older adults (HAROLD) is one of the models describing this process stating that, especially in prefrontal areas, activity during task performance is less lateralized in OA than in YA (Cabeza, 2002). Besides reduced lateralization, occipital activity seems to reduce while prefrontal activity increases, an effect described by the so-called posterior-anterior shift in aging (PASA) model (Davis, Dennis, Daselaar, Fleck, & Cabeza, 2008).

The widespread cognitive and neural decline makes it hard to define what exactly constitutes a ‘healthy older adult’ and what type of participants one should include in a study. Implementing inclusion criteria that are too strict will result in poor generalizability, but being too loose will result in a highly variable sample rendering it difficult to find significant effects of experimental interventions. Participants in the studies reported in his dissertation were invited only when they reported no severe motor problems (including limitations using the fingers or arms), and no history of neurological problems, arthritis or rheumatism. The Montreal Cognitive Assessment (MoCA, Nasreddine et al., 2005) was administered to exclude those with mild or severe cognitive impairment, the latter being associated with pathologies like Alzheimer's disease. As suggested by recent research, the cut-off point we used was lower than the original cut-off of 26 as proposed by the MoCA authors, which has been found to be too strict (Freitas, Simões, Alves, & Santana, 2013).

Motor sequence learning paradigms

Motor sequence learning refers to the acquisition of the skill to perform a fixed sequence of movements quickly with high accuracy and little attentional monitoring. In most studies, the sequence is presented using a computer display and participants perform their task using key-presses or by controlling a lever with goal oriented forearm flexion-extension movements. Over time, performance of the sequence improves in terms of speed and accuracy. An important distinction between different types of sequence learning tasks is the way in which ensuing sequences are presented. This can be either in a serial manner where a single sequence is repeated without interruption, or in a discrete manner where a distinct break is incorporated between ensuing sequences. Examples tasks are the, appropriately named, serial reaction time task (SRT, Abrahamse, Jiménez, Verwey, & Clegg, 2010) and the discrete sequence production task (DSP, Abrahamse, Ruitenberg, de Kleine, & Verwey, 2013). The DSP task is more suitable to study preparatory and motor chunking mechanisms since it involves relatively short sequences that are believed to constitute the building blocks that also underlie everyday skilled behavior (Verwey et al., 2015). Furthermore the DSP task involves short sequences followed by a short break. Therefore, participants usually notice the sequence regularity quickly and develop more explicit sequence knowledge, measured by asking the participant to verbalize their sequence, than in the SRT task. Compared to the DSP, the SRT task is more suited for studying implicit sequence learning, since participants usually improve considerably without becoming aware of the regularity (Abrahamse et al., 2010). More importantly, performance in the SRT task typically does not involve motor chunking (Jiménez, Méndez, Pasquali, Abrahamse, & Verwey, 2011). In all, research with these motor tasks has contributed greatly to our understanding of sequence learning. As the DSP task has been used for three out of four experiments reported in this dissertation, and since work with the DSP task has provided the main theoretical framework used here, it is discussed in detail subsequently. The two other tasks that have been used, the flexion-extension (FE) and sequence-tapping task, will then be shortly considered too.

The discrete sequence production task

The typical experimental setting of the DSP task consists of a participant sitting at a table with a monitor in front of him or her. The fingers of both hands rest gently on the keys of the keyboard (Fig. 1A). A row of boxes, or placeholders, is presented on the screen. Each of the placeholders is related to a spatially compatible key on the keyboard. When one of the placeholders is filled with a color, the participant presses the associated key as quickly as possible. The order in which the placeholders are activated denotes the sequence; the screen turns white shortly between successive sequences. Typically, two sequences composed of 3 to 7 elements are practiced during the practice phase. These are presented in a random order. Because each sequence starts with a different element, with practice the task essentially turns from two series of 6-choice RT tasks into a single 2-choice RT task because after initiation, each sequence is performed as a single, automated response. DSP experiments often consist of as much as 500 practice trials per sequence. This allows the participant to perform the sequence in a relatively automatic fashion at the end of practice.

In most DSP studies, the practice phase is followed by an awareness test in which participants are tested on whether they can verbalize their sequence knowledge. If so, they are said to possess explicit sequence knowledge. This is done with a questionnaire asking the participant to write down the individual key presses that make up each of the sequences (‘recall’ test), and to select the two sequences from a list of alternatives (‘recognition’ test). In recent studies, we also asked participants to denote the learned sequences by using the index finger to point at the placeholders in the correct order (Barnhoorn, Döhring, Van Asseldonk, & Verwey, 2016). After this awareness questionnaire, the DSP test phase is administered. The test phase is used to assess the type of sequence representation that has developed. It typically consists of one condition containing the familiar sequences, and one condition with random sequences. By contrasting performance on these blocks it can be determined whether the developed skill is specific for the practiced sequences or whether some kind of task-general skill has developed. In some studies, an additional single-stimulus test condition displays only the first element of the sequence in order to test whether the participant is able to perform the sequence by heart. As will be discussed later, by contrasting the single-stimulus and familiar test condition it can be determined whether participants still benefits from seeing the stimuli.

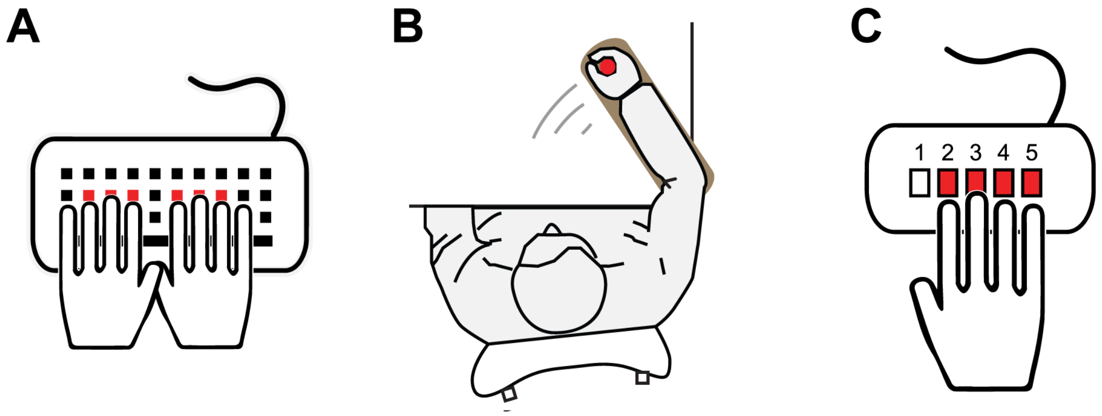

Fig. 1 (A) The DSP task in 6-finger configuration, (B) the FE task, (C) the sequence-tapping task.

The flexion-extension task

The flexion-extension (FE) task requires participants to move a cursor on the screen as quickly and smoothly as possible using elbow flexion-extension movements (Fig. 1B). Participants lay their forearm on a lever that is supported by a near friction-less axle, the handle at the end of the lever is adjusted such that the elbow becomes aligned with the axis of rotation (e.g., Shea, Park, Wilde, & Braden, 2006). The position of the lever is coupled to the position of the cursor on a screen, and in this way, movements can be made to reach a sequence of targets, or to match a wave pattern. The FE task has been used extensively to study effector independent transfer of movement (for a review, see Shea, Kovacs, & Panzer, 2011). Usually, the transfer condition consists of the same type of movements but made with the opposite effector, with either spatially equal or mirrored movement patterns. In the experiment described in Chapter 2, we used the FE task for its lack of overlap in muscle activation patterns with key-press movements. This allowed us to study whether OA are able to use previously developed sequence representations (for instance, after practice with key-presses) in a completely effector independent motor task (using FE movements).

The sequence-tapping task

In the sequence-tapping task, the goal is to perform a sequence that is displayed on the screen continuously (e.g., “3 - 5 - 2 - 4 - 2”) as often as possible. The participant rests the fingers of one hand on a row of keys that are numbered 1 to 5 (Fig. 1C). The keys are then pressed in the sequential order that is presented on the screen, as often as possible in a 3-

minute time window. Because the whole sequence is always displayed, the task involves limited working memory (WM) requirements. In previous studies as well in the study described in Chapter 5, a dedicated response box is used instead of a computer keyboard (Zimerman, Heise, Gerloff, Cohen, & Hummel, 2014), reducing the potential advantage of computer experience that YA often have over OA. Key-presses on this response box take a little more force than on a regular computer keyboard. Compared to the other motor learning tasks, the sequence-tapping task is relatively simple with little cognitive requirements. In Chapter 5, a study is described that used a sequence-tapping task to explore enhancement of motor learning in OA.

Cognitive processing in sequence learning

The main theoretical framework used in this dissertation to describe the development of discrete sequencing skill is the dual processor model (DPM, Abrahamse et al., 2013; Verwey, 2001). This model is based on results from many DSP studies and incorporates features of other sequence learning models (e.g., Hikosaka, Nakamura, Sakai, & Nakahara, 2002; Keele, Ivry, Mayr, Hazeltine, & Heuer, 2003). As the name implies, two processors are assumed to be involved in sequence execution. The cognitive processor is dependent on limited attentional resources while the motor processor is a highly automatic resource. Together, these processors drive three modes of sequence execution as shown in Fig. 2. In the *reaction mode*, the sequence is executed using a stimulus-response (S-R) loop for every element in the sequence. Each response is selected by the cognitive processor and subsequently executed by the motor processor. The reaction mode can therefore be used with familiar and unfamiliar sequences. With practice, associations between ensuing elements of the sequence begin to develop, this is called the *associative mode*. In this mode, external guidance by the movement-specific stimuli is still required, but responses to upcoming stimuli are primed by the preceding response. Note that these associations are potentially represented at a spatial or central-symbolic level (Verwey et al., 2015) and that this level of sequence representation resembles the visuospatial representation in the sequence learning model by Hikosaka et al. (2002). After extensive practice, the associative mode is replaced by the much faster, and less attention demanding, *chunking mode*. The chunking mode relies on motor representations of subsets of the sequence, called *motor chunks*. Motor chunks, a central concept in this thesis, are memory representations of a fixed series of movements. The size of a chunk is limited by working memory capacity (Bo & Seidler, 2009). When performing a short sequence (e.g., 3 elements), one chunk usually holds the whole sequence whereas sequences with over 4 or 5 elements are segmented in multiple chunks. In the chunking mode, the cognitive processor identifies which sequence needs to be performed, which is necessary since in the DSP task it is unknown which sequence will be presented next. After this, it loads the appropriate motor chunk in the motor buffer. The motor processor subsequently executes the sequence of movements. Note that, as depicted in Fig. 2C, the cognitive and motor processors are assumed to race each other in the chunking mode, speeding up the individual responses. Accordingly, in dual-task conditions in which the cognitive processor is engaged in other processes, response times become somewhat slower (Verwey, Abrahamse, & De Kleine, 2010).

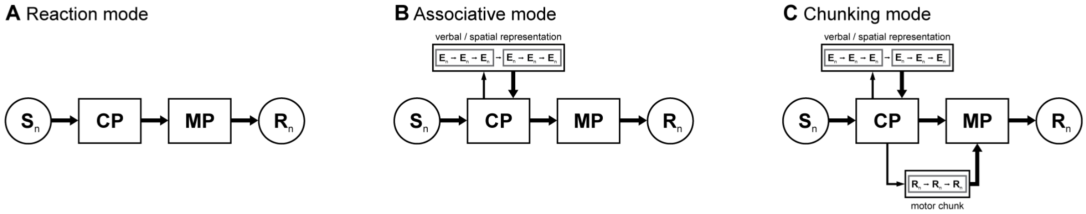

Fig. 2 The DPM consists of 2 processors: the cognitive processor (CP) and the motor processor (MP) that together drive three modes of responding. S_n and R_n denote the current stimulus and response, E_n denotes associations between successive events.

One of the challenges in research on the DPM and motor chunking in general is operationalizing the relevant concepts into measurable dimensions and developing suitable statistical models. The execution modes develop slowly and smoothly over time, and are assumed to overlap partially, these aspects are difficult to model statistically. Furthermore, many factors can influence the pattern of response times (RTs) associated with the performance of a sequence. For instance, regularities in the sequence like trills and runs, or biomechanical properties like reduced flexibility of one of the fingers or wrist rotation to speed up performance all influence RTs in ways that are hard to predict. The usual method to reduce measurement variability (noise) is to average RTs from many trials. However, this is likely to also filter out interesting patterns like changes in chunk structure (Acuna et al., 2014). Numerous interesting algorithms have been developed in order to advance the analysis of chunking (e.g., Acuna et al., 2014; Ramkumar et al., 2016; Wymbs, Bassett, Mucha, Porter, & Grafton, 2012), but these solutions are often applicable only for very specific purposes and using them requires advanced statistical understanding. Furthermore, current methods do not control for biomechanical variability that becomes increasingly prominent with advancing age. In the present work, we have resorted to developing a new, relatively simple outcome measure, the IED, that is based on previous work, easy to interpret and resistant to biomechanical variability in OA. However, finding an optimal solution for this problem remains an important challenge for future research.

The neural basis of sequence learning has been studied extensively over the past decades (for an overview, see Penhune & Steele, 2012). Major brain regions involved include the motor cortex, basal ganglia and the cerebellum. The basal ganglia are likely involved in chunking, as evidenced by an impaired ability to form motor chunks in patients with BG damage (Boyd et al., 2009). The cerebellum is involved in processes related to sensorimotor integration, error correction and the formation of internal models. The primary motor cortex (M1) is the major cortical output to the descending motor system and there is strong evidence for its involvement in the storage and representation of new motor memories (e.g., Wiestler & Diedrichsen, 2013).

Motor learning in OA: Deficits and interventions

Motor performance deficits displayed by OA include coordination difficulty (Seidler, Alberts, & Stelmach, 2002), increased variability of movements (e.g., Contreras-Vidal, Teulings, & Stelmach, 1998), and a pronounced increase in movement duration (e.g., Barnhoorn et al., 2016). The slower movements seem to be partly attributable to physical and neural deterioration, but are probably also driven by a tendency to emphasize accuracy over speed (Goggin & Meeuwsen, 1992; Salthouse, 1979; Walker, Philbin, & Fisk, 1997). This may result from strategic preference or may even be imposed by age-related decrements in brain connectivity (Forstmann et al., 2011). Regarding sequence learning in particular, there is growing evidence that OA have difficulties developing motor chunks. Findings indicate that they prepare upcoming elements, an important indicator of chunking behavior, to a lesser extent than YA do (Verwey, 2010; Verwey et al., 2011). Instead, they remain reliant on external stimuli. And when OA do develop motor chunks, they seem to consist of fewer elements than those of YA because of reduced visuospatial working memory capacity (Bo, Borza, & Seidler, 2009). Whereas these studies used key-press tasks, reduced chunking behavior has been shown when OA use the FE task as well (Panzer, Gruetzmacher, Fries, Krueger, & Shea, 2011; Shea et al., 2006). Building on these insights of reduced motor chunking, a logical next step is to explore opportunities to stimulate the use of chunking behavior in OA, which is what we did in the studies described in Chapter 3 and 4.

The ability to mitigate age-related cognitive and motor deficits is highly relevant in our graying society, and while the current dissertation focuses on motor chunking and tDCS, many other avenues have been explored in previous research. For instance, a recent review concluded that cognitive training programs can enhance memory performance, executive functioning, processing speed, and attention (Reijnders, van Heugten, & van Boxtel, 2013). Regarding motor development, training programs to improve balance have received much attention, even resulting in evaluations of exercise games using the commercially available game platform Nintendo Wii. Results are promising and show that exercise using this platform can improve balance in OA (Laufer, Dar, & Kodesh, 2014). Besides behavioral evaluation, interventions have also been assessed in terms of their success in preventing or compensating for age-related brain changes. Physical exercise has been shown to be associated with greater brain volume, recruitment of additional neural resources (Seidler et al., 2010).

A large body of research on enhancement of motor learning focused on the application of transcranial direct current stimulation (tDCS). Although tDCS research has a long history, systematic investigations started around 1998 (Priori, Berardelli, Rona, Accornero, & Manfredi, 1998). It is an accessible and non-invasive method that works by applying a low-intensity current between two electrodes applied to the scalp. The current running through the cortex alters the excitability of the stimulated brain area as measured with transcranial magnetic stimulation pulses (TMS, Stagg & Nitsche, 2011). Cortical excitability reflects neuron reactivity and specificity and is a fundamental aspect of human brain function. Through this mechanism tDCS can eventually increase long-term potentiation of new motor memories. Evidence for enlarged excitability in OA has been established through studies finding increased responses to TMS pulses after tDCS stimulation (e.g., Fujiyama et al., 2014). Two recent reviews discuss the effects of tDCS on motor learning in OA: Summers, Kang & Cauraugh (2016) discuss 11 motor learning OA tDCS studies; Perceval, Flöel & Meinzer (2016), discuss 13 studies in the motor domain. The studies discussed in these reviews include two sequence tapping studies (Zimerman et al., 2013, 2014); two studies used a finger tapping choice RT task (Heise et al., 2014; Lindenberg, Nachtigall, Meinzer, Sieg, & Flöel, 2013); two studies used a pegboard test (Parikh & Cole, 2014, 2015); the Jebson-Taylor hand function test was used in yet two other studies (Hummel et al., 2010; Marquez, Conley, Karayanidis, Lagopoulos, & Parsons, 2015); and other studies focused on ball rotation (Hoff et al., 2015); postural control (Zhou et al., 2015); reaching (Hardwick & Celnik, 2014); transfer in a tracking task (Goodwill, Daly, & Kidgell, 2015); visuomotor adaptation (Panouillères, Joundi, Brittain, & Jenkinson, 2015); and wrist extension (Goodwill, Reynolds, Daly, & Kidgell, 2013). Overall, the benefit of tDCS on performance in motor tasks is substantial for OA, with a mean effect size of 0.65 (Summers et al., 2016).

In general, research suggests that tDCS can play an important role in enhancing both cognitive and motor performance in older adults (Summers et al., 2016). On the other hand, when studying the tDCS literature, most readers will conclude there is also quite a degree of skepticism, criticism, and unexplained variability in the outcomes (Bestmann, de Berker, & Bonaiuto, 2014; Horvath, Carter, & Forte, 2014; Horvath, Forte, & Carter, 2015a, 2015b; Perceval et al., 2016). Especially the differential effects of tDCS on OA and YA demand attention. That is, in several studies tDCS interventions inducing beneficial effects in YA did not improve or even impaired performance in older adult (Perceval et al., 2016). Accordingly, there has been a call to advance the field by taking a more systematic, incremental approach as opposed to the somewhat haphazard exploratory, proof-of-principle style that has been popular till now. In line with this view, replications, fundamental physiological investigations and modeling studies are increasingly valued (Bestmann et al., 2014; Summers et al., 2016). In the light of these developments we performed a study including a replication condition of an important previous result combined with an incremental step forward, which is described in Chapter 5.

Dissertation overview

The experiments presented in this dissertation follow the research questions of the overarching re-Load project: How do the representations that OA develop differ from those that YA develop, and how can we support OA in learning new motor skills? Accordingly, the first two empirical Chapters focus on characterizing age differences, exploring abilities preserved and potentially lost in OA. The last two empirical Chapters investigate behavioral and neurophysiological interventions to enhance motor learning.

Chapter 2 explores age-related similarities and differences in sequence representations. One of the fundamental features of most models of motor learning is that over time, two types of representations develop. Early in learning, an effector-independent representation similar to the DPM's associative mode improves performance and after extensive practice, a more efficient motor representation similar to the motor chunks formed in DPM's chunking mode is developed (Hikosaka et al., 1999; Keele et al., 2003; Verwey et al., 2015). By investigating transfer of sequence knowledge between movement types that are unrelated in terms of muscle activation and response location (key-presses and FE movements), we investigated whether the early visuospatial (effector-unspecific) representations are as flexible and intact in OA as in YA.

Chapter 3 investigates age-differences in the development of motor representations, that is, motor chunks. Previous research suggested that OA have difficulty developing these efficient representations (Verwey, 2010). Using the DSP task, this experiment aimed to answer the question whether OA are indeed unable to develop motor chunks, or whether they need more practice to develop motor chunks.

Chapter 4 examines whether strategic preference affects whether and how quick OA develop chunking behavior. We hypothesized that the careful, error-averse way in which OA conduct the DSP task may stimulate their reliance on external stimuli (Verwey, 2010) and prevent them from developing more efficient representations. Therefore, this study instructed participants to perform a DSP task focusing either on speed or on accuracy.

The final empirical Chapter describes a study on the potential of tDCS as a technique to enhance motor learning in OA. Because the aim was to contribute to the robustness of existing results, we conducted a study that includes a replication condition of an important previous experiment (Zimerman et al., 2013). We extended on the previous findings by adding an additional test condition allowing us to answer the question whether tDCS enhances sequence-specific learning or the development of task-general skill. Chapter 6 provides a summary and discussion of the results.

Similar representations of sequence knowledge in young and older adults: A study of effector independent transfer

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ABSTRACT

Older adults show reduced motor performance and changes in motor skill development. To better understand these changes, we studied differences in sequence knowledge representations between young and older adults using a transfer task. Transfer, or the ability to apply motor skills flexibly, is highly relevant in day-to-day motor activity and facilitates generalization of learning to new contexts. By using movement types that are completely unrelated in terms of muscle activation and response location, we focused on transfer facilitated by the early, visuospatial system.

We tested 32 right-handed older adults (65 – 74) and 32 young adults (18 – 30). During practice of a discrete sequence production task, participants learned two 6-element sequences using either unimanual key-presses (KPs) or by moving a lever with lower arm flexion-extension (FE) movements. Each sequence was performed 144 times. They then performed a test phase consisting of familiar and random sequences performed with the type of movements not used during practice. Both age groups displayed transfer from FE to KP movements as indicated by faster performance on the familiar sequences in the test phase. Only young adults transferred their sequence knowledge from KP to FE movements. In both directions, the young showed higher transfer than older adults. These results suggest that the older participants, like the young, represented their sequences in an abstract visuospatial manner. Transfer was asymmetric in both age groups: there was more transfer from FE to KP movements than vice versa. This similar asymmetry is a further indication that the types of representations that older adults develop are comparable to those that young adults develop. We furthermore found that older adults improved less during FE practice, gained less explicit knowledge, displayed a smaller visuospatial working memory capacity and had lower processing speed than young adults. Despite the many differences between young and older adults, the ability to apply sequence knowledge in a flexible way appears to be partly preserved in older adults.

INTRODUCTION

Western societies are aging. This development calls for a better understanding of how age interacts with health and capabilities. Older adults show declining performance in the cognitive and physical domains, resulting in reduced motor performance and changes in motor skill development (Salthouse, 2004; Voelcker-Rehage, 2008). These declines are correlated with reduced neural integrity (Seidler et al., 2015) and associated with more widespread engagement of neural resources, possibly in order to compensate for the reduced integrity (Seidler et al., 2010). Research has indicated that aging may have distinct effects on different aspects of motor learning: complex tasks are affected more than low-complexity tasks and fine motor performance is affected more than gross motor performance (Voelcker-Rehage, 2008). We here focus on changes in motor learning and more specifically, how cognitive representations of motor skills differ between older and young adults. We investigated sequence representations using a discrete sequence-learning paradigm (Abrahamse et al., 2013; Verwey, 1999) in which sequence knowledge was transferred between key-press (KP) and lower arm flexion-extension (FE) movements. A flexible application of motor skills is the basis of day-to-day motor activity and allows generalization of learning to new conditions and contexts.

Sequence learning and transfer of sequence knowledge

The ability to apply sequence knowledge in a flexible way is assumed by most models of sequence learning. For instance, the influential scheme of motor learning by Hikosaka et al. (1999) proposes that a sequence is learned simultaneously using two independent systems: an early system based on visuospatial coordinates, and a late system using motor coordinates. The visuospatial coordinate system is more dependent on attentional capacity and is believed to allow for transfer of sequence knowledge to other effectors. A second model of sequence learning that has received much attention is the dual-system theory by Keele, Ivry, Mayr, Hazeltine and Heuer (2003). They propose that a multidimensional and a unidimensional system together facilitate learning. The multidimensional system can be implicit or explicit, is protected by attentional constraints and is associated with the ventral pathway. The unidimensional system only facilitates implicit learning, and is associated with the dorsal pathway. In a transfer task, the multidimensional system is thought to enable the use of previously learned stimulus-stimulus associations with a new response mode. A third model of sequence learning is the Cognitive framework for Sequential Motor Behavior (C-SMB) proposed by (Verwey et al., 2015). This framework suggests that, depending on the task, sequence learning can develop at three levels of cognitive processing: the perceptual, central and motor level. This framework also allows for transfer of sequence knowledge, based on associations on the perceptual (e.g., visuospatial) and central (e.g., central-symbolic, potentially using explicit knowledge) level. Unsurprisingly, none of the three models discussed here perfectly accounts for all aspects of motor learning. For instance, Hikosaka et al. (1999) does not specifically address central levels of sequence representation; the model by Keele et al. (2003) is subject to ongoing debate about the definition of a dimension; and the C-SMB model (Verwey et al., 2015) has not been extensively validated on the neural level. However, the models do share the prediction that early in learning, an effector independent representation develops that can be used in situations where novel effectors are used. Furthermore, in all three models, the system facilitating transfer is attention-driven.

In accordance with these models, there is now much evidence that people are able to apply sequence knowledge flexibly when using different types of movements. For example, studies have shown transfer of sequence knowledge from finger-movements to arm-movements (Cohen, Ivry, & Keele, 1990; Grafton, Hazeltine, & Ivry, 1998), inter-manual transfer of sequence learning with finger-movements (Parsons, Harrington, & Rao, 2005; Verwey & Clegg, 2005; Verwey & Wright, 2004; Wiestler, Waters-Metenier, & Diedrichsen, 2014), and inter-limb transfer of sequence learning with FE movements with the forearm (Kovacs, Muhlbauer, & Shea, 2009). A recent review of the transfer literature is provided by Shea, Kovacs and Panzer (2011). Based on these results, the ability of effector-independent transfer of sequence knowledge in young adults is well supported. However, less is known about how this ability is retained over the life span and whether age affects the representations that are developed.

Older adults, sequence learning and transfer

Studies on sequence learning in older adults have indicated a number of differences in learning compared to young adults. Regarding the rate of acquisition, results have been somewhat ambiguous. Namely, in some studies older adults acquired sequence knowledge less quickly than young adults (Curran, 1997; Daselaar, Rombouts, Veltman, Raaijmakers, & Jonker, 2003; Shea et al., 2006), in other studies at the same rate (Seidler, 2006) and in yet another experiment older adults even showed more skill during acquisition than young adults (Brown, Robertson, & Press, 2009). Sequence complexity may play a role here: differences between young and old become more pronounced with increasing sequence complexity, for instance, when the sequences include a second-order predictive structure (Curran, 1997).

Sequence representations and the corresponding movement patterns that older adults develop seem to be less structured. That is, sequences are less efficiently organized in the smaller subsequences (i.e., called motor chunks) typically found in young adults (Shea et al., 2006; Verwey, 2010; Verwey et al., 2011). These reductions in the ability to apply a structure to the sequence have been found to be related to declines in visuospatial working memory (Bo et al., 2009; Bo, Jennett, & Seidler, 2012). Furthermore, the problems in developing an efficient representation may also be related to the idea that older adults remain more reliant on external guidance (Verwey, 2010). In other words, older adults may be learning the general task, but younger adults also learn the sequence. This explains previous findings that older adults improved more slowly than young adults on a repeated sequence, but improved as much over time as young adults in performing random sequences (Shea et al., 2006). Furthermore, older adults' difficulty in developing and maintaining a sequence representation is also apparent in consolidation, which has been shown to be reduced compared to young adults (Brown et al., 2009). Clearly, a number of previous findings show that older adults have more difficulty developing efficient sequence representations and maintaining them.

Research on transfer of sequence knowledge can help us understand how representations differ between young and older adults. For example, a study by Dickins, Sale and Kamke (2015) showed that older adults were able to transfer sequence knowledge obtained in a sequential finger-thumb opposition task to the non-practiced hand. However, another study suggests otherwise: Panzer, Gruetzmacher, Fries, Krueger and Shea (2011) investigated differences in representations of sequence knowledge between age groups using an interlimb practice paradigm. Young and older adults practiced with their right or left arm on day one and with the contralateral limb on day two. The groups performed either the same visuospatial movement sequence or a visuospatially mirrored movement sequence on the second day. Using this paradigm, the authors found that only the young group benefited from this additional practice on day two, and only when sequence presentation was the same on a visuospatial level (non-mirrored). Older adults did not show a clear benefit of the second day of practice in any of the conditions, suggesting that switching effector imposed more problems for them than for younger adults. The differential outcomes between this study and the Dickins et al. (2015) experiment may have to do with task complexity: Panzer et al. (2011) used much longer sequences (16 vs. 4 elements) that were performed using a novel method of responding, which probably took more time getting familiar with than the simple finger-to-thumb opposition task used by Dickins et al. (2015).

Concluding, although results are not fully consistent, sequence representations in older adults may well be different from those in young people: older adults have more difficulty developing and utilizing sequence knowledge with different effectors.

Current experiment

In most previous transfer studies with young (e.g., Kovacs et al., 2009; Parsons et al., 2005) as well as with older adults (Dickins et al., 2015; Panzer et al., 2011), transfer was to the mirrored arm or hand. A part of this kind of transfer could potentially depend on motor representations because sequence practice with one effector has been found to have a bilateral effect in the primary motor cortex (Wiestler et al., 2014). Hence, we cannot be entirely sure what type of representation facilitates transfer between mirrored movements. To further disentangle potential age differences in sequence learning, we here focused on transfer purely facilitated by the visuospatial system that is described by most models of sequence learning (Hikosaka et al., 2002; Verwey et al., 2015). While we will mainly refer to this system using the term visuospatial representation, note that types of central or relational coding may be part of this system too (e.g., Verwey et al., 2015). Accordingly, we chose to investigate transfer of sequence knowledge between two frequently used sequencing paradigms, namely sequences of KP and sequences of lower arm (FE) movements. With this paradigm, the effectors involved are highly independent in terms of muscles activated during the movements and in terms of response locations so that any transfer relies on applying visuospatial representations and is independent of the motor representations that may have developed. We made the visual presentation of the tasks equal for both types of movements to facilitate optimal use of visuospatial representations.

Recently, it has been suggested that transfer of sequence knowledge between different contexts involves the adjustment of existing visuospatial sequence representations (Verwey, Groen, & Wright, 2016). This adjustment of visuospatial representations may be used also in our task when the movements of a familiar sequence are adjusted to execute different movements. Earlier research showed that in such a situation transfer may be asymmetric. Specifically, it was found that transfer was higher from FE sequences to KP sequences than from KP to FE sequences (Shea & Aranda, 2005, see Dean, Kovacs, & Shea, 2008). This finding is consistent with the notion that executing an aimed movement in a FE sequence involves more feedback processing and attentional demands than executing a key-press movement in a KP sequence (e.g., Cruse, Dean, Heuer, & Schmidt, 1990; Glencross & Barrett, 1992). This cognitive effort is likely to interfere more with the adjustment of existing visuospatial sequence representations during an FE movement than during a KP movement. Another finding corroborating that transfer involves adjustment of existing representations is that movement sequences in an endoscopic task showed more transfer of practice from a complex environment with precise movements to an easier task environment than vice versa (Verwey, Stroomer, Lammens, Schulz, & Ehrenstein, 2005). Hence, we expected more transfer from FE sequences to KP sequences than vice versa.

In the current study, older and young participants practiced two 6-element sequences with either right-hand KP or with right arm FE movements. During the test phase that followed, they performed random and familiar sequences with the non-practiced movement type (e.g., KP practice was followed by a FE test phase). We hypothesized that the visuospatial system that young adults use (Hikosaka et al., 1999; Keele et al., 2003; Verwey et al., 2015) works in a similar way in older adults. Thus, we expected that both age groups would be able to transfer sequence knowledge between the movement types and would perform familiar sequences in the test phase faster than the random sequences. However, because of indications of reduced processing speed in older adults (e.g., Salthouse, 2000), we expected less transfer in the older group than in the younger group. In anticipation of this result, we explored whether processing speed is associated with transfer between the two sequencing tasks because a higher processing speed may allow for faster adjustment of the available sequence presentations (Verwey et al., 2016). In addition, we measured visual spatial working memory (VSWM) capacity as this capacity has been associated with the rate of learning, probably because a larger working memory allows for easier memorizing of sequential elements (Bo et al., 2009). Finally, we assessed explicit knowledge of the practiced sequences. This variable has often been found to be associated with higher execution rates, especially when sequence execution rate is limited by some other factor (Verwey, 2015). It has been frequently argued that explicit sequence knowledge is not associated with motor, but instead with more abstract central representations like visuospatial representations (e.g., Jeannerod, 1997), so explicit sequence knowledge might be associated with the amount of transfer in the present study too.

METHODS

Participants

We recruited older participants (65-75) via advertisements in local newspapers; young participants (18-30) were students participating for course credits. The older adults were only invited for participation when they reported that none of the following applied: severe motor problems; using a wheelchair; limitations in using the fingers or arms; history of neurological problems or stroke; arthritis or rheumatism; color-blindness. Data from 9 older participants was excluded: five stopped participation or were excluded because task performance led to discomfort or pain in the fingers, wrist or arm; one scored below our cut-off of 23 on the Montreal Cognitive Assessment (MOCA, Nasreddine & Phillips, 2005); two others showed extreme error rates in the test phase; one stopped participation because of a lack of motivation. The remaining 32 older adults (20 females) had a mean age of 69.4 ± 2.7, and scored 27.8 ± 1.9 on the MOCA[1]. The 32 young adults (23 females) had a mean age of 22.4 ± 2.7, with a MOCA score of 28.4 ± 1.4. All participants were right-handed as indicated by the Edinburgh handedness inventory (Oldfield, 1971). The ethics committee of the University of Twente approved the study and all participants provided informed consent.

Apparatus

Participants sat at a table with a 22 inch wide-screen monitor placed at 62 cm from the edge of the table. During task performance they responded using either KP movements with the four fingers of the right hand on a standard keyboard or using forearm FE movements with a lever that was fixed to the table (Fig. 1). The lever was supported by a vertical, nearly frictionless axle. The elbow was aligned with the axis of rotation and the participant held a handle that was shifted according to the length of the arm. An A/D converter attached to a potentiometer recorded the location of the lever at 500 Hz. The FE task was presented using 32-bit Matlab 2014b in combination with PsychToolBox 3.0.11 (Kleiner, Brainard, & Pelli, 2007). The KP and visual spatial working-memory tasks were presented using E-Prime 2.0.

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[1] One participant scored 23, and indicated that she was not native Dutch and did not know all the words in the verbal memory task. She fully understood all instructions and was included in the analysis.

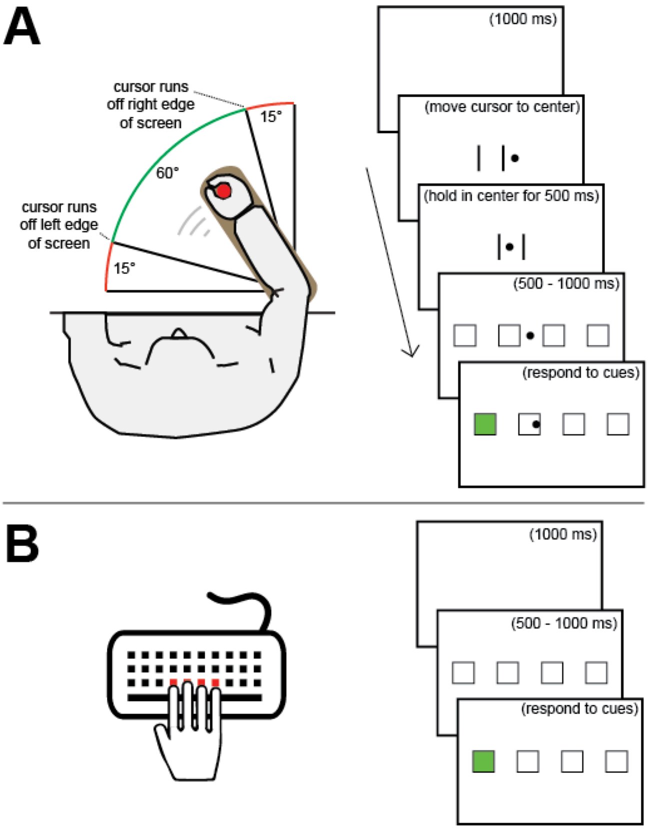

Fig. 1 (A) Task set-up and visual presentation for the flexion-extension (FE) movements. (B) Task set-up and visual presentation for the key-press (KP) movements. The remarks between brackets were not displayed during the tasks.

Design and procedure

All participants were assigned to one of two task-order groups. They either practiced the sequences using FE movements and were tested on sequence knowledge with KP movements (FEtoKP group) or vice versa (KPtoFE group).

Participants first completed (1) a handedness form (Oldfield, 1971) at home. The visit to the lab started with administration of the (2) MOCA followed by (3) a VSWM task and (4) a 90 seconds digit symbol substitution task to assess processing speed (Wechsler, 1955). Then, participants filled in (5) an ad-hoc self-report fatigue scale after which they were given a 3-minute break. After this break, the experiment started with (6) a short familiarization phase for each of the movements, starting with the movement type the participant would use during the later test phase. Participants were shown how errors are made and what the error feedback looked like. Then, participants worked through (7) a practice phase using one of the movement types. Following the practice phase, (8) explicit sequence knowledge was measured in three ways using a questionnaire. Participants were first asked to write down the order of the elements using 1 to indicate the leftmost element, 2 to indicate the second, and so on. Then, the target locations were shown on the screen again and participants pointed out the sequences with their index finger. Finally, they were asked to select their sequences from a list of 18 alternatives. After this, (9) a second self-report fatigue scale was filled in and participants started the test phase using the non-practiced type of movements. During (10) the test-phase, a block of random and a block of familiar sequences were performed; the order of these blocks was counterbalanced across participants. After the test phase (11) a final self-report fatigue scale was filled in, participants were debriefed and the experiment was finished. Note that we examined explicit knowledge before the test phase because the order of random and familiar test phase blocks was counterbalanced and the questionnaire would possibly be affected by interference from the random test block in a different way depending on the order.

Discrete sequence production task

The sequence production task was implemented in a similar way for both types of movements (see Fig. 1). Black outlines of four 38*38 mm placeholders were horizontally presented with 65 mm spacing between them. A placeholder received a green fill when it became the active target. The screen background was white. When using FE movements, a vertically centered, round, black 8 mm cursor was presented to indicate the location of the lever. Before each trial, this cursor had to be held in the center area of the screen, indicated by two vertical black lines 65 mm apart, for 500 ms. Each trial started with a 500 to 1000 ms display of the placeholders. When using KP movements, pressing a key during this period resulted in an error message and the display of the placeholders was restarted. When using FE movements and moving the cursor away from the center during this period, the 2 vertical lines were reinstated and the cursor had to be held in the center for 500 ms again. After the placeholder screen, the first target became active, directly after the correct response the second became active, and so on. When an error was made, the sequence was terminated and a centered red exclamation mark was shown for 500 ms. Between trials, a 1000 ms blank screen was shown.

Before starting the KP familiarization phase, participants were instructed to lay their right-hand fingers on the C, V, B and N keys and press the spatially corresponding key when a target became active. They also received the instruction that pressing the wrong key or responding too slowly would lead to an error. The maximum RT was 2000 ms when using KP and 3000 ms when using FE movements. Prior to the FE familiarization phase, participants received instruction to use the lever to move the cursor to the active target.

Furthermore, the instruction noted that responding too slowly or moving the cursor too far over the target after hitting it (so that the following square or the end of the screen would be hit) would lead to an error. In both familiarization phases, 10 trials of random 6-element sequences were practiced. At the start of familiarization and each practice block, participants received the instruction to respond quickly without making too many mistakes (less than 11%).

Before starting the practice phase all participants were told that they were going to learn two sequences of six elements each. Based on our previous research, six element sequences are sufficiently difficult to find individual differences between participants, but easy enough to make sure all participants will learn the sequence to some extent (Abrahamse et al., 2013). They were not told that they would be tested on their sequence knowledge or that they would need to perform a different type of movement later. Practice consisted of 6 blocks with 48 trials per block and a 120 seconds break in between blocks. In total, each sequence was performed 144 times. Every block held 2 sub-blocks with 40 seconds break in between. During all breaks, the error percentage for the previous sub-block was displayed with a note stating that the participant either made too many errors (when 11% or above), or that he or she did well. Below this, the mean RT in ms was displayed. At the bottom of the screen, a counter showed the remaining time for the break in seconds. The spacebar had to be pressed to start the next block (with the left hand when using FE movements) so that when needed, participants were able to extend the break.

The test phase was performed using the movement type not used during practice. The test phase consisted of one block including the practiced sequences and one block with random sequences. Each test block consisted of 24 trials with a 40 seconds break in between the blocks. Before starting each test block, participants were informed whether the targets would follow the same order as during practice or no fixed order at all. The order of the two test blocks was counterbalanced over participants.

All participants practiced the same two sequences. The order of elements for sequence A was: 1; 3; 2; 4; 1; 2 (where 1 indicates the left-most target). The order for sequence B was: 4; 1; 3; 2; 4; 3. These sequences are balanced in whether the first location is left or right of the starting position, the total distance covered, and the number of times a one- two- or three-element distance is covered. Furthermore, every element is a turning point, making it impossible to hit multiple targets in one sweep, and every target is used three times in total over the 2 sequences. The sequences were presented in random order. For the random test phase block, the same 24 pseudo-random sequences were used for all participants and presented in random order. For these sequences, all elements were turning points too and locations were never immediately repeated.

Visuospatial working-memory task

We used a version of the visuospatial working-memory task published by Luck and Vogel (1997, Experiment 1). Each of the 120 trials of the task started with a 1000 ms fixation screen presenting a centered plus sign. Then, participants viewed a sample array of randomly placed colored squares on a grey background for 100 ms. The colors of the squares were randomly determined as well, multiple squares could have the same color. After this, a blank screen was presented for 900 ms, followed by the test array which was presented until the response or until a threshold of 2000 ms had passed. The test array was equal to the sample array except for the fact that one square was encircled. Participants were asked to press “a” when the color of that square was the same or “l” when it was different compared to the sample array, which happened half of the trials. On the top corners of the front of the monitor, reminder labels for the keys were placed: “same” on the left and “different” on the right. After a trial, participants received feedback about whether the response was correct, and could continue to the next trial by pressing “a” or “l”. The array consisted of 2, 4, 6 or 8 squares; every array size was used 30 times. The possible colors were: blue, red, yellow, purple, green, black, and white.

Analyses

We defined response time (RT) as the time between the onset of an active target and the correct response. Note that after a correct response, the next target became active immediately. For all RT analyses, we excluded the first trial of every sub-block and trials containing an error. Then, we excluded trials with a mean RT that was above a threshold of the mean trial RT plus 2.5 * standard deviation of mean trial RTs in that sub-block. Because absolute RTs in older adults and young adults are quite different, we used a percentage transfer score to allow comparison between the age groups. Transfer was calculated as the percentage speed difference between mean RTs of each participant’s familiar and random test block: (random RT - familiar RT) / random RT * 100. Note that this score does not control for the amount of learning during the practice phase. For that, a random sequence block would be needed at the end of the practice phase. We decided not to include such a block to prevent potential differential interference effects between the age groups. Learning rate was calculated as the percentage difference between mean RTs of the first and last sub-block of the practice phase: (RT sub-block 1 – RT sub-block 12) / RT sub-block 1 * 100. Unless stated otherwise, we report explicit knowledge based on the combined average of the number of elements correctly written down and the number of elements correctly pointed out during the explicit knowledge questionnaire (correct elements were counted from the start to the first mistake). All correlations we report are Pearson product-moment correlations. When the assumptions of sphericity were violated we applied the Greenhouse–Geisser correction, corrected p-values and original degrees of freedom are reported. Proportions of errors were arcsine transformed before analysis (Winer, Brown, & Michels, 1991).

RESULTS

Practice phase

The practice RT and accuracy data were analyzed with a mixed 2 (Age) x 2 (Task) x 12 (Practice Sub-block) repeated-measures ANOVA (see Fig. 2)[2]. We found an effect of Practice Sub-block, $F(11, 660) = 111.74, p < .005, \eta_p^2 = .651$, indicating that participants got faster over time. Older adults were slower than young adults, $F(1, 60) = 68.29, p < .005, \eta_p^2 = .532$. The effect of Task was significant too, $F(1, 60) = 38.05, p < .005, \eta_p^2 = .388$, indicating that KP movements were performed quicker than FE movements. Age group interacted with Task, $F(1, 60) = 8.15, p = .006, \eta_p^2 = .12$, indicating that the RT difference between young and older adults was larger in the KP than in the FE task. Age group interacted with Practice Sub-block too, $F(11, 660) = 8.15, p < .005, \eta_p^2 = .12$, suggesting that, overall, young adults improved more than older adults. Practice Sub-block did not interact with Task, $F(11, 660) = 1.44, p = .226$, indicating that when Age group is disregarded, learning rates were not significantly different between the tasks. The three-way Task x Age group x Practice Sub-block interaction, $F(11, 660) = 11.52, p < .005, \eta_p^2 = .161$, showed that improvement in the KP task was similar for the Age groups, whereas in the FE task it was lower for the older adults.

Analysis of errors made during the practice phase indicated a main effect of Practice Sub-block, $F(11, 660) = 3.13, p < .005, \eta_p^2 = .05$ (see Fig. 2). Furthermore, the amount of errors differed significantly between tasks, $F(1, 60) = 67.3, p < .005, \eta_p^2 = .529$. The interactions with, and main effect of, age group were not significant.

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[2] While we found some indications for heteroscedasticity we report the analyses on the raw RTs. An ANOVA with log-transformed RTs removed the heteroscedasticity but showed the same significance pattern.

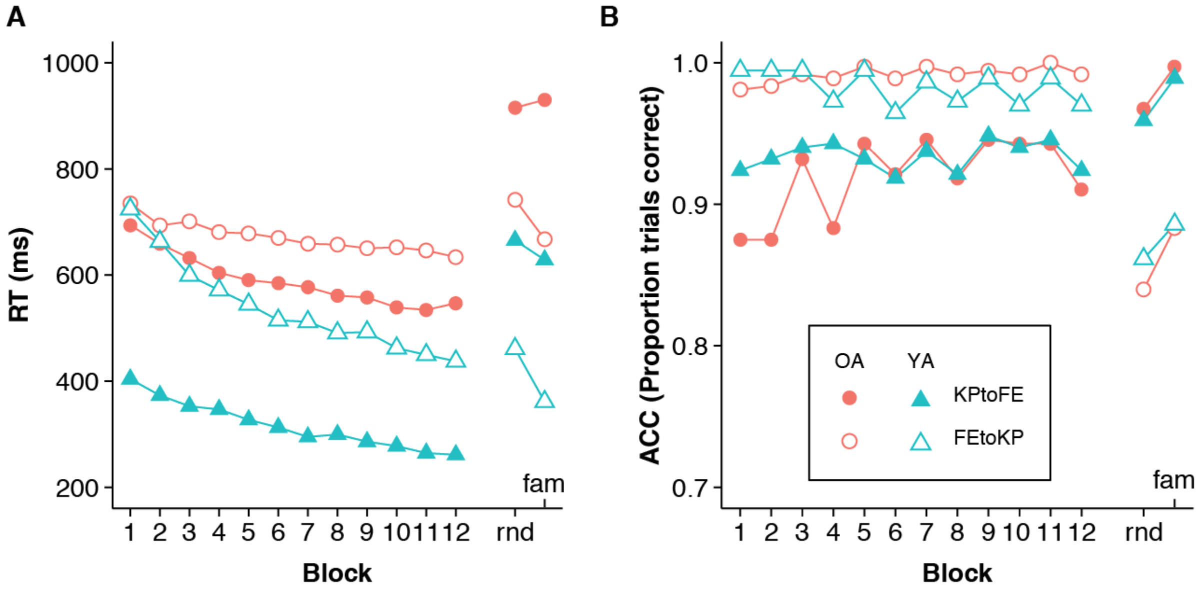

Fig. 2 (A) RT and (B) accuracy development during practice and test blocks. Rnd = random test condition, fam = familiar test condition. The order of test conditions was counterbalanced. Note that regarding FE movements, the older KPtoFE group is slower in the test phase than the older FEtoKP group is in the first block of the FEtoKP condition. Inspection of the FE movements during the familiarization trials suggested a baseline difference between the task groups.

Test phase

To determine whether transfer scores were larger than zero, we performed one-sample t-tests on the sub-samples based on task-order and age. Young adults showed transfer in the KPtoFE condition (*M* = 5.6 %, *t*(15) = 2.39, *p* = .031) and in the FEtoKP condition (*M* = 22.3 %, *t*(15) = 8.17, *p* < .005) (see Fig. 2 and Fig. 3). Older adults showed transfer in the FEtoKP condition (*M* = 11.1 %, *t*(15) = 3.96, *p* < .005) but not in the KPtoFE condition (*M* = -1.8 %, *t*(15) = -0.94, *p* = .361). Group comparison with a 2 (Age) x 2 (Task-order: FEtoKP vs. KPtoFE) ANOVA indicates that older adults showed less transfer than young adults, *F*(1,60) = 14.25, *p* < .005, η_p^2 =.19, and that there was more transfer in the FEtoKP condition than in the KPtoFE condition, *F*(1,60) = 35.90, *p* < .005, η_p^2 =.37. The interaction was not significant, *F*(1,60) = 0.61, *p* = .437, η_p^2 =.01.

Analysis of the errors in the test phases with a mixed 2 (Age) x 2 (Task) x 2 (Test block: familiar vs. random) repeated-measures ANOVA indicated that more errors were made in the random test condition than in the familiar test condition, *F*(1, 60) = 15.1, *p* < .005, η_p^2 = .201 (see Fig. 2). Furthermore, more errors were made in the KP test phase than in the FE test phase, *F*(1, 60) = 119.09, *p* < .005, η_p^2 = .665. The interactions and main effect of Age group were not significant.

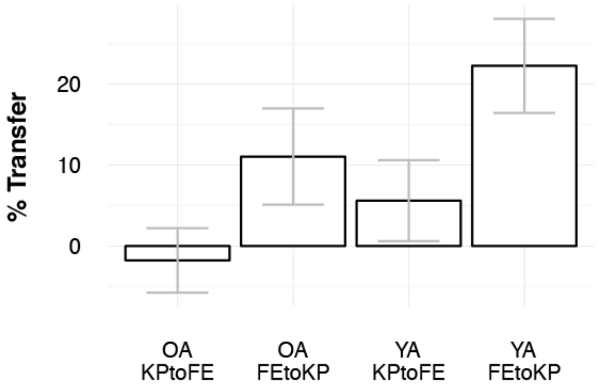

Fig. 3 Percentage transfer for both age groups and task-orders. Error bars indicate confidence intervals.

Explicit knowledge, processing speed, and visuospatial working memory

Results from a 2 (Age) x 2 (Task-order: FEtoKP vs. KPtoFE) ANOVA on explicit knowledge showed that young adults had more explicit sequence knowledge (3.8 elements per sequence) than older adults (2.6 elements per sequence), $F(1,60) = 10.58, p < .005, \eta_p^2 =.15$. There was no difference between Task-order conditions, $F(1,60) = 0.09, p = .771, \eta_p^2 =.00$, indicating that explicit knowledge after the FE and KP practice phases was similar (see Fig. 4). The interaction effect was not significant, $F(1,60) = 0.92, p = .341, \eta_p^2 =.02$. Explicit knowledge was correlated with transfer in the young adults' FEtoKP condition but not in any of the other groups (see Table 1).

Processing speed was higher in the young than in the old group, $F(1,62) = 77.60, p < .005, \eta_p^2 =.56$ (see Fig. 4). Correlations between processing speed and transfer were not significant (see Table 1).

Young adults had a larger visuospatial working memory capacity than the older adults, $F(1,62) = 76.15, p < .005, \eta_p^2 = .55$ (see Fig. 4). For older adults, VSWM capacity was correlated with KP learning rate, but not with the FE learning rate (see Table 1). We found the same pattern for young adults: VSWM capacity is correlated with KP learning rate, but not with the FE learning rate (see Table 1). This VSWM and learning rate relationship for KP sequences is in line with previous research (Bo et al., 2009).

It is important to mention that the small sub-samples (n=16) we used for the correlations together with the added variance from the counterbalanced order of the familiar and random test blocks may have suppressed some effects. Accordingly, inspection of Table 1 shows that four correlation coefficients were close to significance.

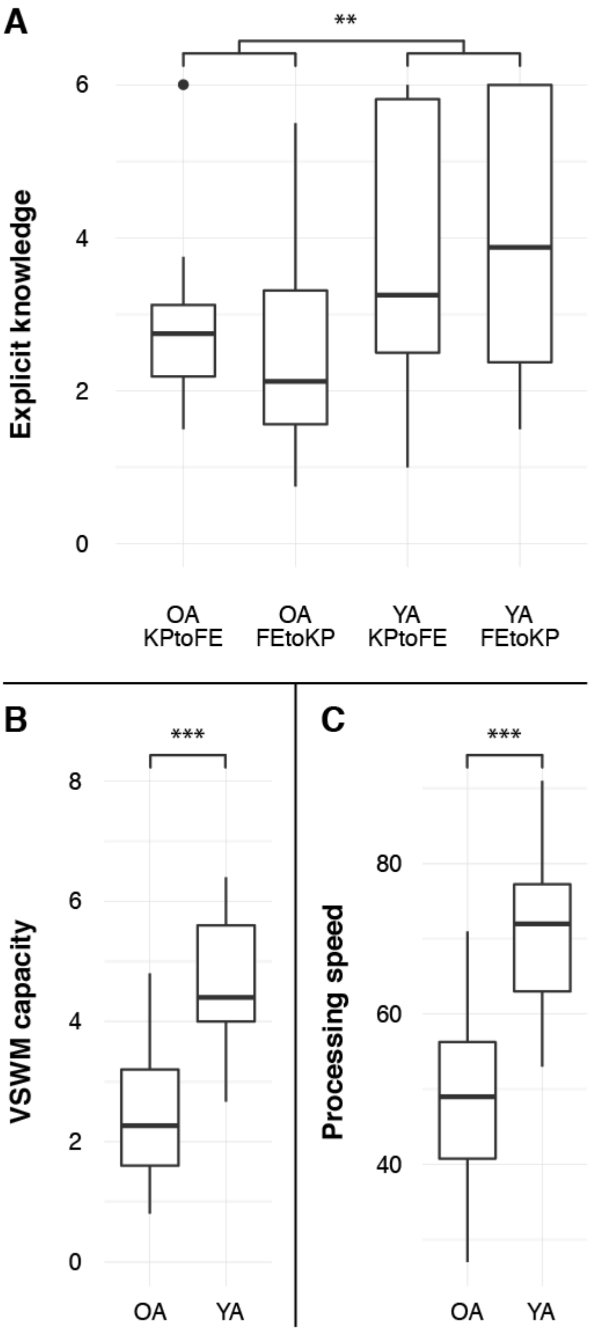

Fig. 4 Age differences in (A) explicit knowledge, defined as average number of elements correctly reproduced, (B) visuospatial working memory capacity, and (C) processing speed. ** = $p < .01$, *** = $p < .005$.

Table 1

Correlations between: explicit knowledge and transfer; processing speed and transfer; and visuospatial working memory and learning rate. P-values are denoted between brackets.

	OA, FEtoKP	*OA, KPtoFE*	*YA, FEtoKP*	*YA, KPtoFE*
*Explicit knowledge * Transfer*	0.31 (0.12)	0.4 (0.062)	**0.55** (0.014)	0.1 (0.354)
*Processing speed * Transfer*	0.41 (0.056)	0.28 (0.151)	-0.03 (0.548)	-0.14 (0.696)
*VSWM * learning rate*	0.15 (0.284)	**0.49** (0.028)	0.36 (0.086)	**0.5** (0.024)

Summarizing, we found that both age groups displayed transfer of sequence knowledge from FE to KP movements, but only young adults showed transfer from KP to FE movements. Older adults showed less transfer than young adults in both tasks. We furthermore found that older adults improved less during FE practice, gained less explicit knowledge, displayed a smaller VSWM capacity and had lower processing speed than young adults. In both age groups, a larger VSWM capacity was associated with quicker sequence learning when performing KP movements but not when performing FE movements.

DISCUSSION

The models of sequence learning discussed in the introduction (Hikosaka et al., 1999; Keele et al., 2003; Verwey et al., 2015) predict transfer of movement sequence knowledge, even when the actual movements are entirely independent from each other. Our results confirm that both young and older adults showed transfer, although for the older group this was significant only in the FEtoKP group and not in the KPtoFE group. In line with our predictions, older adults showed less transfer than young adults. Transfer was asymmetric in both age groups: practice with the FE movements followed by a test phase with KP movements resulted in more transfer than vice versa. This is consistent with our expectation that the additional cognitive effort associated with executing FE movements interferes with the adjustment of visuospatial representations, and reduces the ability to use the available sequence knowledge. The observation of correlations between working memory and learning rate in the KP, but not in the FE practice phase, further corroborated that sequence learning in the FE task requires more attention for movement execution and feedback processing than in the KP task. However, note that the correlation between working memory and learning rate in the FE practice phase did approach significance in the young adults. The finding that both age groups showed a similar asymmetry is also a confirmation that the type of representation older adults develop aligns with those that young adults develop. Together, these results suggest that the older participants, like the young, represented their sequences in an abstract visuospatial manner. Since the movement types as well as the response locations were entirely different, we know that the representation used is independent of the reinstatement of a motor representation but instead relies on visuospatial representations (Hikosaka et al., 2002; Verwey et al., 2015). These results suggest that older adults remain able to apply learned motor skills in novel contexts, just like the young.

We found that for both age groups VSWM capacity was correlated with the learning rate when practicing sequences with KP movements. However, when practicing FE movements, both groups showed no relation with VSWM. The KP results are partly in accordance with a study by Bo et al. (2009), who found that visuospatial working memory is correlated with learning rate in young but not in older adults. Why did we find a correlation between learning rate and visuospatial working memory in older adults while Bo et al. (2009) did not? An important reason may be that they used a learning rate score based on the first 60 practice trials of a 12-element sequence while we used more than twice as much practice trials (144) with 6-elemement sequences. In other words, our participants received more practice on an easier task, this may have allowed them to utilize their cognitive capabilities to a larger extent.

We found a correlation between explicit sequence knowledge and the amount of transfer in only one of the four groups. This is unexpected because explicit knowledge has been shown to contribute to sequence production, especially when performing at moderately fast speeds (Verwey, 2015). These results suggest that the early learning mechanism which is usually thought to be processed explicitly (e.g., Hikosaka et al., 2002), also depends, at least partly, on implicit sequence representations. For processing speed, we found only a marginally significant correlation with transfer for the FEtoKP older adults group and no other correlations. However, the expectation does hold when comparing the groups: older adults showed a lower processing speed along with less transfer. We expect that the small sub-samples (n=16) we used for the correlations together with the added variance from the counterbalanced order of the familiar and random test blocks may have suppressed some of the correlations. Furthermore, because of the participant's limited familiarity with the new type of movements when switching to the test phase, factors other than explicit knowledge and processing speed may have played a relatively large role.

In analysis of our results, it is somewhat difficult to control for initial learning because our study did not include a random sequence block at the end of the practice phase because the interference effect may be different over age groups. Future research could contribute to our findings by using either a random sequence block and controlling for interference, or by having participants practice until full explicit knowledge of the sequences is reached. The latter option would also allow for more precise inspection of contributions of explicit knowledge. Future research could also consider using a larger sample to gain power when conducting correlational analyses on subgroups.

Concluding, our hypothesis that models of sequence learning that are valid for young adults (Hikosaka et al., 1999; Keele et al., 2003; Verwey et al., 2015) also apply to older adults has been largely confirmed. Older adults learned more slowly, and showed less transfer than young adults when the familiar sequences were carried out with different movements,. This is consistent with earlier indications of reduced transfer (Panzer et al., 2011) and reduced learning (e.g., Curran, 1997; Daselaar, Rombouts, Veltman, Raaijmakers, & Jonker, 2003) in older adults. However, the types of representations seem to be similar to those that young adults develop and the ability to apply sequence knowledge in a flexible way is partly preserved in older adults.

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Differences in chunking behavior between young and older adults diminish with extended practice

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Psychological Research, in press

ABSTRACT

Previous research found reduced motor chunking behavior in older adults compared to young adults. However, it remains unclear whether older adults are unable to use a chunking strategy or whether they are just slower in developing them. Our goal was to investigate the effect of extended practice on the development of chunking behavior in healthy older adults. A group of young and a group of healthy older adults between 74 and 85 years of age visited the lab on two days. A sequence of 3 and a sequence of 6 elements were both practiced 432 times in a discrete sequence production task. We found that age differences in chunking behavior, as measured by the difference between initiation and execution of the sequence, diminish with extended practice. Furthermore, in older, but not in young adults, slow responses that are often interpreted as the first response of a next motor chunk were associated with a finger that was also slow during performance of the random sequences. This finding calls for more attention to biomechanical factors in future theory about aging and sequence learning.

INTRODUCTION

Older adults show impaired performance in the physical and cognitive domains. These impairments are associated with increased difficulty in developing new motor skills (e.g., Wu & Hallett, 2005). Since Western societies are aging rapidly, it is important to better understand age-related changes in cognition and motor performance. Age-related cognitive decline has been reported over a broad range of cognitive abilities (Harada et al., 2013), including processing speed (Harada et al., 2013; Salthouse, 2004), and working memory (Borella, Carretti, & De Beni, 2008; Verhaeghen & Salthouse, 1997). Cognitive changes are normally accompanied by ongoing physical decline and these factors together explain limitations in motor performance and learning. For example, reduced hand function in older adults is explained simultaneously by deterioration at the biomechanical level (e.g., joints, muscles, bones) and changes in neural control (Carmeli, Patish, & Coleman, 2003; Seidler et al., 2010). However, more research is needed on how changes in motor learning can be explained by changes in cognitive and physical capabilities.

Sequence learning is one of the major paradigms that have been used to study motor learning. A recent framework for understanding the learning and production of sequences is the dual processor model (DPM, Abrahamse et al., 2013). The DPM is based on results from many studies using the discrete sequence production (DSP) task but also incorporates features of other sequence learning models (e.g., Hikosaka, Nakamura, Sakai, & Nakahara, 2002; Keele, Ivry, Mayr, Hazeltine, & Heuer, 2003). The architecture proposed in the DPM consists of a cognitive processor that is dependent on attentional resources and a motor processor that does not require attentional resources. Together, these processors enable three modes of sequence production (Ruitenberg, Verwey, Schutter, & Abrahamse, 2014; Verwey & Abrahamse, 2012). In the *reaction mode*, the cognitive processor sequentially translates each target into an appropriate response, which is then carried out by the motor processor. As sequence learning progresses, performance may improve because associations between elements begin to develop, in which case the learner has progressed into the *associative mode*. Finally, in the *chunking mode*, series of successive elements in a sequence are integrated into a single representation that can be loaded into a motor buffer as a whole after being triggered by the cognitive processor. This single representation is not necessarily a motor representation, but may also be central-symbolic (Verwey et al., 2015). Response time patterns in the chunking mode are characterized by multiple features. The first key-press is typically slower than later elements. This delay is caused in part by time uncertainty and in part by the loading of a representation consisting of multiple upcoming elements into the motor buffer. After the first response, subsequent elements are quickly performed in one sweep. The DPM predicts that "the difference between the first (initiation) and later (execution) response times (RTs) increases considerably with practice because of the increasing possibility to prepare the later key-presses" (Abrahamse et al., 2013). Hence, an increase in the difference between initiation and execution suggests increased chunking. Longer sequences are often divided into multiple motor chunks and one or more slower elements in the RT pattern are taken to indicate that a next chunk is initiated (Abrahamse et al., 2013). While the term chunking was originally based on this division process, research has shown that, in accordance with the DPM, chunking behavior is reflected in multiple aspects of sequence learning and performance (Acuna et al., 2014).

Previous research on motor chunking in older adults has focused on multiple aspects of chunking behavior. For example, in a study by Verwey (2010), most older participants (aged 75 to 88 years old) were found to remain reliant on external stimuli and the difference between initiation and execution key-presses did not increase like it did in the young participants. Similar results were later found for a group of middle-aged participants (Verwey et al., 2011). Bo, Borza and Seidler (2009) found that a lower proportion of the older adults in their study, compared to the young participants, divided a long 12-element sequence into multiple motor chunks. This study also showed that when the older participants did chunk, their chunks consisted of fewer elements than those of young adults. The movements performed in most studies on chunking consisted of keyboard presses. However, reduced chunking abilities in older adults have also been shown in a task with forearm flexion-extension movements (Panzer et al., 2011; Shea et al., 2006). Clearly, previous research has provided important insights into age-related differences in chunking but since all these studies used a relatively limited amount of practice, an important question remains: Are older adults unable to develop chunking strategies or do they simply need more practice to develop them?

The current study

Our main goal was to investigate the effect of extended practice on the development of chunking behavior in healthy older adults. We used a DSP task with a 3- and a 6-element sequence. These sequence lengths are similar as used in previous studies on chunking in older adults (Verwey, 2010; Verwey et al., 2011). We provided 3 times as much practice compared to these previous studies as each of the two sequences was repeated 432 times, spread over two consecutive days. This number of practice trials is quite typical for DSP studies with young participants (Abrahamse et al., 2013).

Our aim was to see how older adults perform in the light of DPM's predictions. We hypothesized that they would require more extensive practice than young adults to increase chunking behavior. This chunking behavior would be indicated by an increasing difference between the first and following key-presses of each sequence (i.e., the Initiation-Execution Difference or IED). Although it was unknown how much practice would be needed, we expected differences in chunking behavior between older and young adults to gradually reduce during the second day of practice, and perhaps even disappear. In previous research, slow elements in the sequence were taken to indicate the start of a new motor chunk, also called a concatenation point (e.g., Ruitenberg et al., 2014). However, especially with the older adults it may well be that slow elements are due to increased biomechanical variability (e.g., Contreras-Vidal, Teulings, & Stelmach, 1998). To investigate this potential problem, we here determined for both age groups whether slow elements in a learned sequence correspond with slow fingers, as identified when performing random sequences, in older and young adults.

Additional to these primary goals, we measured visuospatial working memory capacity, explicit sequence knowledge, and processing speed in order to enhance our understanding of the factors contributing to differences in sequence learning between older and young adults. Visuospatial working memory (VSWM) capacity has been shown to be associated with the length of motor chunks developed by older and young adults (Bo et al., 2009), and we were interested whether this would be the case for the IED too. Because previous research showed that explicit sequence knowledge is correlated with the initiation-execution difference (Verwey, 2010), we also measured explicit sequence knowledge. Finally, processing speed has not previously been related to chunking behavior, but since processing speed has been suggested to play a central role in many age-related cognitive differences (Salthouse, 1996), we here explored its relationship with chunking behavior and sequence execution, too.

METHODS

Participants

The young participants were students participating for course credit. Older adults, in the range of 74 to 85 years old, were recruited via local media. The older applicants were invited for participation only when they reported that none of the following applied: severe motor problems including use of a wheelchair or limitations in using the fingers or arms; history of neurological problems; arthritis or rheumatism; or color-blindness. Of the older adults who initially visited the lab, 7 were excluded and replaced due to: pain in the wrist (1); limitations in using the fingers (1); more than 30% errors during the last 4 blocks of day 1 (4, participation ended after visit 1 for these participants); and more than 80% errors during the random sequence test phase (1). The 18 older adults (age = 79 ± 3.5, 13 females) that were eventually included for analysis had a score on the Montreal Cognitive Assessment (MoCA) of 26 ± 2.5 on a scale of 0-30. None scored below 22, the threshold for mild cognitive impairment (Freitas et al., 2013). Of the 18 young participants tested (age 21 ± 1.2, 7 females), no participants were excluded or replaced. All participants were right-handed as confirmed by the Edinburgh handedness inventory (Oldfield, 1971). The ethics committee of the University of Twente, faculty of Behavioral, Management and Social Sciences, approved the study and all participants provided informed consent.

Procedure

All participants visited the lab on two consecutive days. The older participants received an information letter and the Edinburgh handedness form (Oldfield, 1971) at home prior to participation. For them, the MoCA was administered at the start of the visit (Nasreddine et al., 2005). Then, on both days, participants completed a series of DSP blocks with breaks and additional questionnaires interleaved (see Fig. 1). After every three DSP blocks, an ad-hoc self-report fatigue scale (11 point Likert scale) was administered. After block six on the first day, a 90 seconds digit-symbol substitution test was administered to measure processing speed (Wechsler, 1955). A visual array comparison test to measure visuospatial working memory capacity was included at the start of day two. In this task, participants view a sample array of 2 to 8 colored squares for 100 ms, then, 900ms later, a test array is presented and the participant is asked whether the test array is identical to the sample array (see Barnhoorn et al., 2016). After the last DSP practice block on the second day, a questionnaire measuring explicit sequence knowledge was administered. In this awareness questionnaire, participants were first asked to write down the order of the elements using the letters corresponding to the keys they had used (while the keyboard remained in sight). Then, the target locations were shown on the screen again and participants were asked to point out the sequences by pointing with their index finger. Finally, participants were asked to select their sequences from two lists of 12 sequences, one for each sequence length. At the end of the first visit, older participants were offered a stress ball to relax hands and fingers.

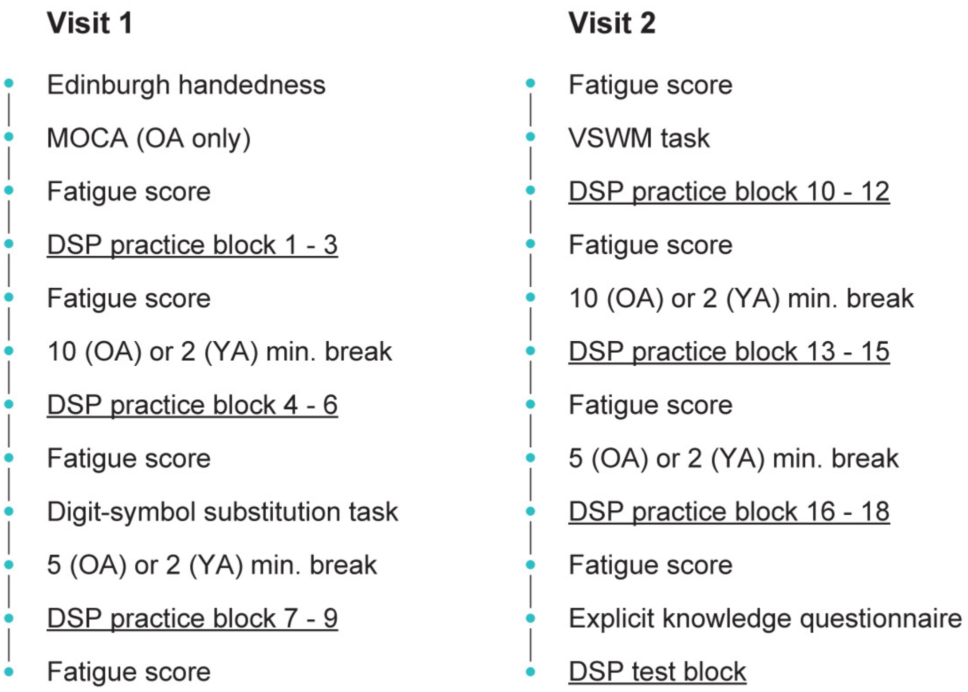

Fig. 1 Study procedure. The main activity participants performed was DSP practice, the other tasks and questionnaires were interleaved with the DSP blocks. Note that the older adults (OA) were provided with longer breaks than the young (YA) participants.

Discrete sequence production task

Participants practiced one 3-element sequence and one 6-element sequence in random order. Across participants, the keys of the sequences were rotated over sequential positions (e.g., G, L, D becomes J, D, F) so that over participants, all fingers were used equally often at each sequence position. Furthermore, the sequences did not involve repeated elements, and did not involve regularities like trills and runs. The DSP task was presented on a 22″ wide-screen monitor using E-Prime 2.0. On the display, black outlines of six 28 * 28 mm placeholders were aligned horizontally with 14 mm spacing in between them. The background was white. These squares corresponded to the buttons D, F, G, J, K and L on the regular QWERTY keyboard on which the participants rested their ring, middle and index fingers of both hands. The spacing between the third and fourth placeholder was 56 mm, a letter H was presented here. A square was filled green when it became the active target, after which the participant pressed the spatially compatible key. Each time the correct key had been pressed the next stimulus was displayed. This continued until the sequence was completed. Note that the response-stimulus interval was zero and hence, the RT is equal to the inter-key interval. We denote the first response RT1, the second RT2, etc. After an incorrect key had been pressed the message “Wrong” was displayed for 1500 ms. When no key was pressed for 20 seconds, the error message “No response” was displayed for 1500 ms. In both cases, a new trial started. Before each trial, the empty placeholders were displayed for 1000 ms. Pressing any key during this period resulted in a 1500 ms error message “Too early” after which the trial was repeated. After each trial, a 1250 ms white screen was presented.

Participants were instructed that they would learn two fixed sequences of key-presses during practice. The task consisted of 18 practice blocks with 48 trials each, rendering 864 practice trials in total. Each block comprised two sub-blocks, between which a 40-second break was provided. Between two full DSP blocks, participants were given a 2-minute break during which the error percentage and mean RT in ms were displayed on the screen, older participants enjoyed a longer break after every three DSP blocks (see Fig. 1). The test phase consisted of two sub-blocks. One sub-block involved the familiar sequences; the other sub-block random sequences that were generated online (without immediate stimulus repetitions). The order of these test phase sub-blocks was counterbalanced over participants.

Analyses

For all RT analyses, we excluded the first trial (i.e., sequence) of every sub-block and trials containing an error. Of the resulting dataset, we excluded 1.47% of trials with a mean trial RT that was above a threshold of the mean trial RT plus 2.5 * standard deviation of mean trial RTs in that sub-block. When Mauchly’s test indicated that assumptions of sphericity were violated we applied the Greenhouse–Geisser correction, and reported corrected p-values and original degrees of freedom. The proportions per block of trials (sequences) with an error were arcsine transformed before analysis (Winer et al., 1991). We report explicit knowledge based on the sum of the number of elements correctly written down and the number of elements correctly pointed out during the explicit knowledge questionnaire (correct elements were counted from the start to the first mistake; maximum explicit knowledge score: 18).

RESULTS

Practice phase general results

Response times of the 3-element sequence were submitted to a mixed 2 (Age group) x 18 (Block) x 3 (Serial position) ANOVA with Age group as the between-subjects variable.

Mauchly's test indicated that the assumption of sphericity was violated for Block, $\chi^2(152) = 664.8$, $p < .001$, $\varepsilon = .226$, Serial position, $\chi^2(2) = 24.7$, $p < .001$, $\varepsilon = .655$, and their interaction, $\chi^2(594) = 1938.3$, $p < .001$, $\varepsilon = .136$. The older adults were substantially slower than their young counterparts (594 ms vs. 239 ms), $F(1, 34) = 53.5$, $p < .001$, $\eta_p^2 = .61$ (see Fig. 2). Furthermore, performance improved over Blocks, $F(17, 578) = 83.1$, $p < .001$, $\eta_p^2 = .71$ and differentially so for older and young adults as indicated by a Block x Age group interaction, $F(17, 578) = 7.6$, $p < .001$, $\eta_p^2 = .18$. Serial position showed a main effect, $F(2, 68) = 90.1$, $p < .001$, $\eta_p^2 = .73$, which is in line with the first key-press being slower than subsequent key-presses. Serial position interacted with Age group, $F(2, 68) = 6.3$, $p = .010$, $\eta_p^2 = .16$. A significant Serial position x Block interaction $F(34, 1156) = 9.7$, $p < .001$, $\eta_p^2 = .22$, provides a first indication that the key-presses developed differently over time.

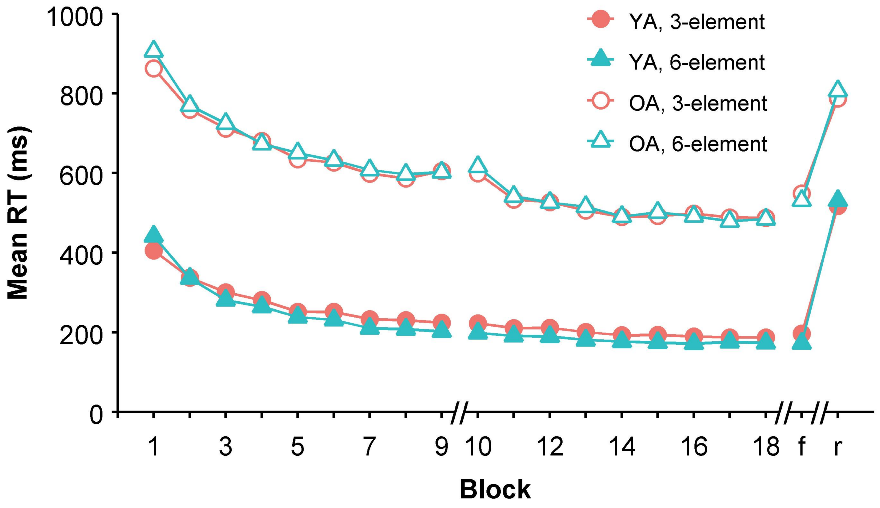

Fig. 2 RT development during the practice and test blocks (r = random, f = familiar), the order of the test phase sub-blocks was counterbalanced, Day 1 ended after Block 9.

Response times of the 6-element sequences were submitted to a mixed 2 (Age group) x 18 (Block) x 6 (Serial position) ANOVA with Age group as the between-subjects variable. The assumption of sphericity was violated for Block, $\chi^2(152) = 765.0$, $p < .001$, $\varepsilon = .184$, Serial position, $\chi^2(14) = 61.2$, $p < .001$, $\varepsilon = .605$, and could not be computed for their interaction. Here too, older participants were much slower than young (601 ms vs. 224 ms), $F(1, 34) = 50.6$, $p < .001$, $\eta_p^2 = .60$. Furthermore, performance improved over Blocks, $F(17, 578) = 80.8$, $p < .001$, $\eta_p^2 = .70$ and there was a Block by Age group interaction, $F(17, 578) = 6.3$, $p < .001$, $\eta_p^2 = .16$. Serial position showed a main effect, $F(5, 170) = 32.6$, $p < .001$, $\eta_p^2 = .49$, which is in line with a relatively slow first key-press. Serial position interacted with Age group, *F*(5, 170) = 4.1, $p = .009$, $\eta_p^2 = .11$. A significant Serial position x Block interaction *F*(85, 2890) = 6.9, $p < .001$, $\eta_p^2 = .17$, indicates again that the key-presses developed differently over time.

Arcsine transformed error proportions for the 3-element and the 6-element sequence were submitted to mixed 2 (Age group) x 18 (Block) ANOVAs with Age group as between-subjects variable. The assumption of sphericity was violated for Block for the 3-element sequence, $\chi^2(152) = 204.2$, $p = .005$, $\varepsilon = .608$, but not for the 6-element sequence. For the 3-element sequence as well as for the 6-element sequence error proportions, none of the main or interaction effects reached statistical significance. This suggests that the speed differences over time and between age groups were not due to speed-accuracy effects. During practice, older participants made errors on 6% of the sequences, young participants on 5% of the sequences.

Development of fatigue was tested separately for both days with mixed 2 (Age group) x 4 (Time of measurement) ANOVAs on the 11-point fatigue scale with Age group as between-subjects variable. The assumption of sphericity was violated for both day one, $\chi^2(5) = 28.6$, $p < .001$, $\varepsilon = .729$, and day two, $\chi^2(5) = 61.6$, $p < .001$, $\varepsilon = .471$. The main reason this analysis was performed was to see if practice had differential effects of fatigue development in young and older adults. Critically, the Time by Age interaction was not significant for either day 1, *F*(3, 102) = 2.0, $p = .133$ or day 2, *F*(3, 102) = 1.6, $p = .215$. This shows that older and young participants did not experience significantly different amounts of increased fatigue and, thus, that differences in fatigue development did not affect differences in learning. The main effect of Age group showed that young participants scored higher on the fatigue measurement on day 1, *F*(1, 34) = 9.8, $p = .004$, $\eta_p^2 = .22$, and day 2, *F*(1, 34) = 5.3, $p = .027$, $\eta_p^2 = .14$. We think this effect is indicative of a general strategic difference in responding baseline between the age groups that is irrelevant for the current study. The effect of Time on fatigue score was significant on both day 1, *F*(3, 102) = 17.3, $p < .001$, $\eta_p^2 = .34$, and day 2, *F*(3, 102) = 7.4, $p = .004$, $\eta_p^2 = .18$, indicating that all participants experienced increasing fatigue during the experiment.

Test phase general results

A mixed 2 (Age group) x 2 (Familiarity: Familiar vs. Random) x 3 (Serial position) ANOVA was conducted on 3-element sequence RTs with Age group as between-subjects variable. The assumption of sphericity was violated for Serial position, $\chi^2(2) = 21.7$, $p < .001$, $\varepsilon = .675$, and for the Serial position by Familiarity interaction, $\chi^2(2) = 6.4, p = .041, \varepsilon = .850$. A main effect of Age group confirmed that age-related slowing (668 ms vs. 357 ms), $F(1, 34) = 61.0, p < .001, \eta_p^2 = .64$. In general, participants were slower in the Random than in the Familiar condition (652 ms vs. 373 ms.), $F(1, 34) = 340.2, p < .001, \eta_p^2 =.91$, confirming that participants had gained sequence knowledge during practice. This effect was stronger for the young than for the older participants, $F(1, 34) = 7.5, p = .010, \eta_p^2 =.18$. Serial position showed a main effect, $F(2, 68) = 46.4, p < .001, \eta_p^2 = .58$. An interaction between Familiarity and Serial position, $F(2, 68) = 90.9, p < .001, \eta_p^2 = .73$, supports the notion that in general, motor chunking was used in the Familiar but not in the Random sequences (see Fig. 3).

A mixed 2 (Age group) x 2 (Familiarity: Familiar vs. Random) x 6 (Serial position) ANOVA on RT was conducted for the 6-element sequence data as well. The assumption of sphericity was violated for Serial position, $\chi^2(14) =27.9, p = .015, \varepsilon = .723$, and for the Serial position by Familiarity interaction, $\chi^2(14) = 36.5, p = .001, \varepsilon = .717$. The effect of Age group was confirmed (669 ms vs. 352 ms), $F(1, 34) = 76.7, p < .001, \eta_p^2 = .69$. The effect of Familiarity was significant too (669 ms vs. 352 ms), $F(1, 34) = 482.8, p < .001, \eta_p^2 = .93$. Similar to the 3-element sequence results, the advantage of the Familiar over the Random sequences was larger for young than for older participants, $F(1, 34) = 8.2, p = .007, \eta_p^2 = .20$. The main effect of Serial position was significant, $F(5, 170) = 25.5, p < .001, \eta_p^2 = .43$, and differed between Age groups, $F(5, 170) = 3.9, p = .007, \eta_p^2 = .10$. Again, like with the 3-element sequences, Familiarity and Serial position showed an interaction suggesting a different RT pattern in the Familiar than in the Random condition, $F(5, 170) = 35.9, p < .001, \eta_p^2 = .51$.

Arcsine transformed error proportions during the test phase for the 3 and 6-element sequences were submitted to 2 (Age group) x 2 (Familiarity: Familiar vs. Random) ANOVAs. Participants made more errors in the Random (old: 10%, young: 11%) than in the Familiar (old: 5%, young: 6%) condition in the 6-element sequence, $F(1, 34) = 9.5, p = .004, \eta_p^2 = .22$, and in the 3-element sequence, $F(1, 34) = 6.8, p = .013, \eta_p^2 = .17$. For both the 3 and 6-element sequences, the main effects of Age group and the interactions were not significant.

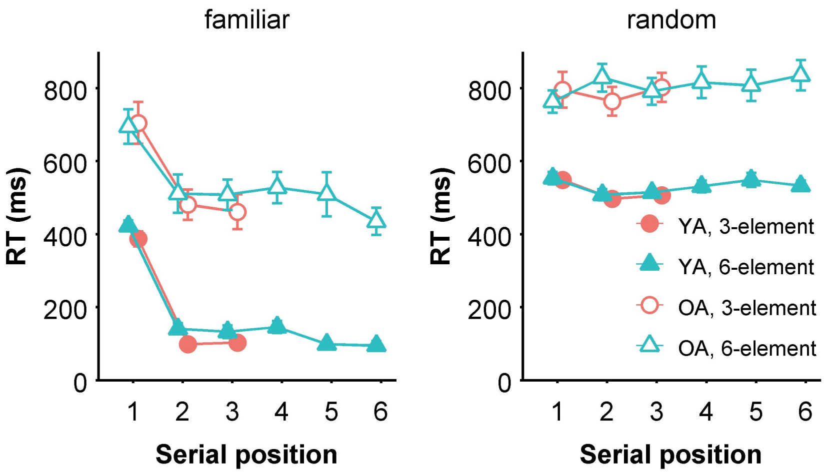

Fig. 3 RT per serial position during the test phase. Error bars denote standard error. Note that the left plot seems to suggest that the 6-element sequence was performed as one large chunk, since no clear slow elements are visible. This is not the case, this RT profile simply results from averaging over multiple participants who have slow elements at different locations (Verwey & Eikelboom, 2003).

Initiation-execution difference

For the 6-element sequences, we defined three types of responses: *initialization* consists of RT1, the initiation of the sequence; a *slow element*[1] is any response after RT1 that is consistently slower than its neighboring responses; all other RT's are *execution* responses. We categorized responses on a block-by-block basis for all blocks with fixed sequences (18 practice phase blocks and one test phase sub-block). A response was classified as a slow element when two one-tailed, paired samples t-tests with alpha set to .1 indicated it to be slower than its neighboring responses in the current block. Consequently, a sequence could have 0, 1 or 2 slow elements. This approach is in line with previous research (Bo et al., 2009; Ruitenberg, Verwey, et al., 2014). Note that RT2 and the last RT can never be a slow element when using this method. This is partly because they do not have two suitable neighbors to compare with[2] and partly because, in line with the aforementioned studies, it is assumed that RT2 is part of the first chunk and the last RT is part of the last chunk. Accordingly, we defined all 3-element sequences to consist of one initialization followed by two execution responses. For the blocks with fixed sequences, we defined an *initiation-execution difference* (IED) to gauge the amount of chunking, as the difference between RT1 and the mean of the

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[1] We intentionally chose a terminology that is not related to any theoretical cognitive concept and refrain from using terms like 'chunk point' or 'concatenation point' since our goal is to establish whether purely biomechanical factors, unrelated to cognitive processes play a role in the occurrence of slow elements.

[2] RT1 is not a suitable neighbor because it is usually slower because of time uncertainty in the presentation of the first stimulus of the sequence.

execution responses, also on a block-by-block basis. The reason we did not include slow elements in the IED calculation (e.g., averaged with RT1) is that these may be slower because of biomechanical factors, especially in older adults, while our aim was to assess a cognitive process that would be associated with the IED.

To test whether the older participants benefited from the additional practice provided on the second day, we submitted the IED for each practice block of the second day to mixed 9 (Block) x 2 (Age group) ANOVAs for each sequence length. The assumption of sphericity was violated for the 3-element sequence, $\chi^2(35) = 190.6$, $p < .001$, $\varepsilon = .313$, as well as for the 6-element sequence, $\chi^2(35) = 122.2$, $p < .001$, $\varepsilon = .367$. For the 3-element sequence, the main effect of Block was significant, $F(8, 272) = 3.9$, $p = .017$, $\eta_p^2 = .10$, the main effects of Age group and the interaction did not reach significance. For the 6-element sequence, the main effect of Block was significant too, $F(8, 272) = 5.2$, $p = .003$, $\eta_p^2 = .13$, and the main effect of Age group did not reach significance either. This time however, Block interacted with Age group, $F(8, 272) = 3.5$, $p = .019$, $\eta_p^2 = .09$, suggesting that the older participants benefited more from the additional practice than the young participants did (see Fig. 4). However, the differential development during day two may be due to a larger decrease of performance at the start of day two. To test this, we submitted the IED's from the last blocks of each day to a mixed 2 (Age group) x 2 (Block: block 9 vs. 18) ANOVA. The main effects of Block and Age group did not reach significance, but the Block by Age group interaction again showed that older participants benefited more from the second day of practice than the young, $F(1, 34) = 4.8$, $p = .036$, $\eta_p^2 = .12$. Additional one-tailed t-tests confirmed that the older participants showed a higher IED at the end of day two than at the end of day one for the 6-element sequence, $t(17) = 2.2$ $p = .02$ (one-tailed), while the young participants did not, $t(17) = 1.6$, $p = .93$.

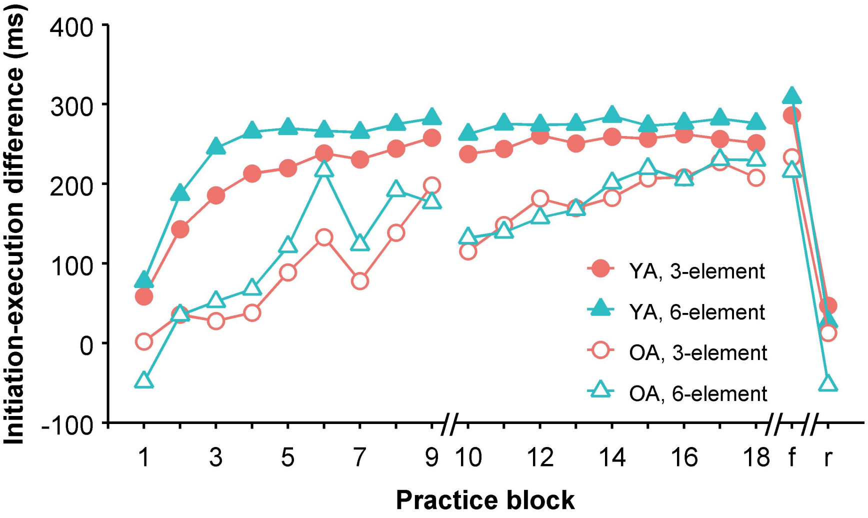

Fig. 4 IED development during the practice and test phase.

For the test phase, IED was submitted to a 2 (Familiarity: Familiar vs Random) x 2 (Age group) mixed ANOVA. For the 3-element sequence, IED was higher in the Familiar than in the Random condition, $F(1, 34) = 127.5, p < .001, \eta_p^2 = 79$. The main effect of Age group and the interaction were not significant. For the 6-element sequence, IED was higher in the Familiar condition as well, $F(1, 34) = 112.7, p < .001, \eta_p^2 = .77$. This time, the main effect of Age group did reach significance, $F(1, 34) = 9.3, p = .004, \eta_p^2 = .22$, the Familiarity x Age interaction was not significant.

Slow elements & biomechanical variation

To establish whether there is an age-related difference in variance between fingers, we calculated the SD of the median finger RTs per participant using the random sequence test block. As expected, older participants showed a larger SD (72.0 ms) than their young counterparts (38.8 ms), $t(34) = 3.9, p < .001$ which is consistent with the presence of larger biomechanical variation among fingers in older adults.

To investigate whether the occurrence of slow elements in older adults is associated with biomechanical factors like a stiff finger[3], we used the data from the random sequence test block (excluding RT1), where sequence knowledge is irrelevant, to determine the median RT of each finger. *Finger speed* was then calculated per finger as the difference between a finger's median RT and the mean of the median RTs of all the fingers used. A positive value

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[3] In the 6-element sequences, each of the six fingers is used once. This means that when any of a participant's fingers is consistently slow, this will show up as a slow response at one point in the sequence.

for finger speed indicates a finger slower than average, a negative value a finger faster than average. Because of the normalization, the average finger speed is zero.

Using the aforementioned t-test method, we found for all participants slow elements for at least one of the practice blocks. To determine whether these slow elements often occur at sequential positions that are performed with a 'slow finger' for a participant, we counted the number of times each finger was used at a slow sequence element. Then, we took the average finger speed of these fingers, taking into account in how many blocks these fingers were associated with slow elements. For example, a participant might display no slow elements in the first 6 blocks of the practice phase, a slow element at sequential position 3 from block 7 to 8, and at position 4 from block 9 to 18. Say that the left index finger was used at sequential position 3, and the right middle finger at position 4, with a finger speed of respectively 40 ms and 70 ms. For this participant, the mean finger speed at the slow elements is than ((2 * 40) + (10 * 70)) / 12 = 65 ms, indicating that the fingers used at slow elements were also slow in the random sequence blocks.

Using the aforementioned method we calculated the mean finger speed at the slow elements for all participants. We then tested the resulting distribution for older and young adults against zero. A two-tailed, one-sample t-test shows that for older participants, the finger speed at slow elements was slower than the mean finger speed, $t(17) = 2.6$, $p = .02$ (see Fig. 5). For young participants, the finger speed at slow elements was not significantly different from the mean, $t(17) = .7$, $p = .52$. The difference between older and young participants was not significant either, $t(34) = 1.7$, $p = .105$.

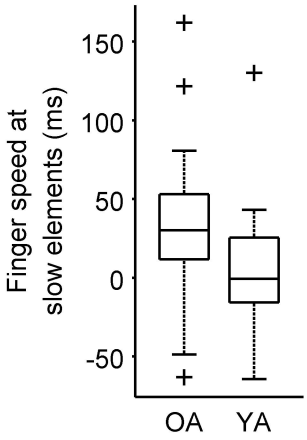

Fig. 5 Finger speed at slow elements. The higher the value, the slower the fingers that were used at slow elements. OA: older adults; YA: young adults.

Awareness, visuospatial working memory capacity & processing speed

Both age groups showed a ceiling effect on explicit knowledge, with 9 out of 18 older and 12 out of 18 young participants reaching the maximum score. A Spearman's rho correlation analysis shows that explicit knowledge and the familiar test-phase IED were correlated for older, r_s = .65, p = .004, but not for young participants. Regarding the VSWM task, most of the older participants mentioned that, although they understood the task well, they found the 100 ms presentation of the sample array (that was to be remembered and compared to an array presented 900 ms later) too short. Since the mean capacity for our older sample is 1.87 and thus higher than the mean capacity of 1.76 found previously a sample with a mean age of 71 (Bo et al., 2009), we decided to report the results regardless. As expected, young participants had a larger VSWM capacity than older participants (VSWM capacity: 4.52 vs. 1.87), *t*(34) = 6.06, p < .001. Contrary to our hypothesis however, VSWM capacity did not correlate with the familiar test-phase IED for older, *r*(16) = . 07, p = .775, or for young participants, *r*(16) = .0, p = 984. Young adults substituted more elements in the digit symbol substitution task than older participants (74 vs. 44 elements) and thus had a substantially higher processing speed, *t*(34) = 9.14, p < .001. However, the number of items substituted did not correlate with the familiar test-phase IED for older, *r*(16) = .39, p = .115, or for young adults, *r*(16) = .14, p = .582. Processing speed did correlate with execution rate in the random test condition for older, *r*(16) = -.51, p = .031, but not for young participants, *r*(16) = -.01, p = .959.

Results summary

In line with our hypothesis, older adults continued to increase their IED during the second day while their young counterparts had already reached a ceiling during the first day. The difference in IED between the age groups eventually diminished. In older adults, slow elements in familiar sequences were associated with a finger that was also slow during performance of the random sequences, such an effect was not found for the young. Older adults with more explicit knowledge showed a higher IED. The IED was not associated with VSWM or with processing speed in either age group.

DISCUSSION

Our primary goal was to test the hypothesis that extended practice would enable older adults to develop motor chunking behavior, which we measured using the initiation-execution difference (IED). Our hypothesis was supported, with the IED reaching almost the same level in the older as in the young adults. This indicates that older adults prepared learned sequences before movement onset to a similar extent as young adults, and thus showed similar chunking behavior. While the pattern of IED development was rather similar for both sequence lengths (see Fig. 4), the second day of practice led to a significantly increased IED in older adults for the 6- but not the 3-element sequence. Apparently, it took the older adults more time to develop chunking behavior for the longer sequence. For younger adults the IED increased faster for the 6-element sequence than for the 3-element sequence. This may be due to accumulating activation in the associative mode which is used early in practice (Verwey & Abrahamse, 2012).

The IED was not equally robust in both age groups, especially during the first day of practice. It seems that the breaks and unrelated tasks between successive blocks of DSP practice negatively affected the IED for older but not for young adults (e.g., see block 6 in Fig. 4). The switch from the first to the second day also negatively affected the IED in the older sample. Previous research found reductions in older adults' sleep-dependent consolidation for sequence performance in general (Gudberg, Wulff, & Johansen-Berg, 2015; Wilson, Baran, Pace-Schott, Ivry, & Spencer, 2012) and for motor chunking in particular (Bottary, Sonni, Wright, & Spencer, 2016). Our results suggest that for older adults performance on the next day can even be worse than on the previous day. Overall, the older adults in our study showed slower development of chunking for the 6-element sequence, but they did manage to develop chunking behavior after extended practice.

Our analysis of the effects of biomechanical variation between fingers on the occurrence of slow elements confirmed our expectations. For the first time we show that for young adults slow elements in familiar sequences were not associated with finger speed in random sequences and, hence, the DPM's interpretation that these elements are locations where motor chunks are concatenated need not be rejected (Abrahamse et al., 2013). In contrast, for older adults slow elements in the learned sequences were associated with fingers we identified as slow using data from the random sequence test condition. It is difficult to estimate to what extent cognitive and biomechanical factors contributed to the slowing of individual sequence elements in the older adults, but these findings suggest that potential indications for concatenation points in this group may in fact have been caused by biomechanical factors (like a stiff finger) rather than cognitive factors (like a concatenation point). As such, the occurrence of occasional slow responses in older adults alone is not sufficient evidence to support the use of motor chunks. An interesting question for further research that emerges from this finding is whether people in general, and older adults in particular, use the additional time introduced by a slow effector to perform additional cognitive processing.

The results presented here regarding chunking behavior and the effects of biomechanical variation provide relevant new insights, but also call for follow-up research to provide more detailed ideas regarding the analysis of sequence learning data. Many factors may affect RTs including, but not limited to, stiff fingers, handedness, wrist rotation, switching the hand used, and differences between fingers (e.g., the ring and little fingers have been found to be slower in piano studies, Aoki, Furuya, & Kinoshita, 2005). Previous research has proposed multiple analyses to analyze, sometimes rather specific, aspects of chunking. The methods used include t-tests (Bo et al., 2009; Ruitenberg, Verwey, et al., 2014), k-means clustering (Song & Cohen, 2014), dynamic network analyses (Wymbs et al., 2012), hidden Markov models (Acuna et al., 2014) and non-parametric rank-order algorithms (Alamia, Solopchuk, Olivier, & Zenon, 2016). An elaborate discussion of each of these methods is beyond the scope of the current work. There were several reasons why we chose for the IED as a measure of chunking. First, the IED provides an estimate of the strength, or extent, of chunking at different moments of practice. Second, it takes into account the potential confounding effects of fingers that are slow in general. Third, chunking structures differ per participant (Verwey & Eikelboom, 2003), something that our analysis took into account. Finally, using this method allows us to, indirectly, compare outcomes of our study to previous DSP chunking studies in older adults (Verwey, 2010; Verwey et al., 2011). A downside of our t-test based method that we could not overcome is that of the 6 elements, only RT 3, 4 and 5 can be a slow element. The result is that when a finger is very slow in the random sequences, but not used at RT 3, 4 or 5, it is not included in our findings regarding finger speed at slow elements. Note that while this downside makes our approach less sensitive, the present finding of a relationship between slow elements and general finger speed only underlines robustness of this finding.

Next to our primary goals, we explored how chunking behavior was related to explicit knowledge, VSWM, and processing speed. Explicit sequence knowledge was correlated with the IED for older adults in keeping with previous findings (Verwey, 2010), suggesting that when older adults are executing keying sequences this may not solely rely on pure motor representations. This is in line with the recently proposed cognitive framework for sequential motor behavior (C-SMB, Verwey et al., 2015), built on the foundations of the DPM, which postulates that the representations underlying motor skill and motor chunks may be mixed. That is, verbal and/or visuospatial central-symbolic representations may underlie skilled sequence performance too. A post hoc interpretation may then be that a mixture of motor and cognitive sequence knowledge drives the chunking mode displayed by older adults. In line with the previous suggestions of enhanced analyses, future research could focus on teasing apart the specific representations underlying chunking behavior.

The expected relationship between VSWM and chunking behavior (in terms of IED) was not observed in either age group. For the older participants, this may be related to the difficulties they reported during the VSWM task. It may also be that the extent of preparation and chunking, as quantified with the IED, is independent of the actual VSWM capacity. Remember that the IED measure also reflects the time uncertainty that is associated with the first response of a discrete sequence. Our results suggest that processing speed does not play a strong role in chunking behavior. This fits the idea that older adults had still been relying more on the motor processor than on the cognitive processor (Abrahamse et al., 2013). That processing speed in older adults is indeed associated with the cognitive processor was indicated by the present finding that processing speed did correlate with random sequence performance.

In summary, we found that age differences in motor chunking behavior, as measured by the difference between preparation and execution of the sequence (i.e., IED), diminish with extended practice. Unlike young adults, older adults appeared to show an association between slow elements in the sequences and fingers that were slow in the random sequences. This finding shows that future research should take into account the possibility that in older adults a slow sequence element may be caused by a slow, perhaps stiff, finger instead of by the start of a next motor chunk.

Acknowledgements

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Reduced motor chunking in older adults cannot be attributed to carefulness

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Manuscript in preparation

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ABSTRACT

Previous research on motor sequence learning showed that older adults have difficulty developing motor chunks. We hypothesized that the careful, error-averse way in which this group often conducts motor tasks stimulates them to perform movements slowly resulting in relatively large intervals between movements. These longer intervals could cause extended decay of response code activation, reducing the development of associations between subsequent response codes and thus hampering the development of motor chunks. To test this idea, we instructed groups of older participants to perform a sequence learning task either as fast, or as accurate as possible.

Participants (62 – 75 years old) practiced a discrete sequence production (DSP) task with 168 practice trials per sequence. A Speed group was instructed to perform as fast as they could while paying little attention to errors committed. An Accuracy group was instructed to make as few errors as possible. After practice participants performed in a test phase containing random sequences, familiar sequences and a single-stimulus condition in which the familiar sequences were to be performed to the first stimulus only.

The intervention induced the expected effect with fast responses and relatively many errors in the Speed group, and the opposite pattern in the Accuracy group. However, our measure of chunking showed no group difference at any moment of practice or during the test phase. Furthermore, in the test phase, the speed group was not more successful in performing the sequences by heart than the accuracy group. We conclude that speedy, error-rich performance during practice does not stimulate the development of motor chunks in older adults.

INTRODUCTION

Motor sequence learning is an important ability to maintain daily living with advancing age. Unfortunately, older adults (OA) show deficits in performing and learning motor sequences. A well-known aspect that is affected strongly is movement speed but numerous other aspects of sequence learning change with advancing age as well. For example, learning is often slower, especially in complex tasks, and task performance requires more cognitive control (King, Fogel, Albouy, & Doyon, 2013; Seidler et al., 2010). Furthermore, OA were found to have greater difficulty than young adults (YA) in developing representations that contain integrated series of movements, often called *motor chunks* (Bo et al., 2009; Panzer et al., 2011; Verwey, 2010; Verwey et al., 2011). Some authors have related OA's inability to use motor chunking to a tendency to remain reliant on external stimuli during task performance (Verwey, 2010). This focus on external guidance has been found in earlier research as well, and might be a consequence of OA's preference for strategies that emphasize accuracy over speed (Goggin & Meeuwsen, 1992; Salthouse, 1979; Walker et al., 1997). In the present study, we investigated whether the emphasis that OA place on accuracy, which may slow them down and fuel their reliance on external guidance, affects the extent to which they develop motor chunks.

Chunking is fundamental to efficient sequence execution, and has been extensively studied with the discrete sequence production (DSP) task (Abrahamse et al., 2013; Verwey, 1996). In this task, participants practice two fixed sequences of 3 to 7 key-presses over a prolonged period of time. In an attempt to better understand the processes underlying sequential motor behavior, the results of many DSP studies have led to the proposal of the Dual Processor Model (DPM). According to the DPM, two processors drive various modes in which the elements of a DSP task sequence can be executed (Abrahamse et al., 2013; Verwey, 2001). A *cognitive processor* underlies performance in the *reaction* mode that involves translating individual stimuli into responses. With practice, associations between ensuing elements of the sequence begin to form, this is called the associative mode. In this mode, still mainly driven by the cognitive processor, external guidance by the movement-specific stimuli is still required, but responses to upcoming stimuli are primed by the preceding response. Finally, a *motor processor* underlies performance in the so-called *chunking mode* that relies on motor chunks that have been developed in the course of extended practice. Defining properties of sequence performance in the chunking mode are increased automaticity (i.e., reduced attentional load); reduced reliance on external stimuli after the first element; and the preparation, or buffering, of elements of the sequence (Abrahamse et al., 2013).

Previous sequence learning studies on chunking in OA have focused on various aspects of chunking behavior. For instance, Panzer et al. (2011) showed that OA have difficulties dividing the sequence in subseries of movements, or chunks. Additionally, Bo et al. (2009) found that when OA do divide a sequence in multiple chunks, these chunks consist of fewer elements than the chunks formed by YA. Two other studies investigated the extent to which OA prepare sequence execution before commencing the first movement. Specifically, Verwey (2010) measured the difference in response time (RT) between the first element (the *initiation response*) of the sequence and the remaining elements (the *execution responses*). He found that the difference between sequence initiation time and mean element execution time is much smaller in OA than in YA, suggesting that OA make limited use of motor chunks. Later, similar results were found for middle-aged adults (Verwey et al., 2011). In line with limited development of motor chunks, the OA also remained highly dependent on guidance by external stimuli in that most of the older participants were not able to produce the sequences without key-specific stimuli. These results suggest that in the course of practice YA are increasingly performing in the chunking mode, while OA continue to perform in the reaction or associative mode.

In the current study, we investigated the hypothesis that encouraging OA to focus on speed instead of accuracy increases chunking behavior in a DSP task. This is suggested by the notion that faster responses allow for less decay of response code activation in between responses (Hommel, 1994), which in turn could lead to stronger sequence representations because of increased associations between ensuing sequence elements (Verwey et al., 2015). In line with this idea, previous research found that longer response-stimulus intervals cause reduced sequence learning in a serial reaction time task (Frensch & Miner, 1994; Verwey & Dronkers, n.d.). It should be noted, though, that this beneficial effect of speed might be counteracted by the increased error rate that could accompany an increased focus on execution speed. To test our hypothesis, we randomly assigned older participants to either a Speed or an Accuracy group. They practiced a 3- and a 6-key sequence, the 3-key sequence was included because OA may be more likely to use motor chunking with short sequences (Bo et al., 2009). We predicted that increases in speed would stimulate the transition to the chunking mode, and that this would mostly affect key-presses after the first key-press since these benefit most from the enhanced preparation assumed to accompany the speed instruction. Hence, we predicted a larger difference between initiation and execution responses in the Speed than in the Accuracy condition. Additionally, we tested whether participants were able to perform the sequences without external guidance (past the first stimulus), as predicted by the notion that participants execute their sequences in the chunking mode (Abrahamse et al., 2013). Note that unlike several previous studies (e.g., Ruitenberg, Verwey, Schutter, & Abrahamse, 2014), we did not focus on the potential division of a sequence into multiple subseries of movements. We do this because previous research showed that the most commonly used indicator for a chunk start within a sequence – a slow element in the sequence – may in OA be caused also by a slow (e.g., stiff) finger (see Chapter 3).

METHODS

Participants

Participants were recruited via local media. Interested OA were invited for participation only when they reported that none of the following applied: severe motor problems including use of a wheelchair or limitations in using the fingers or arms; history of neurological problems; arthritis or rheumatism. One participant was excluded due to extremely slow mean RTs (3 standard deviations above from the sample mean). The 24 participants (aged 62 – 75, mean age 69 ± 4, 15 females) who were eventually included in the analysis had a score on the Montreal Cognitive Assessment (MoCA, Nasreddine et al., 2005) of 26.8 ± 1.7. None scored below 22, the threshold for mild cognitive impairment (Freitas et al., 2013). According to the Edinburgh handedness inventory (Oldfield, 1971), 18 participants were right-handed, four left-handed, and two were ambidextrous. The ethics committee of the University of Twente, faculty of Behavioral, Management and Social Sciences, approved the study. All participants provided written informed consent and received a financial compensation of € 20,- and reimbursement for travel costs.

Apparatus

The task was presented on a 22″ LCD wide-screen monitor using E-Prime 2.0 running under Windows 7. Participants used a standard USB keyboard to perform the sequences.

Discrete sequence production task

Participants practiced a 3- and a 6-key sequence in random order using the ring, middle and index fingers of both hands. They used the D, F, G, J, K and L keys of a standard computer keyboard to respond to targets presented in one of six horizontally aligned 28 * 28 mm placeholders. After pressing the spatially compatible key, the next target was immediately displayed. This continued until a sequence was completed. We use the term trial to denote performance of one sequence. After each trial, a 1250 ms white screen was presented, the next trial then started with a 1000 ms presentation of the placeholders. When a key was pressed during this presentation period, an error message "too early" was presented for 1500 ms in Dutch and the presentation period was restarted. To ensure that all fingers were used equally often at each sequential position across participants, the sequence elements were rotated across sequential positions (e.g., the sequence G, L, D for one participant becomes J, D, F for the next, and so on). As a reminder of the keys to be used, the letter H was displayed in between placeholder 3 and 4 to emphasize that the three keys left and right of the H key were associated with the placeholders. The horizontal spacing was 56 mm between the third and fourth placeholder, and 14 mm between the other placeholders. The screen background was white and the placeholder outlines were black. A placeholder was filled green when it became the active target.

The task involved 7 practice blocks each containing 2 sub-blocks of 24 trials each (48 trials per block, 336 trials in total). Although there was no specific familiarization phase, the experimenter monitored performance of the first few sequences to ensure that the participant understood the task. Participants were given a 40-second break between sub-blocks and a 120-second break between blocks. The test phase consisted of three blocks, each containing 32 trials and involving a different experimental condition. The familiar condition included the two practiced sequences. The random condition consisted of random sequences that were generated online (and contained no repetitions). These two test blocks were presented in counterbalanced order and were separated by a 40-second break. Finally, the single-stimulus test condition included the familiar sequences too but, after responding correctly to the first stimulus, no targets were displayed and the participant was instructed to complete the sequence by heart. Since the two sequences that participants practiced always started with a different first key-press, the first stimulus was sufficient for the participant to determine which of their sequences was to be performed. When participants were not able to produce one correct sequence during the first 10 trials, the single-stimulus condition was terminated prematurely. Otherwise, all 32 trials were performed. The participants were not informed about this. The single-stimulus condition was always introduced as the last test block to prevent interference with the other two test blocks. A short additional instruction screen was presented before the single-stimulus block explaining that stimuli after the first would not be displayed anymore. The participant started after he or she confirmed to the experimenter that the instructions were clear.

The instructions and feedback during practice urged the participants to produce the sequence either fast or accurately. During the breaks, the Speed group received information about their mean RT during the completed sub-block. When the mean RT was 2.5% faster than the previous block, the instruction read (translated from Dutch): "This was faster than the previous block, good job! Try to be faster again in the next block". When RT improvement didn't meet the 2.5% criterion, the instruction read: "Unfortunately, you didn't improve yourself sufficiently! Try to be faster in the next block". When error-rates, calculated as the percentage of trials containing an error, were below 10%, participants were urged to be faster with the instruction "You are allowed to make more errors". Only when error-rates were above 40% the instruction was "You are making too many errors, please try to make fewer errors". In the Accuracy group, participants were stimulated to perform the task without making errors. The message during the breaks was either "You have not made any errors during the previous block, good job! Please try to maintain this", or "You made X errors during the previous block, try to make fewer errors". When a participant's mean key-press RT across a sub-block surpassed 2000 ms, the only instruction was "You responded a little too slowly, try to respond faster". After committing an error, the message "wrong" was presented for both groups. To penalize errors to a stronger extent in the Accuracy group, the error feedback duration was 3000 ms in the accuracy group, and 1500 ms in the speed group.

Before starting the test phase, all participants were shown the same message: "The instruction changes now: Respond as fast and accurately as possible". When participants asked for additional explanation, the experimenter added that, "unlike before, both speed and accuracy of responding are now equally important". During the test phase, no instructions or feedback was provided during the breaks.

Procedure

Participants were randomly assigned to either the Speed or the Accuracy group. The procedure started with administration of the MoCA (Nasreddine et al., 2005). Then, participants filled in a first ad-hoc self-report fatigue scale (11 point Likert scale) before commencing the DSP task practice phase. Instructions before and after each of the 7 practice blocks stimulated participants to either perform fast or accurately. After the practice phase, a questionnaire measuring explicit sequence knowledge was administered. In this awareness questionnaire, participants were first asked to write down the sequences using the letters of the keys they had been pressing. The instruction provided a reminder of the letters / keys used and their location on the keyboard. Then, the target locations were displayed on the screen again and the participants were asked to point out, with their index finger, the sequences they had just practiced. The experimenter registered the participant's pointing sequence. Finally, participants were asked to select their sequences from two lists of 12 sequences, one for the 3-key and one for the 6-key sequence. After the awareness questionnaire, another fatigue scale was administered followed by the DSP task test phase. The test phase was followed by the last fatigue scale. Finally, participants were debriefed and compensation was arranged. A session lasted about 1 hour and 45 minutes.

Analyses

We used a method described previously (see Chapter 3) to classify per participant, for each practice and familiar test block separately, all responses from the 6-element sequence as *initialization responses*, *slow responses*, or *execution responses*. Every first RT was classified as initialization. A response was classified as a slow response when two one-tailed, paired samples t-tests with alpha set to .1 indicated it to be slower than its neighboring responses in the current block (Ruitenberg, Verwey, et al., 2014). All other RTs were execution responses, the second and sixth RT were always classified as execution responses. We then calculated, after excluding the slow responses, the *Initiation-Execution Difference* (IED) as an index for the extent to which sequence performance was prepared before onset of the first movement.

For all RT analyses including calculation of the IED, we excluded the first trial of every sub-block and trials containing an error (erroneous trials were not replaced). Next, we excluded all trials that had a mean RT exceeding a threshold of the mean trial RT plus 2.5 * the standard deviation of mean RTs in that sub-block. For accuracy analyses we calculated across all trials in each block the proportions of trials containing an error. We then performed an arcsine transformation on the proportion of erroneous trials before submitting the resulting variable to the ANOVA (Winer, Brown, & Michels, 1991). When assumptions of sphericity were violated for any of the analyses we applied the Greenhouse–Geisser correction, but we report the corrected p-values and original degrees of freedom.

Using the explicit knowledge questionnaire results, we computed an aggregate explicit knowledge score based on the sum of the number of elements correctly written down and the number of elements correctly pointed out during the questionnaire (correct elements were counted from the start to the first mistake; maximum explicit knowledge score: 2 times 3 + 6 = 18). Data for the single-stimulus condition was included for RT analysis only when a participant had finished the single-stimulus block, and when he or she performed at least five sequences correctly. This was done separately for the 3-key and 6-key sequences.

RESULTS

Practice phase results

Response times of the 3-key sequence were submitted to a 2 (Speed-accuracy group) x 7 (Block) x 3 (Key) mixed ANOVA with Speed-accuracy group as between-participants variable. Participants in the Speed group were faster than those in the Accuracy group (490 vs. 610 ms), $F(1, 22) = 4.9, p = .038, \eta_p^2 = .181$, showing that the speed-accuracy intervention had induced the intended effect (see Fig. 1). Performance improved over Blocks, $F(6, 132) = 55.3, p < .001, \eta_p^2 = .715$, and the main effect of Key was significant too, $F(2, 44) = 11.9, p < .001, \eta_p^2 = .350$. Furthermore, Key interacted with Block, $F(12, 264) = 13.2, p < .001, \eta_p^2 = .376$, showing that the RT-pattern per sequence changed over the successive blocks. The Block by Speed-accuracy group interaction was marginally significant, $F(6, 312) = 2.7, p = .059$ (Fig. 1). The Key by Speed-accuracy group did not reach significance, $F(2,44) = 0.4, p = .700$, and the three-way interaction did not reach significance either, $F(12, 264) = 0.9, p = .468$.

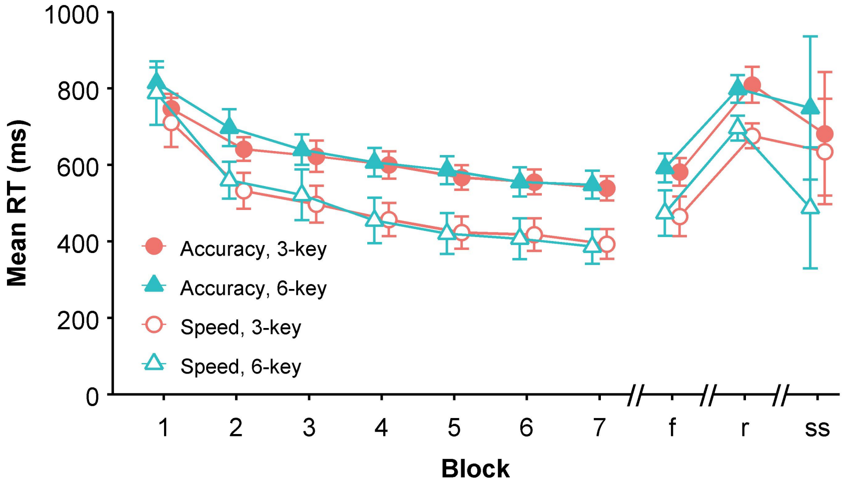

Fig. 1 Mean response times per sequence in the practice and test blocks. The familiar (f) and random (r) block order was counterbalanced over participants, the Single-stimulus (ss) block was always last. Note that 3- and 6-key data-points are offset on the horizontal plane to enhance legibility. Error bars denote standard error.

Response times of the 6-key sequence were submitted to a similar 2 (Speed-accuracy group) x 7 (Block) x 6 (Key) mixed ANOVA. This time, participants in the Speed group were only marginally faster than those in the Accuracy group (505 vs. 635 ms), $F(1,22) = 3.9, p = .062$,

η_p^2 = .149. Participants did improve over Blocks, *F*(6, 132) = 61.8, $p < .001$, η_p^2 = .738, and again, we found a main effect of Key, *F*(5, 110) = 7.9, $p < .001$, η_p^2 = .265. Similar to the 3-key sequence, Block interacted with Key, *F*(30, 660) = 7.4, $p < .001$, η_p^2 = .252, showing that the RT pattern across each sequence changed during practice. The Block by Speed-accuracy group interaction was marginally significant, *F*(6, 132) = 2.6, $p = .078$, η_p^2 = .107. The Key by Speed-accuracy group interaction was not significant, *F*(5, 110) = 0.8, $p = .539$, and neither was the three-way interaction, *F*(30, 660) = 0.7, $p = .675$.

To validate whether our intervention led to faster performance of the 6-key sequences in the Speed group at the end of practice, we conducted the same ANOVA including only the final block of practice. The Speed group was indeed faster during the final block, *F*(1, 22) = 7.7, $p = .011$, η_p^2 = .259. Furthermore, the main effect of Key was still significant, *F*(5, 110) = 13.5, $p < .001$, η_p^2 = .381, but the Key by Speed-accuracy group interaction was not significant, *F*(5, 110) = 0.4, $p = .849$.

For the 3- and 6-key sequences, arcsine transformed proportions of trials correct per block were submitted to separate 2 (Speed-accuracy group) x 7 (Block) mixed ANOVAs. Participants in the Speed group made more errors in the 3-key sequence (91% vs. 98%), *F*(1, 22) = 13.5, $p = .001$, η_p^2 = .380, and in the 6-key sequence (81% vs. 97%), *F*(1, 22) = 57.2, $p < .001$, η_p^2 = .722 (see Fig. 2). This confirms that our intervention resulted in faster RTs and higher error rates in the Speed compared to the Accuracy group. For the 6-key sequence, participants made more errors with successive Blocks, *F*(6, 132) = 2.4, $p = .034$, η_p^2 = .097. For the 3-key sequence, the main effect of Block was not significant, *F*(6, 132) = 0.9, $p = .467$. The Block by Speed-accuracy group interaction did not reach significance for the 3-key sequence, *F*(6, 132) = 1.2, $p = .335$, or for the 6-key sequence, *F*(6, 132) = 1.4, $p = .210$.

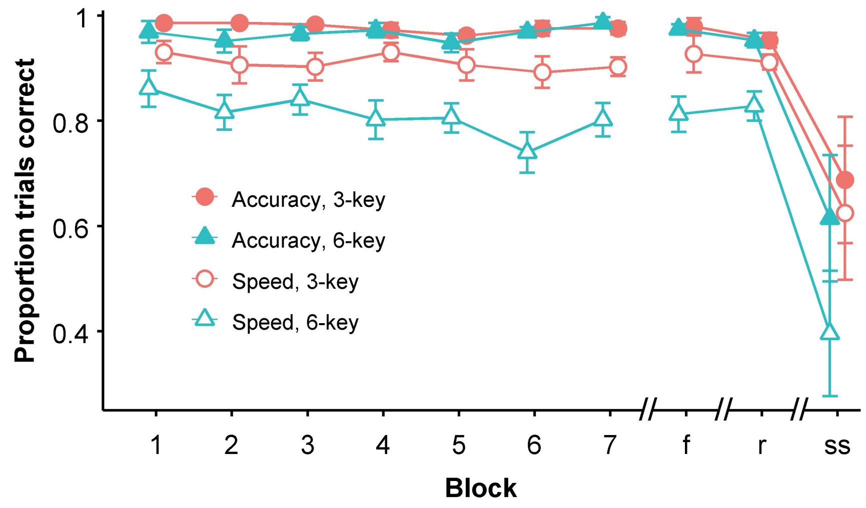

Fig. 2 Accuracy in the practice and test blocks for the Accuracy and the Speed groups. Error bars denote standard error.

We submitted the 3- and 6-key sequence IEDs of the practice phase, assumed to index chunking, to separate 7 (Block) x 2 (Speed-accuracy group) ANOVAs with Speed-accuracy group as between-participants factor. The IED increased with practice across blocks for the 3-key sequence, $F(6, 312) = 21.9$, $p < .001$, $\eta_p^2 = .499$, and for the 6-key sequence, $F(6, 132) = 8.1$, $p < .001$, $\eta_p^2 = .269$ (see Fig. 3). However, the IEDs did not differ between the Speed-accuracy groups (3-key: $F(1, 22) = 0.4$, $p = .518$, 6-key: $F(1,22) = 0.6$, $p = .454$) and neither did the interaction between Speed-accuracy and Block reach significance, 3-key: $F(6, 312) = 1$, $p = .409$, 6-key: $F(6, 132) = 1.5$, $p = .228$. These results do not support the hypothesis that Speed-accuracy influenced chunking during practice.

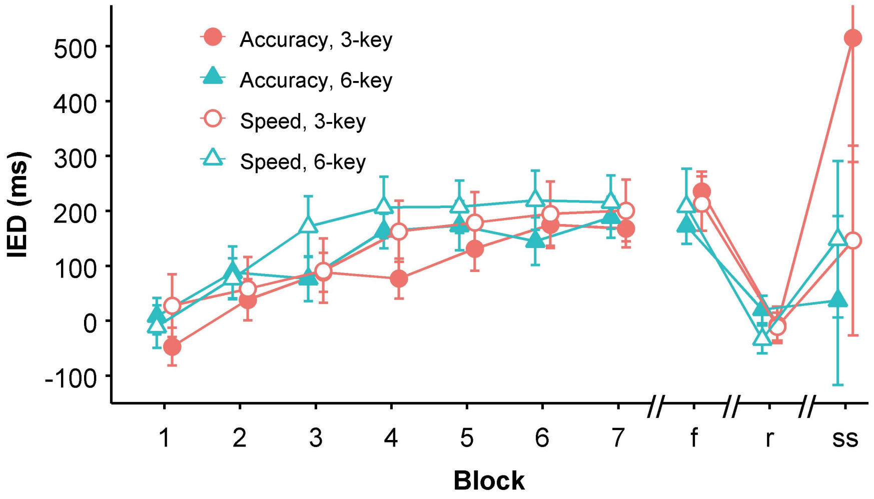

Fig. 3 Development of the IED over practice and test blocks. Error bars denote standard error (we cut off part of the 3-key Single-stimulus error-bar).

Test phase results: familiar and random sequence conditions

The RTs of the 3-key sequences in the first two test phase conditions were submitted to a 2 (Test condition: Familiar vs. Random) x 2 (Speed-accuracy group) x 3 (Key) mixed ANOVA with Speed-accuracy group as between participants factor. Despite the same performance instruction for both groups in the test phase, responses across both Test conditions were still faster in the Speed than in the Accuracy group (588 vs. 696 ms), $F(1, 22) = 5.6, p = .027, \eta_p^2 = .202$. Furthermore, participants responded faster in the Familiar than in the Random Test condition, $F(1,22) = 57.4, p < .001, \eta_p^2 = .723$. Like in the practice phase, we also found a main effect of Key, $F(2, 44) = 19.4, p < .001, \eta_p^2 = .468$ (see Fig. 4). Finally, Test condition and Key showed a significant interaction, $F(2,44) = 38.5, p < .001, \eta_p^2 = .636$. The Test condition by Speed-accuracy group interaction was not significant, $F(1, 22) = 0.1, p = .768$, and neither were the Key by Speed-accuracy interaction, $F(2, 44) = 0.1, p = .880$, and the three-way interaction, $F(2, 44) = 0.2, p = .776$.

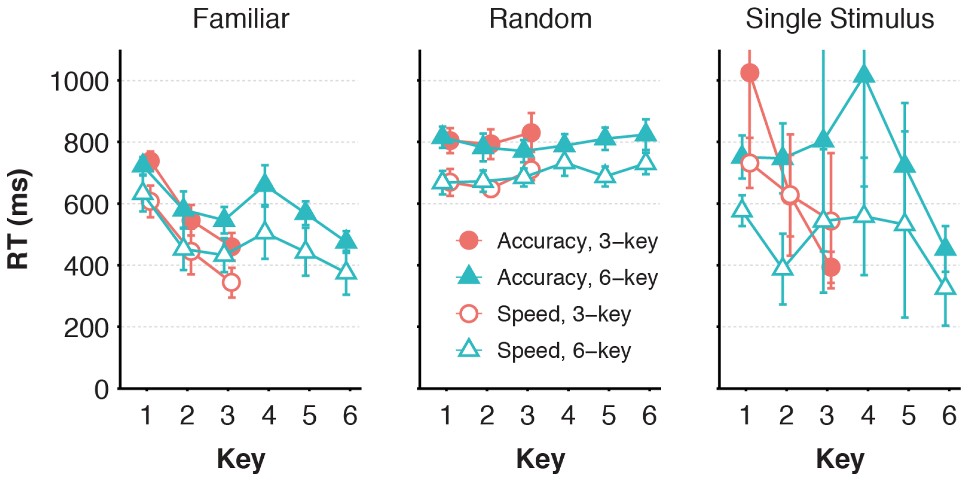

Fig. 4 Response times obtained in the test phase. The Single stimulus condition included 18 (out of the 24) participants for the 3-key sequence, and 15 for the 6-key sequence. Error bars denote standard error (for legibility, we cut off parts of some of the Single-stimulus error-bars as these are symmetric anyway).

The same ANOVA performed for the 6-key sequence data showed a trend for faster performance by the Speed group (618 vs. 710 ms), $F(1, 22) = 4.2, p = .052, \eta_p^2 = .160$. Similar to the 3-key sequences, performance in the Familiar Test condition was faster than in the Random condition, $F(1, 22) = 57.8, p < .001, \eta_p^2 = .724$. Furthermore, we again found a main effect of Key, $F(5, 110) = 7.7, p < .001, \eta_p^2 = .258$, and an interaction of Key and Test condition, $F(5, 110) = 13.6, p < .001, \eta_p^2 = .382$. The Test condition by Speed-accuracy group interaction, $F(1, 22) = 0.1, p = .778$, the Key by Speed-accuracy group interaction, $F(5, 110)$

= 0.1, $p = .936$, and the three-way interaction, $F(5, 110) = 1.0$, $p = .418$, did not reach significance.

For the 3- and 6-key sequences, arcsine transformed proportions of trials correct per block were submitted to 2 (Test condition: Familiar vs. Random) x 2 (Speed-accuracy group) mixed ANOVAs. Participants in the Accuracy group continued to make fewer errors than those in the Speed group (95% vs. 92%) when performing the 3-key sequence, $F(1, 22) = 5.5$, $p = .029$, $\eta_p^2 = .199$, and when performing the 6-key sequence (96% vs. 82%), $F(1,22) = 26.9$, $p < .001$, $\eta_p^2 = .550$**.** The effect of Test condition reached significance for the 3-key sequence with more errors in the Random condition (95% vs. 93%), $F(1,22) = 5.1$, $p = .034$, $\eta_p^2 = .189$, but not for the 6-key sequence, $F(1,22) = 0.6$, $p = .471$. The Test condition by Speed-accuracy group interaction did not reach significance for the 3-key sequence, $F(1, 22) = 0.0$, $p = .942$, nor for the 6-key sequence, $F(1, 22) = 0.5$, $p = .488$.

The 3- and 6-key IEDs for the test phase were submitted to separate 2 (Test condition: Familiar vs. Random) x 2 (Speed-Accuracy group) mixed ANOVAs with Speed-Accuracy group as between-subjects factor. Participants showed a higher IED in the Familiar Test condition than in the Random condition for the 3-key sequence, $F(1, 22) = 65.6$, $p < .001$, $\eta_p^2 = .749$, as well as for the 6-key sequence, $F(1, 22) = 40.2$, $p < .001$, $\eta_p^2 = .646$. However, for both sequence lengths, there was no main effect of Speed-accuracy group (3-key: $F(1, 22) = 0.1$, $p = .771$, 6-key: $F(1, 22) = 0.0$, $p = .857$), and neither was there a significant interaction between Speed-accuracy group and Test condition (3-key: $F(1, 22) = 0.1$, $p = .743$, 6-key: $F(1, 22) = 2.1$, $p = .163$).

Summarizing it seems that, in the test phase, participants still performed largely according to the Speed-accuracy instruction that had been provided during the practice phase. Compared to the Accuracy group, participants in the Speed group still made more errors and were faster, although only marginally so in the 6-key sequences. The IED still did not differ between the Speed-accuracy groups.

Test phase results: Single stimulus condition

Of the 24 participants in our sample, five were unable to perform one correct 3- or 6-key sequence during the first 10 trials of the Single-Stimulus Condition. For them, the task was terminated prematurely and their Single-Stimulus RT and IED data were not included in the analyses. For the remaining participants, data were included in the RT and IED analyses and figures only when a participant had performed at least five correct trials of a specific sequence length. For the 3-key sequence analysis 18 participants adhered to these criteria (9 from the Speed group). For the 6-key sequence analysis 15 participants adhered to these criteria (6 from the Speed group). Note that the data of all participants were included in the accuracy analyses.

Submitting the 3-key sequence RTs of those who adhered to our error criterion to a 2 (Speed-accuracy group) x 3 (Key) mixed ANOVA showed a main effect of Key, $F(2, 32) = 4.5, p = .030, \eta_p^2 = .221$. The main effect of Speed-accuracy group did not reach significance, $F(1, 16) = 0.0, p = .830$, and neither did the interaction, $F(2, 32) = 1.4, p = .271$. Submitting the 6-key sequence data to the same analysis showed no significant main effects of Key, $F(5, 65) = 1.7, p = .214$, and Speed-accuracy group, $F(1, 13) = 1.0, p = .342$, and their interaction was not significant either, $F(5, 65) = 0.4, p = .636$. For both the 3- and 6-key sequences, there was no difference between the Speed and Accuracy groups in the number of sequences performed correctly during the Single stimulus test block as tested with Mann-Whitney tests (3-key: $U = 67, p = .799$, 6-key: $U = 50, p = .219$).

For the Single-stimulus Test condition, there was no significant difference in IED between the Speed and Accuracy groups for both the 3-key sequence, $t(16) = 1.3, p = .213$, and the 6-key sequence, $t(13) = 0.5, p = .625$.

Explicit knowledge and fatigue

A t-test on explicit knowledge, defined as the sum of the number of elements written down and pointed out correctly, indicated that there was no difference in the amount of explicit knowledge between the Speed (mean = 8.3 correct elements out of 18) and Accuracy (mean = 10) groups, $t(22) = 0.6, p = .565$. To analyze fatigue differences over time, we used the R package nparLD (Noguchi, Gel, Brunner, & Konietschke, 2012) to perform nonparametric longitudinal analysis according to a 2 (Speed-accuracy group) x 3 (Time of measurement) design with the ANOVA-type statistic (ATS) as test statistic. We found a main effect of Time, ATS(df = 1.3) = 22.4, $p < .001$, indicating that fatigue increased over time. Yet, there was no main effect of Speed-accuracy group, ATS(df = 1) = 1.8, $p = .177$, and neither was there an interaction, ATS(1.3) = 2.0, $p = .155$. These results suggest that the absence of an effect of the Speed-accuracy instruction on chunking was not due to increased fatigue in one of the conditions.

DISCUSSION

In this study, two groups of OA performed a DSP task, one group focusing on completing the sequences as fast as possible, and the other group focusing on obtaining highly accurate performance. As intended, the speed-accuracy intervention resulted in fast responses with relatively many errors in the speed group, and slower responses with fewer errors in the accuracy group. Both groups showed improvements in RTs during the practice phase, and both groups showed an increase in the IED, indicating learning and possibly development of chunking. However, the results show that the reduced tendency of OA to develop motor chunks found in earlier studies (Verwey, 2010; Verwey et al., 2011), cannot be attributed to OA focusing on accuracy at the expense of speed. The IED did not differ between the groups in the practice or in the test blocks, and neither did the speed group perform better in the single-stimulus test condition. Development of fatigue and the formation of explicit knowledge were not different between groups, implying that these factors did not affect the results.

Our results indicate that carefulness does not explain limited chunking in OA. A few reasons may explain the absence of the hypothesized effect. First of all, the expected relationship between chunk development and carefulness may simply not be as strong as expected. Second, it may also be that our sample of OA was too skilled and that a sample of older adults with higher baseline RTs would show a benefit from a speed-accuracy intervention. For example, the OA in Verwey (2010) had a mean RT of 1157 ms in a largely similar DSP test phase compared to 642 ms in our sample. This was probably caused by the way in which the OA had been recruited. In the present experiment, OA were recruited via an advertisement whereas Verwey (2010) had students visit other students' grandparents. This may have yielded a selection of less fit OA. A third explanation for the absence of an effect of instruction may be that the higher error rate in the speed group counteracted the development of chunking. A recent study investigated post-error slowing in OA performing the DSP task and showed that like YA, middle-aged OA as well as high-aged OA revealed post-error slowing (Ruitenberg, Abrahamse, De Kleine, & Verwey, 2014). Interestingly, this slowing was functional only for YA and middle-aged OA as only these groups showed improved accuracy following an error. The authors suggested that the high-aged OA reverted to execution based on stimulus-response translation (i.e., the reaction mode) after an error, a similar process may have reduced the development of chunking representations in our study.

Overall, our speed-accuracy intervention yielded the expected effects in term of lower RTs and increased errors in the speed group. However, both the IED and performance in the single-stimulus test condition did not provide any indications for increased chunking during or after practice with a focus on fast responses. We conclude that, although OA are well able to speed up task performance when instructed to, their tendency to work more carefully at the expense of execution rate does not explain why OA seem to develop motor chunks to a lesser degree than YA.

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Non-invasive brain stimulation enhances motor learning in healthy older adults

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Manuscript in preparation

ABSTRACT

Transcranial direct current stimulation (tDCS) has shown the potential to enhance motor learning in older adults. However, results have not been consistent and only little research to date has focused on sequence learning. We aimed to add robustness to previous results and extend our understanding. Therefore, we conducted a study that includes a replication of a previous study (Zimerman et al., 2013) that found enhanced motor sequence learning with tDCS in older adults. Our study further involved a condition to determine whether potential tDCS benefits are sequence-specific or task-general.

We tested 16 older (62 - 75) and 16 young adults (18 - 30) in a double-blind cross-over experiment. All participants learned two different key pressing sequences in separate sessions. During practice they received 20 minutes of anodal stimulation with one, and 20 minutes of sham tDCS stimulation with the other sequence. A bipolar montage was used with the anode over left M1 and the cathode over the right supraorbital area. Motor learning was measured using a sequential tapping task in which participants used four fingers to tap a fixed 5-element sequence as often as possible in 3-minute time blocks. Six blocks contained fixed sequences. Additional blocks at the beginning and end of practice contained random sequences to tease apart sequence-specific and task-general learning. In line with Zimerman et al. (2013), we show that motor sequence learning, especially in older adults, can be enhanced with tDCS. We further established that tDCS improved sequence-specific learning, while task-general performance was not influenced.

INTRODUCTION

From learning to drive to preparing breakfast and brushing one's teeth, the development and maintenance of motor skills is essential in daily living. Unfortunately, the learning of motor sequences is impaired in healthy older adults (OA, Seidler et al., 2010). Thus, enhancement of motor learning in healthy older adults is a promising line of research that could aid in maintaining independent living. The present study attempts to aid motor sequence learning in OA using transcranial direct current stimulation (tDCS). tDCS has been shown to be effective in improving motor learning and performance in a wide variety of motor tasks such as sequence tapping, the Grooved Pegboard Test, and the Jebson-Taylor hand function tests in OA (Heise et al., 2014; Marquez et al., 2015; Parikh & Cole, 2014; Zimerman et al., 2013, 2014). Moreover, a recent review by Summers et al. (2016) concluded that cognitive performance can also be enhanced by tDCS.

Despite the positive effects of tDCS, when studying the tDCS literature readers will also encounter some skepticism given the large degree of unexplained variability in response to tDCS (Bestmann et al., 2014; Horvath et al., 2014, 2015a, 2015b; Perceval et al., 2016). For example, it is not fully understood why tDCS often has differential effects in young adults (YA) and OA (Perceval et al., 2016). Additionally, recent studies have reported null-effects of tDCS on motor learning in OA (Kaminski et al., 2017; Raw, Allen, Mon-Williams, & Wilkie, 2016) and substantial inter- and intra-individual variability of tDCS response in YA (Horvath, Vogrin, Carter, Cook, & Forte, 2016). Following these observations, there has been a call to advance the tDCS field by taking a more systematic, incremental approach. Accordingly, replications, fundamental physiological investigations and modeling studies are increasingly valued (Bestmann et al., 2014; Summers et al., 2016). In light of these developments we performed a replication of a previously published motor skill enhancing tDCS study in OA (Zimerman et al., 2013). We focused on this study because it is one of the very few that combined tDCS with sequence learning in OA.

Zimerman et al. (2013) investigated whether tDCS enhances motor sequence learning in OA and YA. Using a within-subject design, participants received anodal tDCS (a-tDCS) during one visit and sham stimulation during the other visit, with a wash-out period of at least 10 days. A different sequence was practiced during each visit. The participants were instructed to tap a 5-element sequence as often as possible in successive 3-minute windows. The authors found a facilitating effect on motor learning with a-tDCS to the primary motor cortex (M1) in OA but not in YA. This beneficial effect extended to a retention test 24 hours later. The results from this study provide important insights into the effects of tDCS on motor learning in OA, but a few key issues remain. First of all, the OA in this study showed no learning when performing in the sham condition. Second, the authors did not report whether task performance was influenced by the order of stimulation conditions and whether this differed between age groups. Since tDCS effects are partially dependent on task difficulty and likely also on experience with a task (Summers et al., 2016), it is good to scrutinize the effect of previous exposure to the task. It is likely that there was an order effect such that exposure to the task during the first session improved performance in the second session (Robertson, Pascual-Leone, & Miall, 2004). Finally, it is unknown whether the enhanced learning was caused by sequence-specific, or by task-general learning (e.g., Verwey, 1999). Dexterity has been shown to be enhanced in OA with tDCS (Hummel et al., 2010), and this is a viable explanation for Zimerman et al.'s (2013) beneficial effects of tDCS. Understanding which mechanism actually underlies enhanced performance in the Zimerman et al. (2013) experiment is important in order to estimate where and how this type of enhancement can be relevant in real-life applications. We believed that scrutinizing the effects of tDCS would allow us to explain some of the current differential findings between OA and YA in tDCS motor learning studies.

Our study included the same sequence-tapping task and the same stimulation conditions as Zimerman et al. (2013), but we added a pre- and post-test of random sequence performance to assess task-general learning. Note that while Zimerman et al. (2013) included retention tests 90 minutes and 24 hours after the practice phase, we did not include these tests because our random-sequence post-test might interfere with retention. Excluding these retention tests does not affect our ability to reproduce the main result found by Zimerman et al. (2013) since tDCS enhancement of motor learning was found during the practice phase, but tDCS did not affect consolidation. In other words, tDCS modulated motor learning in an online fashion. Our study served a number of goals. First, we aimed to reproduce the result of enhanced learning in OA with a-tDCS in the Zimerman et al. (2013) study. Second, we aimed at determining whether a-tDCS affects sequence-specific or task-general learning. We predicted that task-general learning would be enhanced in OA, in line with previous studies showing dexterity enhancement in OA when stimulated with a-tDCS (Hummel et al., 2010; Parikh & Cole, 2014). Our third goal was to investigate whether task experience obtained in the first session benefits the second session. We predicted that, especially for OA, baseline performance in the second session would be improved compared to the first session. We believe that studies like the present one play an important role in science since they provide added control for sampling error and artifacts, and therefore increase confidence in the generalization of the results (Open Science Collaboration, 2015; Schmidt, 2009).

MATERIALS & METHODS

Participants

We recruited nineteen healthy OA (aged 62 – 75) and sixteen healthy YA (aged 18 – 30) for the current study. OA were recruited via local media whereas the YA were mostly students living in the vicinity of the university campus recruited via the university participant pool or flyers. Interested OA received an information letter at home and were contacted at least seven days later to make an appointment. All participants were right-handed according to the Edinburgh handedness inventory (Oldfield, 1971). Two OA participants dropped out: one due to poor vision while another could not make the second session due to illness. Data from one other OA participant was excluded due to difficulties with performing the task. The 16 OA (8 females), that were eventually included in the final analysis, had a mean age of 69.5 ± 3.8. The OA had a mean score of 27.4 ± 1.5 on the Montreal Cognitive Assessment (MoCA, Nasreddine et al., 2005). All OA scored well above the threshold of 22 (Freitas et al., 2013). Participants were screened with the standard questionnaire for contra-indications when conducting non-invasive brain stimulation (Rossi, Hallett, Rossini, & Pascual-Leone, 2009). None of the included participants suffered from severe motor problems or limitations in using the fingers or arms, chronic joint pain, arthritis, rheumatism, sensitive skin, frequent headaches, clinical depression, poor vision, neurological or heart disorders. The 16 YA (10 females) had a mean age of 21.8 ± 4.0, the MoCA was not administered to them. The study was approved by the Medical Ethical Committee of the Medical Spectrum Twente (MST), Enschede, The Netherlands and conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent.

Design and procedure

The study followed a randomized crossover, double-blind design with Age group (YA versus OA) as between-subjects factor and tDCS condition (a-tDCS versus sham) as within-subjects factor. Two sequences were used, counterbalanced over tDCS condition order and Session. The tDCS conditions were spread over two sessions separated by at least 10 days. After set-up of the tDCS, the motor task was initiated (see Fig. 1). The motor task consisted of three parts: 2 baseline blocks, 5 practice blocks, and one post-test block. Before and after the baseline measurements as well as before and after the post-test block, visual analog scales (VAS) were administered, these measures are easy to administer and have shown high reliability (Folstein & Luria, 1973). Using three scales, participants rated their attention, hand fatigue, and general fatigue from 0 (indicated as "lowest possible level") to 100 (indicated as "highest possible level") by placing a cross on a 14 cm horizontal line, the scores were converted to percentages afterwards.

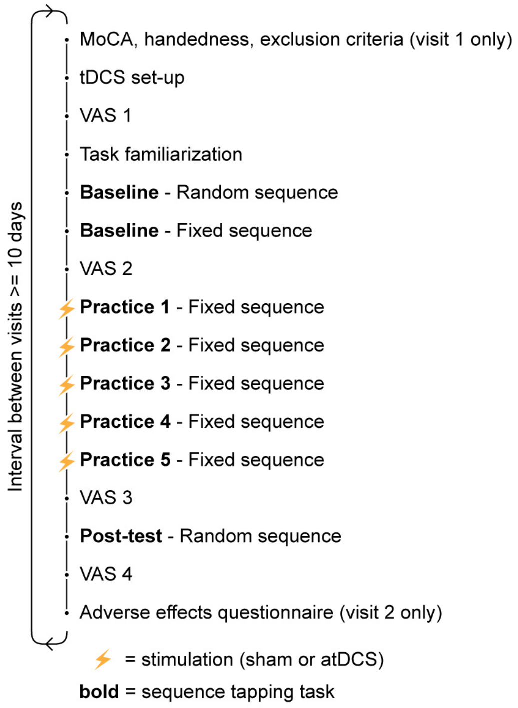

Fig. 1 Overview of the experiment. The procedure was virtually identical in two successive sessions, with half the participants starting with 20 min. anodal tDCS and the other half with the sham condition in Practice blocks 1 to 5. VAS = visual analog scale.

Sequence tapping task

Participants sat at a table behind a 24″ wide-screen LCD monitor. The viewing distance was approximately 65 cm. The task was presented using E-Prime 2.0. Participants responded using a 5-button Chronos response box (Psychology Software Tools, 2016). The screen background was white, the sequence to be performed (e.g., 3 - 5 - 2 - 4 - 2, digits measured 1 cm in height) was presented in black font in the center of the screen. Participants used the four right-most buttons of the response box (labeled 2 to 5, respectively) to perform the sequence presented on the screen using the fingers of their right hand except the thumb. In a fixed-sequence block, participants continuously cycled through the same sequence which was presented continuously. In a random-sequence block, a random sequence was generated online by E-Prime (without direct repetitions) after completion of each sequence or after an error. Thus, each participant likely saw a different random series of sequences in the random-sequence blocks. Participants were instructed to perform as many sequences as possible per 3-minute block, this poses requirements on speed as well as accuracy. In line with Zimerman et al. (2013), we used the number of sequences performed correctly in a block as primary outcome measure. The baseline blocks consisted of one random-sequence block followed by one fixed-sequence block (see Fig. 1). The practice blocks were all fixed-sequence blocks using the same sequence as in the baseline block, the post-test consisted of one random sequence block. The same fixed sequences were used for all participants: 3 - 5 - 2 - 4 - 2 and 5 - 2 - 4 - 3 - 4 (the same as used by Zimerman et al., 2013). Participants performed one fixed sequence in each session. The two fixed sequences were counterbalanced over sessions and tDCS conditions. The random sequences were always different from the previously used sequence and contained no repeated keys. As long as fixed sequences were performed correctly the display did not change. When an error was made in a fixed- or random-sequence block, a grey rectangle with red outline appeared in the background behind the digits for 400 ms. Responses made during this period were not registered. Next, the participant either restarted the sequence (in case of a fixed sequence block), or started the next sequence (in case of a random sequence block). Before onset of the baseline blocks, participants shortly familiarized with the task by performing a 30-second block with a fixed sequence (2 - 3 - 4 - 5 - 3) and a 30-second block with random sequences. A familiarization block was repeated when necessary until participants fully understood the task. Two aspects of our task differed from that of Zimerman et al. (2013): we added the random sequence block before and after the task, and we included feedback after an error whereas in the Zimerman et al. (2013), the display did not change when an error was made.

Transcranial Direct Current Stimulation

Stimulation was delivered with a battery-driven tCS stimulator (Starstim tCS, Neuroelectrics, Barcelona) through rubber electrodes housed in circular 25 cm^2 saline-soaked sponges. A bipolar montage was used with the anode over left M1, centered at C3, and the cathode over the right supraorbital area, centered at Fp2. This is a common montage for M1 stimulation (e.g., Nitsche et al., 2003). Electrode localization was performed using the 10-20 EEG system. The impedance was monitored before and during stimulation to ensure good contact of the sponges with the scalp. The stimulation was started at the onset of the practice phase (practice block 1) of the sequence-tapping task. For both stimulation conditions, the current ramped up linearly from 0 to 1 mA (0.04 mA/cm^2) over 8 s. In the sham control stimulation condition, the current was delivered for 30 seconds and then ramped down over 8 s. In the stimulation condition, the current continued for 20 minutes before being ramped down (over 8 s). The participants and the experimenter were blind to the type of stimulation. All participants were instructed that they could feel a mild itching sensation under the electrodes and received a minor demonstration (a few seconds of 0.3 mA stimulation) during tDCS set-up while measuring impedance. In line with recommendations from Brunoni et al. (2011), we administered an adverse effects questionnaire after every session.

Analyses

The main outcome variable was the number of sequences performed per 3-minute block. We used R (R Core Team, 2015) and the lme4 package (Bates, Mächler, Bolker, & Walker, 2015) to perform linear mixed-effects (LME) analysis. Model significance was evaluated using likelihood ratio tests, estimates of parameter significance were obtained using the lmerTest package which uses Satterthwaite approximations to the degrees of freedom (Kuznetsova, Brockhoff, & Christensen, 2016). In order to conduct likelihood ratio tests we initially fitted our models using a log-likelihood criterion (by including REML = FALSE in the lmer call). After model comparison, we re-fitted the model of interest using restricted maximum likelihood, allowing us to estimate p-values for the fixed effects that are not anticonservative for small sample sizes (Luke, 2016). For the fixed sequences, the predictor Block was coded to 0 for the fixed-sequence baseline Block, and 1-5 for the practice Blocks, and then centered. For the random sequence analysis, the baseline block was coded -.5, the post-test block .5. Contrast codes (-.5 or .5) were used for the factors, with -.5 representing respectively OA for the factor Age, Session 1 for the factor Session and sham for the factor tDCS condition. Centering makes interpretation more straightforward because each coefficient now represents the mean effect of each variable so that lower order effects can be interpreted as average effects (West, Ryu, Kwok, & Cham, 2011).

Results

The central analysis as reported in Zimerman et al. (2013) is a t-test comparing the amount of improvement from practice block 1 to 5 between tDCS conditions. The same analysis was conducted on our data and showed a trend towards a larger improvement in the OA a-tDCS group (which improved by 14 sequences during the session) than in the OA sham group (7 sequences), $t(15) = 1.6$, $p = .061$, while the improvement did not differ between tDCS conditions for YA, $t(15) = .03$, $p = .512$.

Visual inspection of our data confirmed our expectations of transfer from the first to the second session. Specifically, Session seems to affect the intercept and slope of performance, and differentially so for the Age groups (Fig. 2). Clearly, a proper model of our data includes Session, Age group and tDCS condition as predictors. We included Block as continuous predictor in order to model the full learning slope. In this way we used all available information, making our model less susceptible to noise. While development of motor skill is non-linear (Heathcote, Brown, & Mewhort, 2000), we still opted for a linear improvement model given the limited number of blocks and given that almost no participants reached an asymptote. We were mainly interested in 2-way interactions of Block with tDCS condition, Session and Age. Furthermore, we wanted to know whether the Block x tDCS condition interaction would be different for the two Age groups (i.e., whether there would be a 3-way interaction). We started with an intercept-only model including Subject intercept as random factor. The intra-class correlation coefficient for this model was .90, suggesting a high degree of dependency within individuals and thus supporting our decision to use a mixed-effects model. Then, we fitted our model of interest which was a significant improvement over the intercept-only model, $\chi^2(10) = 331.3$, $p < 0.001$. The Akaike information criterion for model fit decreased from 3156 to 2845, indicating better fit.

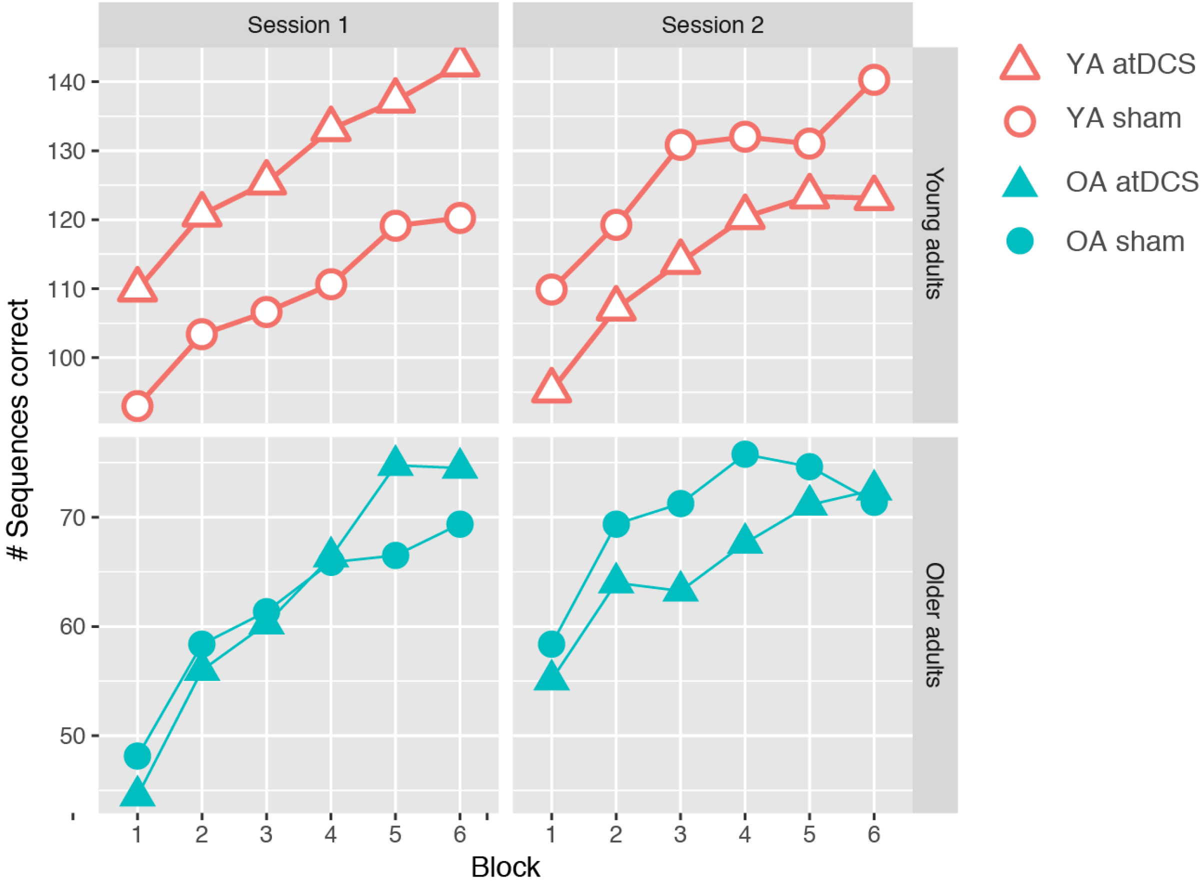

Fig. 2 Number of sequences performed correctly over the fixed sequence blocks. Block 1 is baseline, 2-5 are practice blocks. Note from session 1 to session 2, participants switched from atDCS to sham, or vice versa.

Parameter estimates are displayed in Table 1. We found main effects of three predictors: participants improved over Blocks, participants completed more sequences in Session 2 than in Session 1, and YA completed more sequences than OA. The Block x tDCS condition interaction shows that participants learned faster in the a-tDCS than in the sham group, confirming the beneficial effects of a-tDCS across age groups. Block also shows an interaction with Session, indicating that in Session 2, participants learned slower. Furthermore, YA learned faster than OA as indicated by a Block x Age interaction. The Session x Age interaction shows that the effect of Session was stronger for OA than for YA. The tDCS x Age condition interaction shows a larger baseline effect of the tDCS condition in YA than in OA. This is probably related to a sampling bias in the allocation of participants to YA group (see Fig. 2), starting at the baseline measurement. Importantly, this does not affect the aforementioned Block x tDCS condition interaction. The three-way interaction failed to reach significance. However, the direction of the effect suggests that the beneficial effects of a-tDCS were weaker for YA than for OA.

Table 1

Parameter estimates for model of interest for the fixed-sequence blocks.

	Estimate	Std. Error	df	t value	Pr(>|t|)	
(Intercept)	92,263	4,408	30	20,931	< 2e-16	***
Block	4,7719	0,2359	343	20,226	< 2e-16	***
Session	3,8698	0,8058	343	4,802	2,35E-06	***
tDCS condition	0,6406	0,8058	343	0,795	0,427182	
Age	54,4948	8,816	30	6,181	8,41E-07	***
Block: tDCS condition	1,0277	0,4719	343	2,178	0,030091	*
Block: Session	-1,2473	0,4719	343	-2,643	0,008584	**
Block: Age	1,7527	0,4719	343	3,714	0,000238	***
Session: Age	-3,6563	1,6117	343	-2,269	0,023916	*
tDCS condition: Age	4,6771	1,6117	343	2,902	0,003948	**
Block: tDCS condition: Age	-0,9339	0,9437	343	-0,99	0,323052	

R syntax for our model of interest: lmer(trialsCorrect ~ Block + Session + tDCS condition + Age + Block: tDCS condition + Block:Session + Block:Age + Session:Age + tDCS condition:Age + Block: tDCS condition:Age + (1|Subject), data, REML = T)

Random sequence performance

We fitted the random-sequence data using the same model as used for the fixed-sequence blocks. The intercept-only model shows an intra-class correlation coefficient of .88, supporting the decision to use a mixed-effects model. The model of interest was a significant improvement over the intercept-only model, $\chi^2(10) = 102.97$, $p < 0.001$, the Akaike information criterion for model fit decreased from 899 to 816, indicating a better fit. Parameter estimates are displayed in Table 2. Results indicated that YA performed more random sequences than OA (see Fig. 3). Furthermore, a main effect of Session shows that participants performed more sequences during session two than during session one, suggesting that they benefited from previous task exposure. The effect of Block indicates that participants performed more random sequences at the end than at the beginning of each session.

Comparisons of the total improvement in the random sequence blocks vs. the total improvement in the fixed sequence blocks shows much lower improvement on the random sequences than on the fixed sequences for OA (2.75 vs. 20.41 sequences), *t*(15) = 6.9, *p* < .001 and YA (2.84 vs. 29.53), *t*(15) = 8.5, *p* < .001.

Table 2

Parameter estimates for the model of interest for the random-sequence blocks.

	Estimate	Std. Error	df	t value	Pr(>|t|)	
(Intercept)	45,42969	2,10005	30	21,633	< 2e-16	***
Block	2,79687	0,60412	87	4,63	1,27E-05	***
Session	6,17187	0,60412	87	10,216	< 2e-16	***
tDCS condition	0,39062	0,60412	87	0,647	0,519593	
Age	17,17187	4,2001	30	4,088	2,99E-04	***
Post-test:tDCS condition	-0,59375	1,20824	87	-0,491	0,624369	
Post-test:Session	-1,03125	1,20824	87	-0,854	0,395719	
Post-test:Age	0,09375	1,20824	87	0,078	0,938331	
Session:Age	-1,78125	1,20824	87	-1,474	0,144024	
tDCS condition:Age	0,15625	1,20824	87	0,129	0,897403	
Post-test:tDCS condition:Age	-4,1875	2,41648	87	-1,733	0,086659	

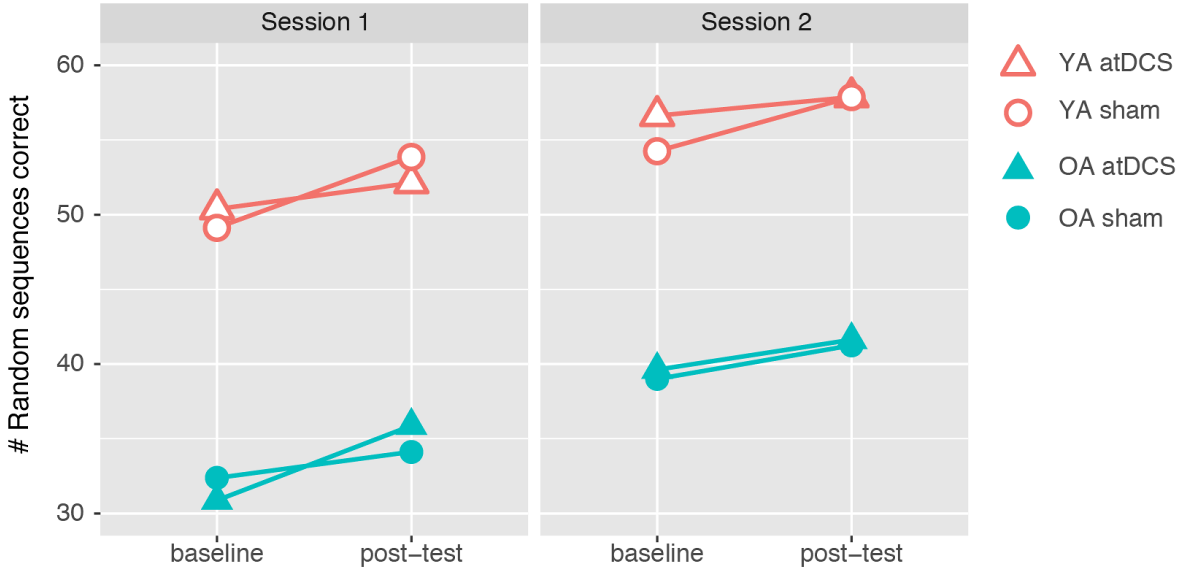

Fig. 3 Number of sequences performed during the random sequence blocks.

Attention and fatigue

We used the VAS scores to control for any differences between intervention conditions in features that might affect skill acquisition. We used the R package nparLD (Noguchi et al., 2012) to perform nonparametric longitudinal analysis for each of the 3 VAS scales according to a 4 (Moment of measurement) x 2 (Intervention: a-tDCS vs. Sham) design with the ANOVA-type statistics (ATS) as test statistic. All measures show a main effect of Moment, ATS(dfs > 1.3) > 8.5, *ps* < .005, showing that across the experiment, all participants experienced reduced attention and increased general- and hand fatigue (see Table 3). None of the main effects of Intervention was significant, ATS(dfs = 1) < 3.1, *p* > .08. Importantly, none of the interaction effects between Moment and Intervention was significant, ATS(dfs < 2.8) < 1.4, *ps* > .250, showing that reduction of attention and increased general- and hand fatigue did not affect differences in skill acquisition between the intervention conditions.

Table 3

Mean scores on VAS scales of attention and fatigue during the experiment.

		Sham				**a-tDCS**			
		T 1	**T 2**	**T 3**	**T 4**	**T 1**	**T 2**	**T 3**	**T 4**
OA	**Attention**	86.1	85.1	75.7	75.8	90.5	88.3	80.1	77.6
	Fatigue	6.9	14.3	25.1	22.0	7.1	14.7	18.2	23.5
	Hand fatigue	5.5	25.7	29.1	26.9	4.7	25.6	28.9	28.9
YA	**Attention**	75.7	70.6	60.8	60.4	79.0	79.3	65.2	63.1
	Fatigue	28.2	28.4	39.3	41.1	26.7	25.9	35.1	36.9
	Hand fatigue	13.0	25.1	40.6	41.1	10.4	23.7	37.4	38.7

* T = Time of measurement, see Fig. 1 for a timeline of the experimental procedure.

Adverse effects

The results of the adverse effects questionnaire can be found in Appendix A. Wilcoxon signed rank tests, performed separately per age group, indicated no differences between the tDCS conditions.

DISCUSSION

Our main findings demonstrate that a-tDCS stimulation over M1 enhances motor sequence learning in both age groups. These results provide support for the earlier findings of enhanced learning in OA (Zimerman et al., 2013). We also hypothesized that a-tDCS enhancement in OA would be explained by improvements in task-general performance as evidenced by shorter response times in the random blocks, and more so in OA than in YA (Verwey, 2010). However, in the present task, task-general performance, as indicated by the random blocks, was not affected by tDCS. This implies that the enhancement of motor learning caused by tDCS was sequence-specific. Previous exposure to the task did improve task-general performance for OA, as indicated by better baseline performance in the second session. In the second session and regardless of sequence type, participants started at a higher level of performance and improved to a lesser extent than in the first session. This effect was stronger for OA than for YA. This is a relevant finding as it provides insight into a potential reason why tDCS does not always affect motor learning in OA and YA in the same manner (Summers et al., 2016). Specifically, when OA benefit from previous task exposure, the task becomes easier and we know that motor tasks have to be sufficiently challenging to be able to enhance performance with a-tDCS (Berryhill, Peterson, Jones, & Stephens, 2014). This means that in future crossover studies comparing YA and OA, measuring and reporting the effects of earlier task exposure is advised so that potential moderating effects of task difficulty can be monitored.

We predicted that task-general learning in OA would be enhanced by a-tDCS because previous studies found enhanced dexterity when practice was coupled with a-tDCS (Hummel et al., 2010; Parikh & Cole, 2014). This prediction was not confirmed. Perhaps, the sequence tapping task does not require much dexterity, and the manual requirements were lower than in the Jebsen-Taylor hand function tests. At the same time, cognitive requirements might have been higher in our sequence tapping task.

Did a-tDCS support learning in both age groups, or only in OA as reported by Zimerman et al. (2013)? The three-way interaction with intervention, block, and age group did suggest a smaller effect of tDCS on motor learning for YA, but it did not reach statistical significance. Thus, we cannot conclude that tDCS affected learning differentially for OA and YA. In line with this observation, the data does suggest that a-tDCS improved learning for YA in the first session too. Improving motor sequence learning through M1 a-tDCS in YA is best achieved with multi-day protocols or retention tests, whereas single-session protocols render weaker results (Hashemirad, Zoghi, Fitzgerald, & Jaberzadeh, 2016). So, although we did not find a significant difference in tDCS enhancement between YA and OA, we do still think it is likely that there is more opportunity for enhancement in OA than in YA.

As anticipated, our findings show clear learning in the OA sham condition, whereas Zimerman et al. (2013) reported no learning at all in this condition. What explains this difference? While we aimed to keep the task and instructions as similar as possible to the Zimerman et al. (2013) study, our experiment deviated because it included error-feedback and a random-sequence block preceding the experiment. Error-feedback, or knowledge of results, is known to boost motor learning (Salmoni, Schmidt, & Walter, 1984), and this probably explains partially why our participants learned more. However, we doubt this completely explains the difference because OA have been found to show clear improvement on sequence learning tasks without error feedback as well (Howard & Howard, 1989, 1992). Potentially, the complete absence of learning in the OA sham condition in Zimerman et al. (2013) was incidental. Importantly, the effect of tDCS on learning in OA was smaller in our study than in the study by Zimerman et al. (2013). This seems to be partially explained by the increased learning in the sham condition in our study. This discrepancy in results between the two studies underlines the importance of reproduction between research groups (Horvath et al., 2015b).

In short, we reproduced the earlier finding that motor sequence learning in OA is enhanced by tDCS, and we showed that this effect was not significantly larger than in YA. We established that this beneficial effect can be attributed to sequence-specific learning rather than to a general task effect. Our results further suggest that in future within-subjects tDCS studies, the effect of task exposure should be monitored closely because the effect of tDCS may reduce as the task becomes easier to the participants.

Acknowledgements

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APPENDIX A

Table 1.

Mean scores on the adverse effects questionnaire administered after each session. Wilcoxon signed rank tests, performed separately per age group, indicated no differences between the a-tDCS and sham conditions.

	Did you experience … ?*				**Was … caused by the stimulation?****			
	a-tDCS		**sham**		**a-tDCS**		**sham**	
	YA	**OA**	**YA**	**OA**	**YA**	**OA**	**YA**	**OA**
Headache	1.1	1.1	1.1	1.0	1.0	1.1	1.2	1.0
Neck pain	1.2	1.1	1.1	1.1	1.0	1.0	1.1	1.0
Scalp pain	1.1	1.1	1.3	1.0	1.4	1.0	1.4	1.0
Itching	1.6	1.2	1.5	1.1	2.2	1.6	1.7	1.2
Tingling	1.7	1.6	1.6	1.5	3.2	2.3	2.6	2.5
Burning sensation	1.8	1.3	1.9	1.3	3.3	1.8	3.1	1.8
Skin redness	1.1	1.0	1.2	1.0	1.3	1.0	1.6	1.0
Sleepiness	1.8	1.0	2.1	1.1	1.6	1.0	2.0	1.3
Trouble concentrating	1.7	1.3	1.8	1.3	2.1	1.3	2.0	1.1
Acute mood change	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0

* 1, absent; 2, mild; 3, moderate; 4, severe

** 1, none; 2, remote; 3, possible; 4, probable; 5, definite

General discussion and conclusions

J. S. Barnhoorn

6

GENERAL DISCUSSION AND CONCLUSIONS

The aging society calls for increased understanding of age-related cognitive and neural changes in motor learning. Why do healthy older adults (OA) have difficulties learning new skills, and how can we support them learning new motor skills? In this dissertation, we zoomed in on the age-related differences in the cognitive representations underlying sequence skill, and explored avenues for enhancing motor learning in OA. This final Chapter will start with a summary of the results from the experiments. Then, new insights regarding motor skill development and enhancement of motor learning based on the aggregated results are presented. Finally, the practical implications of the current results and suggestions for future research are discussed.

Chapter 2 examined whether OA are able to use the effector-independent, visuospatial sequence representation that young adults (YA) have been shown to develop during the early stages of learning a motor sequence (Hikosaka et al., 1999; Keele et al., 2003; Verwey et al., 2015). This type of representation is thought to facilitate the flexible application of learned motor skills in multiple contexts and therefore, it is relevant to know whether this mechanism is affected by advanced age. In the experiment, OA indeed displayed the ability to use sequence knowledge developed using forearm flexion-extension (FE) movements in a test phase where the same sequence was to be performed using key-presses. However, when the practice phase consisted of key-presses and the ensuing test phase of FE movements, OA showed no benefit from practice while YA did show slight transfer. We concluded that, although high age affects the amount of transfer, the ability to apply sequence knowledge in a flexible manner seems to be largely preserved in OA.

Chapter 3 scrutinized OA's ability to develop motor chunking behavior. It complements Chapter 2 because the motor level representation of a sequence is developed after the visuospatial representation. Being able to develop and use motor chunks is important because it is associated with reduced attentional demands and thus frees capacity to focus on things besides controlling movement (Abrahamse et al., 2013), like watching the road while shifting gears in a car. The results confirmed that OA are indeed able to develop chunking behavior, but just need more practice than YA to develop this execution mode. Another important insight gained from this study was that, in older but not in young adults, slow responses that are often interpreted as chunk points were associated with a finger that was also slow during performance of the random sequences. This finding calls for more attention to biomechanical factors, which may lead to one or multiple slow fingers, in future theory and analysis concerning aging and sequence learning.

Chapter 4 tested the hypothesis that the careful, error-averse way in which OA perform tasks, which slows them down and stimulates their reliance on external guidance (Verwey, 2010), prevents them from developing efficient, chunking based representations. The participant sample was divided into a speed group that received the instruction to perform the task as fast as possible, and an accuracy group instructed to make as few errors as possible. The intervention sorted the expected effect with fast responses and relatively many errors in the speed group, and the opposite pattern in the accuracy group. However, our measure of chunking showed no group difference at any moment of practice. Furthermore, in the test phase, the speed group was not more successful in performing the sequences by heart than the accuracy group. Based on these results we concluded that speedy, error-rich performance during practice does not have a beneficial effect on the development of motor chunks in OA.

Chapter 5 explored the potential of tDCS as a technique to enhance motor learning in OA. While previous research suggested that tDCS indeed offers beneficial effects, the literature also calls for replications and incremental steps to add much-needed robustness to the existing results. We therefore tried to replicate the results of a particular sequence learning study (Zimerman et al., 2013). In line with the results of that study, the replication condition in our study showed that tDCS indeed accelerates skill development in a simple but elegant sequence-tapping task. Importantly, we also showed for the first time that tDCS affected the development of sequence-specific skill, and not the general ability to perform such sequencing tasks.

Integrated conclusions: Motor skill development in OA

Aggregating the findings from the empirical studies, one of the central insights that emerge is that, at a qualitative level, OA and YA still appear to function in the same way. Or put differently, the cognitive models of sequence learning that generally have been developed using YA as a model still seem to apply with advanced age. On the one hand, this might be expected because these mechanisms are very fundamental to our daily functioning. On the other hand though, functional changes in neural activity (Seidler et al., 2010) during aging could have induced changes at the functional cognitive level as well. The insights from Chapters 2 and 3 confirm that during motor sequence learning OA develop, like YA, a flexible visuospatial representation first, and with extensive practice, continue to develop a more efficient representation using motor chunks. Furthermore, both age groups showed the asymmetry of transfer between FE and key-press movements and similar correlations between visuospatial working-memory and learning rate in Chapter 2. Additionally, the pattern of development of task-general versus sequence-specific sequence knowledge in the sequence-tapping task in Chapter 5 was also similar. Naturally, differences remain. First and foremost, all of the studies described in this dissertation confirm the substantial speed difference between OA and YA. Second and more interestingly, an insight emerging from Chapter 3 is that because of physical differences (e.g., the presence of one or more stiff fingers), analyses that were developed for YA cannot be applied on OA data in a straightforward way. We will elaborate on this in the "Future research" section of the current Chapter.

In the first DSP studies including OA (Verwey, 2010; Verwey et al., 2011), the authors presented a number of potential reasons for diminished chunking behavior in OA. With the current findings in hand, it is interesting to re-evaluate these explanations. First, the authors note that OA may simply require more practice to develop and use motor chunks. This prediction is supported by the results from Chapter 3. Second, the authors suggest that "motor chunks may develop slower in elderly simply because cognitive slowing induces long inter-key intervals" (Verwey, 2010). Chapter 4 tested this idea, and results suggest that faster responses do not have a beneficial effect on chunking development. As a third explanation for reduced chunking in OA, Verwey (2010) suggested that OA may have developed chunks still, but reduced cognitive flexibility prevented them from switching from the reaction to the chunking mode. This explanation seems to imply that using motor chunks is associated with a particular moment in time during which one switches from the reaction to the chunking mode. The results from Chapter 3 imply this is the case neither for OA or YA, and that instead, the development of chunking is a gradual process. A fourth and final explanation Verwey (2010) offers is that OA's limited working memory capacity reduces efficiency of the motor buffer. Support for this idea is provided by a study by Bo et al. (2009) that showed a correlation between chunk length and visuospatial working memory capacity. Using the same working memory test, Chapter 3 tested whether our measure of motor chunking was correlated with working memory as well, results indicated this is not the case. Hence, the relationship between working memory capacity and chunking seems to be limited to the number of sequential elements contained in a chunk and not the strength of chunking. Concluding, the explanation, as put forward by Verwey (2010), that reduced chunking in OA is a consequence of OA needing more practice is supported by the results from this dissertation, while the other explanations can be rejected.

Integrated conclusions: Enhancing motor skill development in OA

How can we support OA in developing new motor skills in an efficient manner? First of all, simply providing more practice is a good start. While this may not come as a surprise, a new insight emerging from the studies here is how improvement in RTs in OA is related to improvement in skill. Importantly, comparing RT reduction between age groups is complicated because OA can be up to twice as slow as YA when initiating practice. Does a 100 ms improvement from practice onset mean the same thing in both age groups? Methodological studies have suggested this is not the case and that age by treatment interactions may be somewhat inflated because of baseline differences between the groups (Faust, Balota, Spieler, & Ferraro, 1999). The authors suggest solutions using specific Z-Score transformations or linear regression models to augment traditional analyses. Here, we followed usual procedures in line with most previous studies relevant for this dissertation, while keeping an eye on the potential pitfalls of this approach.

Chapter 3 of this dissertation confirms that similar improvements in RT between age groups should be interpreted with caution. While RTs improved relatively similarly in both age groups, the underlying skill improvement as measured by the IED (Initiation-Execution Difference) showed differences in development over time. Importantly, YA reached a ceiling quickly, while OA showed more benefit from additional practice trials. Similar results were found by Verwey (2010) who found similar improvement in RTs between age groups but less learning of the sequence in OA. These insights might serve as a motivation for future researchers and potentially even professionals to think carefully about the time they provide OA for learning a new skill.

In extension to the idea of providing sufficient time, an interesting insight for future researchers and even practitioners may also be that rushing OA provides no benefit for skill development, as we found in Chapter 4. Such a strategy might appear effective at first sight as speed may increase, but the development of the underlying motor skill is not necessarily accelerated while it may well be experienced as frustrating for the learner. Finally, when one aims to enhance motor skill development in OA, tDCS may be an effective method. This tool is cost-effective, non-invasive and supported by a growing body of research.

Practical implications

How does society benefit from the research described in this dissertation? First and foremost, the current work is fundamental in nature, meaning that the eventual benefits need to be considered in a long time frame and are hard to predict. Still, a number of recommendations and applications can be identified already. First of all, the suggestions put forward in the previous paragraph considering the provision of additional practice and refraining from rushing OA can be of relevance for those working with OA. Furthermore, the insight that motor chunks, and with them automaticity, develop so much slower in OA is an important insight for those concerned with safety and training for OA. For example, OA need more practice to get used to the physical control of a new device before continuing with explanation of functionality. These suggestions can be relevant when designing work environments in such a way that they optimally accommodate the aging workforce, something that is increasingly necessary in some countries. A great example of workspace design optimized for older adults is the recent redesign of one of BMW's factories in Germany. Results were encouraging with similar production quantities from the older as from a younger team of workers, and an increase in production quality (Clegg, 2012).

As said, it is hard to predict the eventual benefits that fundamental research brings, this is true especially in the case of the aging society since age affects so many aspects of life. An example of a surprising application of the current results is that some of the datasets and insights brought forward by this dissertation are currently being used to study the effects of aging on the effectiveness of novel, behavior based, authentication methods in cyber security (Haasnoot, Barnhoorn, Spreeuwers, Veldhuis, & Verwey, 2017). Regarding the potential use cases of tDCS, time will need to tell in which areas application will be most effective. Currently, research focuses mostly on clinical tDCS applications like treatment of major depression, aphasia, chronic pain, and enhancing effectiveness of rehabilitation in the critical time period directly following stroke (Kim, Ohn, Yang, Park, & Jung, 2009). Whether tDCS will ever be used as a tool for enhancing OA's learning in a non-clinical setting is difficult to predict.

Future research

Although research on motor sequence learning is decades old, statistical methods to model motor learning processes and especially motor chunking have been lacking, making it difficult to validate theoretical models. Many theories in psychology can be tested in an appropriate manner using traditional statistics applied to relatively simple dependent measures. However, the process of developing motor skills and chunking is highly complex due to large individual differences and alternative execution modes. Therefore, a simple ANOVA or regression is usually unable to capture the complete development process. Besides being able to validate theories, an additional benefit of considering more complex statistical models is that it challenges theorists to operationalize concepts in a coherent, specific manner.

Fortunately, significant progress has been made in recent years regarding the modeling of chunking. Many approaches have been explored and many different aspects of chunking have been measured. Researchers have experimented with different analyses including simple t-tests (Bo et al., 2009; Ruitenberg, Verwey, et al., 2014), k-means clustering (Song & Cohen, 2014), dynamic network analysis (Wymbs et al., 2012) and even a hidden Markov model (Acuna et al., 2014) and a non-parametric rank-order algorithm (Alamia et al., 2016). It is important to realize that that while all these methods refer to 'chunking', they are developed to measure specific aspects of chunking. And for algorithms that do focus on the same aspect, it is unknown whether different methods render the same results. For example, are results always the same when finding chunk boundaries with k-means clustering, t-tests or a rank-order algorithm? Furthermore, the different analyses are associated with many different outcome variables, including chunk length, chunk consistency, correlation between elements (RT and accuracy), and transition between chunk structures. It is at times difficult to estimate how these features are related based on separate studies. Unfortunately, authors don't always elaborate on how they define and correspondingly measure chunking, and to facilitate this a thorough review including an extensive comparison of model performance on simulated data from multiple types of motor tasks would be very helpful. Such an overview should ideally also include a discussion about the temporal resolution at which analyses are performed. For example, a recent method to analyze chunking in a reaching task uses minimum jerk, focusing on movement smoothness on the millisecond time-frame (Ramkumar et al., 2016), while many DSP studies use key-press RTs, which are usually ~100 to 700 ms per movement. How do results from these different tasks compare? And how similar or different are the underlying representations developed in reaching and key-press tasks?

One of the most encompassing algorithms currently available for modeling chunking dynamics is the aforementioned Bayesian chunk inference model provided by Acuna et al. (2014). Three features make this approach especially interesting. First of all, the algorithm is based on a hierarchical Markov model (HMM) and thus it is one of the few methods that models slow development of chunking over time. The output includes a transition matrix that can provide novel insights regarding the way chunk structures emerge. A second feature, that most clearly sets this algorithm apart from alternatives, is that multiple features are used to estimate the chunking state, including RTs, errors and their correlations. And third, a range of outcome parameters is provided, including estimated RT and error correlations (i.e., whether errors are often commenced at the same location in the sequence) and the RT difference between chunk starts and elements within a chunk. In order to make this algorithm even better, future research would benefit from extending it to a hierarchical HMM, in which case it would also allow comparison of chunking behavior between groups (e.g., OA and YA). Furthermore, an interesting extension would be to include the option to view the contribution of different parameters to the final estimation. For example, were the RT correlations most informative for estimating the chunking structure, or the presence of errors? And a final suggestion concerns modeling the influence of biomechanical factors since, as we concluded in Chapter 3, these can have a big impact on the validity of features usually used to infer chunk boundaries. Specifically, RTs from a set of data based on participants performing random sequences could be used to estimate effects that are not associated with sequence knowledge, like fingers that are slower in general.

Regarding the potential of tDCS to enhance motor learning, Chapter 5 provided additional support for the robustness of the effect. Moreover, our results also offered some insights for future research. First of all, while the original study by Zimerman et al. (2013) found no learning in the OA control condition, we showed clear learning in the same circumstances. This is a remarkable result since one would expect that, with the same age group, largely the same task and the same instructions, such a basic finding as the absence of learning would be replicated. These findings underline the importance of replications. If even these basic experimental outcomes differ between labs, how can we be sure of the effects of tDCS? The most promising approach to solving this problem lies in methodological studies, replications and follow-up studies. In the general tDCS field, this approach is gaining momentum (e.g., Horvath, Vogrin, Carter, Cook, & Forte, 2016) and delivers important new insights such as a surprisingly high intra-individual variability related to individual differences in factors like skull anatomy and baseline neural activation states. Similar studies should be performed for OA.

How relevant is our knowledge of laboratory learning for real-world learning? In the literature on motor learning theory, applicability of models to motor performance in daily life is usually discussed in a relatively sparse way. Overall, it seems that the more general theories (e.g., Hikosaka et al., 2002) are useful to explain a wide range of real-world phenomena, while the more specific theories (e.g., the DPM) explain a certain task very well but can be hard to use in a broader context (Wulf & Shea, 2002). Although it is understandable that the dynamic, real-time control system underlying motor learning is usually studied using basic and highly controlled tasks, steps toward expanding the range of tasks may provide relevant new insights (Wolpert, Diedrichsen, & Flanagan, 2011). In the case of OA and the DPM, a potentially interesting avenue would be to explore whether the development of motor chunks indeed underlies automaticity, as is assumed for YA (Abrahamse et al., 2013). This assumption, that chunking underlies automaticity, is an important reason to study motor learning and chunking in OA, since reduced potential for automaticity can have considerable real-world consequences. Hence, investigating whether strong chunking behavior is associated with good dual-task performance in OA would increase our understanding of when and how to apply our knowledge in real-life applications.

Conclusion

Increasing our understanding of the aging process is vital to ensure that we can maintain our standard of living in the aging society. This dissertation aims to contribute to this understanding. The first two Chapters described age-related differences in the cognitive representations underlying motor sequence skill. The final two Chapters explored avenues for enhancing motor learning in OA. In general, the findings suggest that the cognitive processes underlying skill acquisition are largely the same for the age groups investigated. OA proved to be able to develop the visuospatial representation necessary for the flexible application of motor skill, and also showed the ability to develop motor chunks, albeit after extensive practice. Our attempt to speed up the development of motor chunks by motivating participants to practice sequences as fast as possible was not successful. On the contrary, non-invasive brain stimulation did improve motor learning, confirming the promise this technique brings for enhancing skill development in older adults.

Many myths exist considering older adult's (in)abilities. So much in fact, books have been written dedicated to debunking them (e.g., Erber & Szuchman, 2014). This is relevant because such misunderstanding can lead us to work and interact with OA in ways that are wrong and that deny or overestimate their potential. In the light of the aging society, the results presented here are promising. Provide sufficient practice, a cup of tea, and use novel stimulation techniques when appropriate, and OA will reach their full potential.

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Summary

J. S. Barnhoorn

The aging society calls for increased understanding of age-related cognitive and neural changes in motor learning. Why do healthy older adults (OA) have difficulties learning new skills, and how can we support them in learning new motor skills? In this dissertation, we zoomed in on the age-related differences in the cognitive representations underlying sequence skill, and explored avenues for enhancing motor learning in OA.

The tasks used in this research were all centered on motor sequence learning, a flexible paradigm that has been used extensively in previous research on the cognitive underpinnings of motor learning (e.g., Rhodes, Bullock, Verwey, Averbeck, & Page, 2004). Figure 1 shows an overview of the motor tasks that we used. In the discrete sequence production (DSP) task (Fig. 1 A), participants perform a sequence by responding to series of succeeding cues as quick as possible. The flexion-extension (FE) task (Fig. 1 B) requires participants to move a cursor on the screen as quickly and smoothly as possible to succeeding targets using elbow FE movements. Finally, in the sequence-tapping task (Fig. 1 C), the goal is to perform a sequence (e.g., "3 - 5 - 2 - 4 - 2") that is continuously displayed on the screen as often as possible.

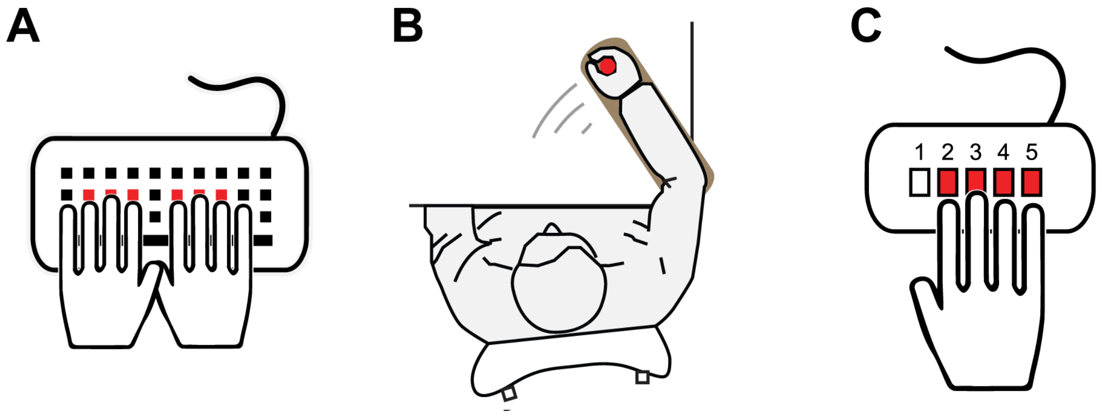

Fig. 1 The DSP task (A) in 6-finger configuration, the FE task (B), the sequence-tapping task (C).

Chapter 2 examined whether OA are able to use the effector-independent, visuospatial sequence representation that young adults (YA) have been shown to develop during the early stages of learning a motor sequence (Hikosaka et al., 1999; Keele et al., 2003; Verwey et al., 2015). This type of representation is thought to facilitate the flexible application of learned motor skills in multiple contexts and therefore, it is relevant to know whether this mechanism is affected by advancing age. In the experiment, OA indeed displayed the ability to use sequence knowledge developed using FE movements in a test phase where the same sequence was to be performed using key-presses. However, when the practice phase consisted of key-presses and the ensuing test phase of FE movements, OA showed no benefit from practice while YA did show slight transfer. We concluded that, although high age seems to affect the amount of transfer, the ability to apply sequence knowledge in a flexible manner seems to be largely preserved in OA.

Chapter 3 scrutinized OA's ability to develop motor chunking behavior. It complements Chapter 2 because the motor level representation of a sequence is developed after the visuospatial representation. Being able to develop and use motor chunks is important because it is associated with reduced attentional demands and thus frees capacity to focus on things besides controlling movement (Abrahamse et al., 2013), like watching the road while shifting gears in a car. The results confirmed that OA are indeed able to develop chunking behavior, but just need more practice trials than YA to develop this execution mode. Another important insight gained from this study was that, in older but not in young adults, slow responses that are often interpreted as chunk points were associated with a finger that was also slow during performance of the random sequences. This finding calls for more attention to biomechanical factors, which may lead to one or multiple slow fingers, in future theory and analysis concerning aging and sequence learning.

Chapter 4 tested the hypothesis that the careful, error-averse way in which OA conduct motor tasks stimulates their reliance on external guidance (Verwey, 2010) and prevents them from developing more efficient, chunking based representations. The participant sample was divided into a speed group that received the instruction to perform the DSP task as fast as possible, and an accuracy group instructed to make as few errors as possible. The intervention sorted the expected effect with fast responses and relatively many errors in the speed group, and the opposite pattern in the accuracy group. However, our measure of chunking showed no group difference at any moment of practice. Furthermore, in the test phase, the speed group was not more successful in performing the sequences by heart than the accuracy group. Based on these results we concluded that speedy, error-rich performance during practice does not have a beneficial effect on the development of motor chunks in OA.

Chapter 5 explored the potential of transcranial direct current stimulation (tDCS) as a technique to enhance motor learning in OA. While previous research suggested that tDCS indeed offers beneficial effects, the literature also calls for replications and incremental steps to add much-needed robustness to the existing results. We therefore tried to reproduce the results of a particular sequence learning study (Zimerman et al., 2013). In line with the results of that study, the replication condition in our study showed that tDCS indeed accelerates skill development in a simple but elegant sequence-tapping task. Importantly, we also showed for the first time that tDCS affected the development of sequence-specific skill, and not the general ability to perform such sequencing tasks.

In general, the findings suggest that the cognitive processes underlying skill acquisition are largely the same for the age groups investigated. OA proved to be able to develop the visuospatial representation necessary for the flexible application of motor skill, and also showed the ability to develop motor chunks, albeit after extensive practice. Our attempt to speed up the development of motor chunks by motivating participants to practice sequences as fast as possible was not successful. On the contrary, non-invasive brain stimulation did improve motor learning, confirming the promise this technique brings for enhancing skill development in older adults.

List of publications

J. S. Barnhoorn

Peer-reviewed publications

Barnhoorn, J. S., Van Asseldonk, E. H. F., & Verwey, W. B. (In press). Differences in chunking behavior between young and older adults diminish with extended practice. *Psychological Research*

Barnhoorn, J. S., Döhring, F. R., Van Asseldonk, E. H. F., & Verwey, W. B. (2016). Similar representations of sequence knowledge in young and older adults: A study of effector independent transfer. *Frontiers in Psychology*, 7:1125.

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Barnhoorn, J. S., Tsoneva T., & Garcia-Molina G. (2014). EEG-Based comparison of repetitive visual stimulation at frequencies in the alpha band. *Proc. 36th IEEE Engineering in Medicine and Biology Society* (Piscataway, NJ: IEEE) Late-Breaking-Research Papers

Presentations & other publications

Barnhoorn, J. S., van Asseldonk, E. H. F., & Verwey, W. B. (2017, November). *Differences in motor sequence learning in younger and older adults: The effect of extended practice.* Oral presentation by Verwey at 58th Psychonomic Society Meeting, Vancouver, Canada.

Haasnoot, E., Barnhoorn, J. S., Spreeuwers, L., Veldhuis, R., & Verwey, W.B. (2017, May) *Towards understanding behavioural biometric recognition performance over time and practice.* Paper presented at Symposium on Information Theory and Signal Processing in the Benelux, Delft, The Netherlands

Barnhoorn, J. S., Greeley, B., van Asseldonk, E. H. F., & Verwey, W. B. (2017, May). *Non-invasive brain stimulation improves motor learning in healthy older adults.* Poster presented at the Neural Control of Movement Society Meeting. Dublin, Ireland.

Verwey, W. B., Barnhoorn, J. S., van Asseldonk, E. H. F., Panzer, S., Döhring, F., Vieweg, J., Voelcker-Rehage, C., Godde, B., Hübner, L., Greeley, B., Seidler, R.D. (2017, May). *The Re-LOAD project: motor Learning in Older ADults.* Poster presented at the Neural Control of Movement Society Meeting, Dublin, Ireland.

Greeley, B., Barnhoorn, J. S., Verwey, W. B., Seidler, R. (2017, May). *Multi-Session Transcranial Direct Current Simulation During Motor Sequence Learning in Young and Older Adults*. Poster presented at Neural Control of Movement Society Meeting, Dublin, Ireland.

Greeley, B., Barnhoorn, J. S., Verwey, W. B., Seidler, R. (2016, May). *Multi-Session Transcranial Direct Current Stimulation Concurrent with Discrete Sequence Production Task in Young and Older Adults*. Poster presented at Geriatrics Center Research Symposium, Ann Arbor, USA.

Barnhoorn, J. S., van Asseldonk, E. H. F., & Verwey, W. B. (2016, April). *Older adults show increased chunking behavior with extended practice.* Poster presented at Neural Control of Movement Society Meeting, Montego Bay, Jamaica.

Greeley, B., Barnhoorn, J. S., Verwey, W. B., & Seidler, R. (2016, April). *Multi-Session Transcranial Direct Current Stimulation Concurrent with Discrete Sequence Production Task in Young and Older Adults*. Poster presented at Neural Control of Movement Society Meeting, Montego Bay, Jamaica.

Barnhoorn, J. S., Döhring, F., van Asseldonk, E. H. F., & Verwey, W.B. (2015, December). *Age effects on the transfer of sequence knowledge between different types of movements*. Poster presented at Meeting of the Dutch Psychonomic Association, Egmond aan Zee, The Netherlands.

Barnhoorn, J. S. (2015, September). *The Qualtrics Reaction Time Engine*. Invited oral presenation at Workshop Online Data Acquisition in Experimental Psychology, Epos Graduate Network, Leiden, The Netherlands.

Barnhoorn, J. S., Döhring, F., van Asseldonk, E. H. F., & Verwey, W. B. (2015, October). *Age effects on the transfer of sequence knowledge between different types of movement.* Poster presented at the Society for Neuroscience, Chicago, USA.

Greeley, B., Barnhoorn, J. S., Verwey, W. B., & Seidler, R. (2015, October). *Modifying the discrete sequence production task for a multiday tDCS study in young and older adults*. Poster presented at the Society for Neuroscience, Chicago, USA.