KU LEUVEN

GROEP BIOMEDISCHE WETENSCHAPPEN

FACULTEIT BEWEGINGS- EN REVALIDATIEWETENSCHAPPEN

The neural correlates of the contextual interference effect in the learning of a complex bimanual task in younger and older adults: an fMRI study

door Celine Maes

masterproef aangeboden tot het behalen van de graad van Master of Science in de revalidatiewetenschappen en kinesitherapie

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Opgesteld volgens de richtlijnen van *Neurobiology of learning and memory*

Woord vooraf

Graag wil ik mijn oprechte dank betuigen aan enkele mensen die deze thesis mede mogelijk gemaakt hebben. Zo wil ik ten eerste mijn promotor, prof. dr. Swinnen, bedanken om dit uiterst interessante onderwerp aan te bieden als masterproef. Verder wil ik ook mijn beide co-promotoren, Lisa Pauwels en dr. Sima Chalavi, hartelijk bedanken voor hun begeleiding, opbouwende kritiek en het delen van hun expertise binnen dit onderzoeksdomein. Dankzij hun enthousiaste bijdrage maakte ik op een erg aangename manier kennis met de wereld van het wetenschappelijk onderzoek en kreeg mijn masterproef verder vorm. Vervolgens wil ik ook graag de leden van de jury bedanken voor de tijd die ze investeerden om deze masterproef kritisch door te lezen. Daarnaast zou ik ook graag volgende personen bedanken: prof. Dominique Maes van de VUB voor haar input aangaande de statistische dataverwerking, Eline Monos voor de samenwerking binnen onze deels gelijklopende masterproef en Britt Sneyers voor haar hulp bij het testen van de proefpersonen. Tot slot ben ik ook dankbaar voor de interesse en motiverende woorden van familie en vrienden.

Leuven, 5 mei 2016 C.M.

Situering Masterproef

Deze masterproef kadert binnen een doctoraatsproject van de onderzoeksgroep bewegingscontrole en neuroplasticiteit van de faculteit bewegings- en revalidatiewetenschappen aan de Katholieke Universiteit Leuven. Zoals de naam reeds doet vermoeden, wordt in deze onderzoeksgroep gekeken naar de plasticiteit van het menselijke brein. Dit gebeurt enerzijds tijdens de uitvoering van verschillende taken en anderzijds binnen het verouderingsproces. Om de werking van de hersenen te bestuderen kunnen twee soorten onderzoek onderscheiden worden. Enerzijds wordt in sommige projecten de hersenactiviteit beïnvloedt om zo het effect hiervan op het menselijk gedrag na te gaan. Anderzijds zijn er projecten, zoals dit project, die een eerder observationele aanpak hanteren. Hierbij gaat men na wat gebeurt in de hersenen tijdens de uitvoering van een bepaalde taak.

Binnen dit doctoraatsproject wordt de neurologische grondslag van motorisch leren onder de loep genomen. Meer specifiek wordt het effect van de organisatie van een trainingsschema op het leerproces van motorische vaardigheden onderzocht. Zo bleek uit voorgaand onderzoek dat een gerandomiseerd oefenschema voordelen heeft ten opzichte van een geblokt oefenschema wat betreft motorisch leren. Hoewel de prestatie tijdens de aanleerfase benadeelt wordt door een gerandomiseerd oefenschema, zorgt dit voor betere resultaten op een retentie- of transfertest (Shea & Morgan, 1979). Dit fenomeen, waarbij het toevoegen van complexiteit tijdens training resulteert in een voordelig effect op motorisch leren, wordt contextuele interferentie (CI) genoemd.

Hoewel het CI-effect wetenschappelijk sterk onderbouwd is voor de uitvoering van relatief eenvoudige taken door jongeren of volwassenen, is er weinig en tegenstrijdige informatie aangaande het voordeel van CI bij complexere taken en ouderen. Daarom wordt er binnen dit onderzoek gekeken naar het CI-effect tijdens de uitvoering van een complexe bimanuele taak bij zowel ouderen als jongeren. Aanvankelijk werd er op gedragsniveau bekeken of een gerandomiseerd oefenschema nog steeds gunstigere effecten toonden voor motorisch leren bij de uitvoering van een complexe taak. Dit werd bekeken voor zowel jongeren als ouderen. Vervolgens wordt in het huidige onderzoek eenzelfde opzet herhaald met gebruik van magnetic resonance imaging (MRI) tijdens uitvoering van de taak om op deze manier de hersenactivatie gelinkt aan de taak en motorisch leren te kunnen achterhalen en vervolgens ook een vergelijking te kunnen maken tussen jongere en oudere proefpersonen.

Referentie

Shea, J. B., & Morgan, R. L. (1979). Contextual interference effects on the acquisition, retention, and transfer of a motor skill. *Journal of Experimental Psychology: Human Learning & Memory*, *5*(2), 179–187. http://doi.org/10.1037//0278-7393.5.

The neural correlates of the contextual interference effect in the learning of a complex bimanual task in younger and older adults: an fMRI study

1. ABSTRACT

Contextual interference (CI) is defined as the variance in presentation of different task variants, with a randomized practice schedule incorporating higher levels of CI as opposed to a blocked practice schedule. The effect of CI, i.e. the beneficial effect of a random practice schedule on motor learning, is well established in behavioural studies investigating rather simple tasks within younger adults. Nevertheless, the generalization of the CI effect to older adults remains debatable. Given the well-known aging of our population, research examining the effect of aging is of increasing importance. Furthermore, little is known about the neural correlates of the CI effect. Therefore, the underlying mechanism that gives rise to the CI effect is not fully captured by current research. On these grounds, the aim of this study was to investigate the CI effect in a complex bimanual task on a behavioural and neuroimaging level by using functional magnetic resonance imaging (fMRI). To this end, 10 younger and 10 older adults were included and randomly assigned to either a random or a blocked practice group. Each participant completed a baseline assessment followed by three days of training. Finally, a retention test was carried out six days after training. ***Behavioural results*** tend to support the advantage of random practice on retention, despite a poorer performance during the acquisition phase compared to blocked practice. This was true for both younger and older adults. Furthermore, all subgroups expressed an improvement of performance over time during the acquisition phase, despite an overall poorer performance of older adults compared to younger adults. On the contrary, post-acquisition processes needed for retrieval did not seem to be affected by age. Regarding the ***neural correlates***, our results support previous literature, stating that various sensorimotor areas as well as subcortical structures and the cerebellum are activated during the execution of a bimanual coordination task. However, older adults recruited a more widespread neural network in order to compensate for their age-related decline in motor function. With regard to the CI effect, differences in activation were found when comparing the blocked and random group of each age group during the acquisition phase. Whereas the blocked groups predominantly rely on sensorimotor areas (primary motor and sensory area and supplementary motor area) the random groups rely more on higher level cognitive cortices (premotor cortex and other frontal regions), suggesting that random practice initiates a more profound dependence on cognitive resources. During retention, the random practice, as opposed to the blocked practice, demonstrated an additional activation of the higher order structures to retrieve memory and optimize the integration of sensory information (precuneus, cerebellum and hippocampus). When comparing the age groups, the elderly recruited additional non-motor areas enabling them to increase attention and feedback dependent performance. Nonetheless, the low amount of subjects in this study restrains us from drawing firm conclusions. Hence, more powerful studies are needed to validate our findings. Keeping in mind the increasing number of elderly in our society, the result of this study could have major implications in the field of geriatrics as well as neuromotor rehabilitation.

Key words: Contextual interference, bimanual coordination, aging, fMRI

2. INTRODUCTION

2.1 Motor learning and aging

Motor learning is a very important aspect in our daily lives. From birth, people develop all different kind of skills such as writing, eating with cutlery, throwing a ball, sewing etc. Because of the significant presence of motor skill learning in our daily lives, it has become a point of interest for many researchers. Since a few decades, numerous studies have investigated the underlying mechanism of motor learning and the factors contributing to the learning of a motor skill. These studies showed that practice is the most prominent factor affecting motor skill learning (Kantak & Winstein, 2012). Abundance possible practice conditions, such as the level of task difficulty, the amount of trials, etc., may affect the learning of a motor skill. Depending on the elected practice conditions, performance and retention will be affected in a specific manner (Wulf & Shea, 2002). Therefore, several studies have tried to determine how to reach the maximum potential for learning by manipulating those different practice conditions. Given the fact that learning new skills as well as maintaining achieved performance levels is present throughout our entire life span, we are interested in motor skill learning in both younger and older adults. To this end, some researchers focused on the learning of motor skills in older adults and its discrepancy or similarities with motor skill learning in younger adults (Seidler et al., 2010). Given the highly increased life expectancy in the latest century and a decline in human fertility, the amount of people above the age of 60 is expected to rise from 9.2% in 1990 to 21.1% by 2050 (Sander et al., 2014). As such, it is of increasing importance to pay attention to the elderly. Besides the well-known cognitive declines, older adults show motor performance deficits due to central nervous system declines as well as changes in the peripheral nerves, sensory receptors and muscles (Seidler et al., 2010). These deficits can have profound consequences with regard to their independence. Namely, when older adults lose their ability to perform daily tasks, they have to rely on relatives to compensate for their deterioration. On the one hand, this can be difficult for the elderly to cope with psychologically, whereas on the other hand it can be a burden for relatives and other caregivers. Furthermore, older adults show balance and gait difficulties as a consequence of a decline in motor performance, making them in danger of falls (Seidler et al., 2010). Therefore, it is highly important for elderly to maintain their performance level in order to stay autonomous as long as possible.

Research examining motor learning in older adults showed that, although a decline in motor performance is seen with aging, they remain capable of learning motor skills and thus increasing their performance level (Voelcker-Rehage, 2008). Nevertheless, literature shows equivocal results concerning the degree of performance gains in older as opposed to younger adults. Whereas some studies stated that performance gains are hardly affected by age (Carnahan, Vandervoort, & Swanson, 1996; Durkin, Prescott, Furchtgott, Cantor, & Powell, 1995; van Dijk, Mulder, & Hermens, 2007; Voelcker-Rehage & Willimczik, 2006), other studies argued that a clear difference exists between younger and older adults regarding their ability to enhance performance levels (Seidler, 2006; Swinnen, 1998; Voelcker-Rehage, 2008). These contradictory findings may be a result of a heterogeneity of various factors contributing to the amount of performance gains among different studies such as task structure, task difficulty and familiarity level (Voelcker-Rehage, 2008). Despite this controversy, researchers agree that older adults try to compensate for their age-related performance loss trough extra activations of cortical and subcortical functions (Seidler et al., 2010). To explain this overactivation pattern in elderly, Reuter-Lorenz and Capell (2008) introduced the compensation-related utilization of neural circuits hypothesis (CRUNCH). According to the authors, older adults will activate additional areas in the brain in order to match the performance level of younger adults. In simple tasks, they generally succeed to keep up with their younger counterparts by this enhanced activation of specific brain regions. However, with increasing task difficulty, these brain regions show activation in the younger adults as well, suggesting that these areas are reserve resources to keep performance levels high. Because of the need for elderly to recruit these brain regions already in simple tasks, they may fail to compensate with tasks getting more difficult, leading to a decrement in performance (Reuter-Lorenz & Cappell, 2008). Nonetheless, research showed that training interventions in elderly can lead to an additional recruitment of brain regions together with an enlarged brain volume, resulting in enhanced motor performance or an improved maintenance of motor skills (Seidler et al., 2010). These confirmed beneficial effects of training interventions in older adults will be a very important issue in our future society.

2.2 Contextual interference

Research examining the effects of different practice conditions on learning and retention is tremendous. In this regard, Guadagnoli and Lee (2004) developed a framework for conceptualizing the effects of different practice conditions on the learning of a motor skill. This framework explains the interactions among information, task difficulty and skill level of the performer leading to an optimal challenge point for learning. This optimal challenge point, also known as a desirable difficulty in performance (Bjork, 1994), is established by manipulating different practice variables.

In the learning of a motor skill, practice consists of multiple trials to become familiar with the task to be learned. These exercise trials can be either completely identical to each other, i.e. constant practice, or they can consist of different variants of the same task, i.e. variable practice (Kantak & Winstein, 2012). In case of variable practice, the order of the different trial variants can be chosen as well. This composition of variable practice trials determines the amount of contextual interference (CI) (Shea &

Morgan, 1979). More specifically, when practicing multiple task variants following a blocked or repetitive practice schedule, the amount of CI is low. On the contrary, the amount of CI is high when practicing multiple task variants following a randomized practice schedule. In other words, the CI effect is the influence that the composition of various practice trials has on motor skill learning. This is one of the most important practice variables affecting motor skill learning and was first introduced in the verbal learning domain by Battig (1966). The author stated that random practice, i.e. high CI, led to results that are more beneficial on retention compared with blocked practice, i.e. low CI, although performance during acquisition was poorer for the random group compared to the blocked group. Thereupon, Shea and Morgan (1979) were the first to support Battig's concept in the learning of a motor skill using a barrier-knock-down-task (see appendix 8.1). These findings gave rise to performance of numerous researches regarding the CI effect which resulted in introducing the CI effect as a robust phenomenon in motor skill learning. Hence, the beneficial effects of CI have been confirmed in various tasks such as simple aiming tasks, anticipation timing tasks, movement patterning task, etc. (Magill & Hall, 1990).

Numerous research groups have tried to capture the underlying mechanisms of the CI effect by creating a theoretical background of the effect (Magill & Hall, 1990). In general, we can distinguish two important points of view to explain the mechanisms underlying the CI effect. The first hypothesis, i.e. the elaboration perspective, was introduced by Shea and Morgan (1979) stating that multiple and variable encoding processes are used in conditions with high CI, leading to a more distinctive and elaborate memory representation (Magill & Hall, 1990; Shea & Morgan, 1979). This hypothesis implies that multiple tasks are simultaneously present in working memory. Hence, the learner is capable of comparing these tasks, resulting in an embellished memorial representation (Brady, 1998; Shea & Morgan, 1979). However, Lee and Magill (1983) argued that the elaboration perspective could not explain the poorer performance of random practice during the acquisition phase. Therefore, the authors introduced an alternative hypothesis, i.e. the action plan reconstruction hypothesis, attributing the benefit of random practice to a continuous reconstruction of the action plan in response to constantly changing contextual demands, leading to a stronger representation of the action plan. This is not the case in blocked practice, where the learner is not challenged to develop a control structure for processing problem-specific information because of the fixed contextual demands (Lee & Magill, 1983; Magill & Hall, 1990). Although these hypotheses were considered as conflicting theories, Young (1993) argued that they also share some common aspects regarding the crucial needs for retention. Firstly, both emphasize the need for an engagement in effortful processing in random practice, which is not necessary in blocked practice. Secondly, they both point out the importance of developing retrieval processes to perform well on retention tests, what is seen in random practice as opposed to blocked practice. According to Young, these two general aspects, which are essential for retention, are present in both the elaboration perspective and the action plan reconstruction hypothesis, despite the different specificities that they receive in each theory (Young et al., 1993).

Although the CI effect is a well-studied and robust concept in motor learning literature, there are still some questions to be answered. Magill & Hall (1990) suggested that the magnitude of the CI effect might be influenced by different factors such as experience characteristics, task complexity and age. Studies investigating the CI effect in older adults are scarce and it is still not clear whether the beneficial effects of high CI can be generalized to the aged population. Secondly it is crucial to consider the generalization of the CI effect to complex motor skill learning taking into account that most of the current results are based on simple motor tasks. In a review from Wulf and Shea (2002), the effects of high CI appeared to be equivocal when learning more complex tasks. The authors claimed that the cognitive effort and processing demands might exceed the capacity of the learner when performing a complex skill following a random practice schedule. Phrased differently, when the task covers a wide range of difficulties, the learner will already be challenged by the task itself. Therefore, the extra demands attributed to a random practice schedule may cause a system overload, nullifying the beneficial effects of random practice (Wulf & Shea, 2002). Nevertheless, this theory of system overload remains hypothetic because until now, little imaging studies are available to confirm this theoretical framework. As most studies are limited to the behavioural aspects of the CI effect, they fail to verify the theories put forward to explain the established results.

Currently, only a few studies have investigated the neural correlates of the CI effect. Cross et al. (2007) were the first to explore the neural substrates of the CI effect in a functional magnetic resonance imaging (fMRI) study using a sequence task. Besides the confirmation of the beneficial effects of random over blocked practice on retention performance, the authors discovered enhanced activation of sensorimotor and premotor areas during random practice, reflecting a more active preparation of motor responses (Cross et al., 2007). However, only younger adults were tested in this study whereas Lin et al. (2012; 2016) investigated the CI effect at both a behavioural and neural level in both younger and older adults, wherefore a serial reaction time task (SRTT) was used. At present, this is the only research group considering the CI effect and its neural basis in elderly. Although the authors confirmed the CI effect in both younger and older adults at a behavioural level, a clear interaction between age and the CI effect was found regarding brain mechanisms. While the left dorsal lateral prefrontal cortex (DLPFC) contributes to the benefits of random practice in younger adults, older adults rely on enhanced engagement of sensorimotor regions, such as the primary and the supplementary motor cortices. These findings clearly demonstrate the modulatory effects of aging on neuroplasticity. The authors concluded that the benefits of high levels of CI are demonstrated in behavioural performance and haemodynamic response (Lin et al., 2012). Although these studies provided a basis for research on the neural correlates of the CI effect, one needs to expand this knowledge to confirm the theoretical background put forward in behavioural research in order to capture the underlying mechanism that gives rise to the CI effect.

2.3 Research purpose

By and large, we can state that the current literature is not profound enough to fully master the CI effect. Hence, there are two main gaps in literature, namely the generalization of the CI effect, both to complex task learning and aging, and its underlying neural correlates. Although random practice schedules, i.e. high CI, are shown to be favourable in rather simple motor tasks, its generalization to more complex tasks is doubtful. In addition to the lack of the investigation of complex skills, studies providing a comparison between younger adults and their older counterparts have been scarce. Thereby, it is debatable if the findings concerning younger adults can be expanded to older adults. Along with this shortage in literature, evidence regarding the neural substrates of the CI effect is strongly limited as a consequence of the behavioural nature of most studies. Nevertheless, imaging studies are necessary to confirm the developed theories aiming to explain the established findings regarding the CI effect.

To this end, the purpose of this pilot study was to compare the performance of younger and older adults in a complex bimanual coordination task, investigating both the behavioural level and the neural correlates of the CI effect. Subjects of both age categories were divided into a blocked and a random practice group. The training intervention consisted of three task variants of a complex bimanual coordination task, distributed over three days of practice. The first and last day of practice were performed in a MRI scanner in order to assess functional brain activity during the acquisition phase. Retention was administered six days later and was also assessed in the MRI scanner. We hypothesized that a high amount of CI, i.e. a random practice schedule, as compared with low CI, i.e. a blocked practice schedule, will lead to a better performance during retention despite poorer performance during acquisition (Magill & Hall, 1990). In agreement with the findings of Lin and colleagues (2009; 2010; 2012), we hypothesized that the beneficial effects of random practice are valid for both younger and older adults, although the latter will encounter a bigger challenge to overcome the difficulties of high levels of CI during the acquisition phase due to the need for a more pronounced cognitive effort. Consequently, the neural correlates addressed by older adults will partially differ from those addressed by the younger adults. More specifically, we hypothesized that younger adults will mainly rely on frontal activity during random as opposed to blocked practice. Furthermore, older adults are expected to rely more on supplementary activation of sensorimotor areas cortices to conquer the difficulties of high levels of CI in random practice compared to blocked practice (Lin et al., 2012).

3. MATERIALS & METHODS

3.1 Subjects

For the recruitment of subjects, flyers were distributed in pharmacies and public places such as the swimming pool. On the whole, 10 younger subjects and 10 older subjects participated in our study. Both younger and older participants were randomly assigned to either a blocked or a random subgroup in order to compare between different amounts of CI. This subdivision led to a totality of four subgroups, i.e. a young blocked (YB) group, a young random (YR) group, an old blocked (OB) group and an old random (OR) group. For a more detailed overview of group specificities, see table 1. To avoid performance bias, subjects were blinded to the concept of CI. All participants declared to be in good physical as well as mental health and had no contraindications for MRI scanning. Whereas the Oldfield Handedness scale was completed to define the laterality of all subjects, the Montreal Cognitive Assessment (MoCA) was conducted for each subject in order to assess their cognitive ability (Oldfield, 1971). Within each age group, participants were matched with regards to age, laterality and MoCA score (all p-values > 0.05). Prior to testing, written informed consent was obtained from all subjects. The protocol was approved by the local ethical committee of KU Leuven, Belgium, and was in accordance with the Declaration of Helsinki (1964).

Table 1: Group specificities

Group	Amount of subjects	Mean ± SD		
		Age	Laterality	MoCA
YB	5	22.8 ± 2.04939	88 ± 16.43168	28.2 ± 1.48324
YR	5	21.6 ± 1.140175	96 ± 5.477226	28.8 ± 0.83666
OB	5	66.4 ± 5.458938	98 ± 4.472136	28 ± 1.581139
OR	5	65 ± 4.795832	54 ± 55.04544	29 ± 1.224745

3.2 Study outline

As our aim was to investigate motor learning following a training schedule with either low or high levels of CI, each participant followed a specific training schedule consisting of different days of practice (see figure 1). A first acquaintance, day zero (D0), was primarily used to complete administration and fill in questionnaires. Consecutively, participants received an explanation regarding the execution of the task, followed by a familiarisation test with the task in a dummy scanner. Furthermore, baseline performance was assessed. This introductory day was followed by a training schedule consisting of three days (D1 – D3) of practice within one week. The first and last day of practice were performed in the MRI scanner, whereas the second day of practice was performed in a dummy scanner. At last, retention, both in a blocked and a random order, were administered six days after the last day of practice (DR).

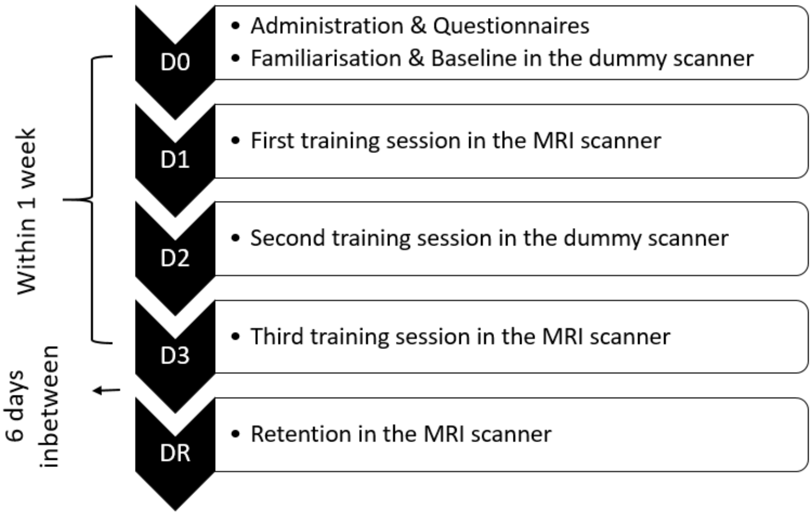

Figure 1: Study Outline *This figure provides an overview of the schedule presented to each subject*

3.3 Behavioural procedure

3.3.1 Instrumentation and task description

Instrumentation

Subjects were placed supine on the extendible table of the MRI (or dummy) scanner, whereupon the task device was positioned over their legs and fixated in the lateral ramps of the MRI table (see figure 2). The device consisted of a rectangular tripod with a dial, i.e. a flat disc whereupon a peg was attached, on both sides. To ascertain stability, towels were used to fill up the blank space between the device and the legs of the subject if necessary. Participants were instructed to move the device back and forth in order to search for an optimal positioning to facilitate the execution of the task. Consecutively, the head coil was placed over the subject's head and a mirror was placed on top of the head coil to assure a clear vision of the screen that was located at the back of the scanner. After explaining the application of the buzzer and a final check-up to make sure the participant was feeling comfortable, the table was slid into the MRI scanner. To avoid interference with task execution, experimental environment during testing in the actual MRI scanner and the dummy scanner were kept as similar as possible.

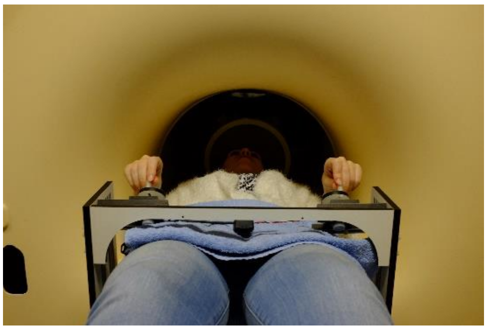

Figure 2: Positioning of the subject in the MRI or dummy scanner with the task device

Task description

Participants performed a PC-based visuo-motor bimanual tracking task, similar to the task used in the studies of Pauwels et al. (Pauwels et al., 2015; Pauwels, Swinnen, & Beets, 2014). The aim of the task was to follow a white target dot that started in the middle of the screen and progressed over a blue line towards the periphery (see figure 3). This goal could be achieved by rotating the two dials on the task device. The actual movement of the participant was represented by a yellow cursor that moved along the screen. Thus, the purpose of the task was to minimise the distance between the white target dot and the yellow curser, controlled by the subject. To enable participants to plan their movement, the line to be followed was pictured two second before the participants needed to start executing the task. As our goal was to determine the activated neural regions corresponding to task performance and learning, we needed to extract this activation pattern from the total brain activation. Therefore, we included both move and no-move trials within each run (see figure 3). The no-move trials were used as a reference (baseline) measure. In these trials, participants were provided with the task on the screen, but were instructed to stay as still as possible. The difference between the normal move and no-move trials was made by changing the colour of the circle presented in the middle of the screen during the planning phase. When a yellow dot was present, subjects were instructed to move, whereas a pink dot represented a no-move trial.

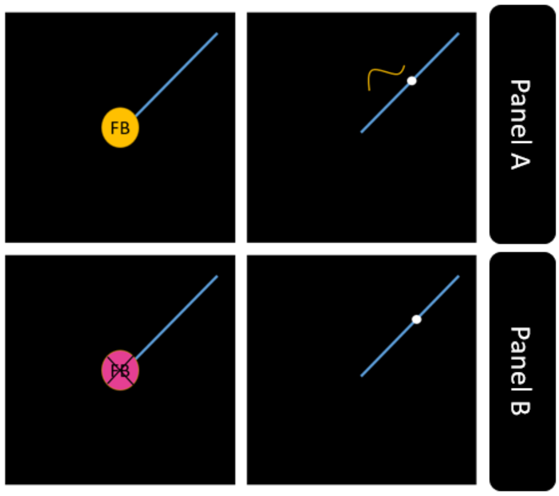

Figure 3: Goal of the task *A yellow dot (panel A) represents a move trial, whereas subjects were asked to stay as still as possible when a pink dot was shown, i.e. a no-move trial (panel B). During the first two seconds the target line is presented, subjects have the opportunity to plan their movement. Afterwards, a white dot, i.e. the target dot, starts moving over the proposed line. In the trials that continuous feedback is provided, a yellow line shows the actual movement of the participant.*

On the whole, participants needed to pursue three lines with a specific slope, progressing to either the upper right corner or the lower left corner of the screen. This resulted in a total of six different lines that were displayed during practice (see figure 4). To track these lines, subjects needed to rotate both dials using a specific *coordination direction* and *frequency ratio*. Rotation of the dial on the right hand side determined horizontal movements, whereas rotating the left dial controlled vertical movements. In order to follow the white target dot on the proposed line, a specific *coordination direction* was needed. More specifically, rotating both dials clockwise (CW) resulted in a movement of the yellow cursor to the upper right corner of the screen, whereas the yellow cursor moved towards the lower left corner by rotating both dials counter clockwise (CCW). Besides the correct coordination direction, the *frequency ratio* of rotations between both hands was also determinative to follow the white target dot. Dependent on the slope of each line, a particular frequency ratio needed to be performed. This implies an amount of rotations of the left hand combined with a specific amount of rotations of the right hand (number of rotations left hand: number of rotations right hand). For example, the line with the easiest slope, i.e. an inclination of 45°, required a 1:1 frequency ratio. In other words, both hands needed to rotate at the same speed in order to move the yellow cursor along the proposed line. Besides this rather simple line, participants also needed to perform two more challenging ratios, i.e. a 1:2 and a 2:3 frequency ratio, in which both hands had to be decoupled to different speeds (see figure 4).

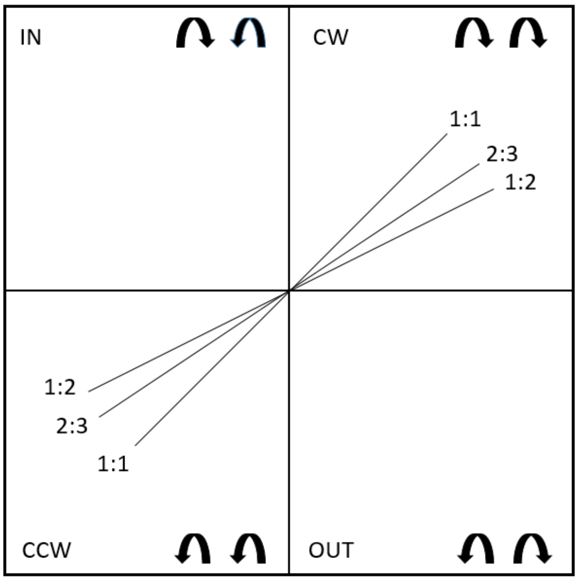

Figure 4: coordination directions & frequency ratios *Schematic presentation of the three lines, all with a different slope, presented to the subjects in two directions. In order to follow these target lines, rotations of both dials either clockwise (CW) or counterclockwise (CCW) were needed in a 1:1, 1:2 or 2:3 frequency ratio.*

3.3.2 Behavioural design

Feedback

During training, feedback was incorporated to facilitate motor learning (see figure 5). Nonetheless, we wanted the participants to perform as well as possible independent of online visual feedback. Therefore, two different types of feedback were used during training, i.e*. continuous feedback (cFB)* and *after-trial feedback (atFB)*. With respect to cFB, which was available in 50% of the total amount of trials during training, feedback was continuously available. This feedback was provided by a yellow cursor during task execution that represented the actual movement of the subject. Thus, subjects could correct their movement at any point in time. In the other 50% of trials, feedback was only provided after the task execution was finished, making it impossible for the subject to base their performance on feedback. Nonetheless, a line, which indicated their performance over the whole trial, was shown after finishing task execution. This after-trial feedback line was coloured in red and/or green, depending on the performance of the participant (see figure 5, panel B). When the subject followed the proposed line perfectly or when they moved parallel relative to this expected line, the after-trial feedback line was coloured in green since this represented a combined rotation of both hands in the correct frequency ratio. Thus, the green colour represented a good performance. On the other hand, the feedback line was coloured in red when the subject was not following the correct slope, i.e. bad performance. In this way, subjects were able to judge their own performance by interpreting their individual movement pictured in the feedback line composed of green and/or red fragments. To assure that the performance on the task was independent of any type of feedback, baseline and retention tests were conducted without the presence of feedback, i.e. no feedback condition (noFB).

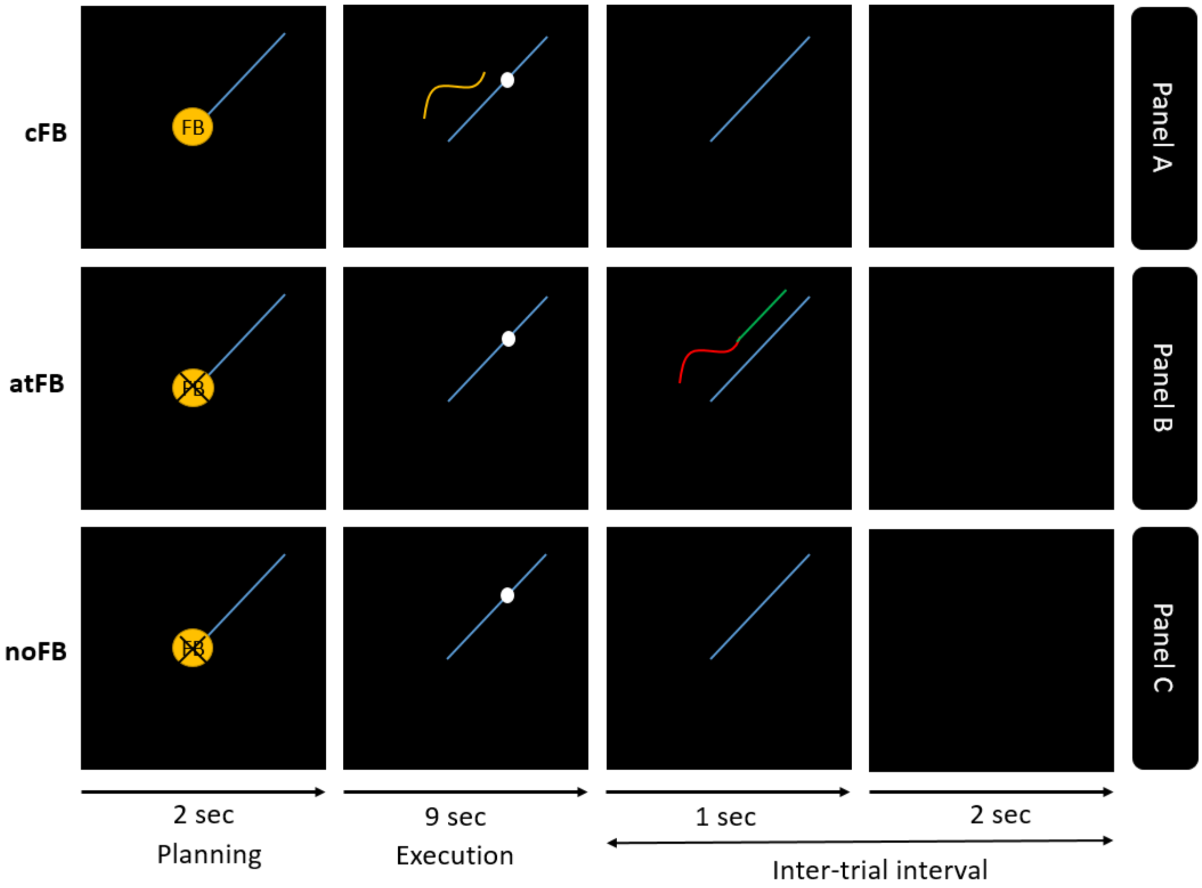

Figure 5: Feedback *The different conditions of feedback are shown in this figure. When continuous feedback (cFB) was present (Panel A), subjects could see their actual movement represented by a yellow cursor during task execution. When after-trial feedback (atFB) was given (Panel B), subjects had no reference of their own movement during the execution phase itself but only after the execution was fully completed. Within the inter-trial interval, their performance over the whole trial was visualised in a line coloured red and/or green for one second. A red line indicated that the subject did not move parallel along the blue line, i.e. bad performance, whereas a green line represented a movement of the subject parallel or on the proposed line and thus good performance. Afterwards, a black screen was provided for both types of feedback during two seconds in order to prepare for the next trial. During baseline and retention tests, no feedback (noFB) was given (Panel C).*

Trial distribution

This section provides an overview of the distribution of trials during baseline, acquisition and retention phase. A schematic resume can be found in figure 6.

Baseline assessment On D0, a pretest consisting of 18 trials, i.e. 12 move and 6 no-move trials, was administered in order to assess the baseline performance level of the participant. All six different lines, i.e. 1:1, 2:3 and 1:2 frequency ratio in both CW and CCW directions, had to be performed without any form of feedback (noFB condition). This baseline assessment was identical for all the participants from both the blocked and random groups.

Acquisition phase The acquisition phase consisted of three consecutive days of practice (D1, D2, D3). During this training, subjects performed 6 runs during each day of practice, whereby each run was composed of 36 trials, i.e. 24 move and 12 no-move trials. During blocked practice, only one frequency ratio was practiced during each day of training. The order in which frequency ratios were provided was counterbalanced in order to avoid a confounding factor with regard to practice order, leading to a total of 3 different orders in the blocked practice condition (see table 2). During the first three runs of each practice day, frequency ratios were practiced in the CW coordination direction, whereas frequency ratios were practiced CCW in the last three runs. As opposed to blocked practice, subjects needed to perform all the three frequency ratios, both in a CW as CCW direction, within each day of practice during random practice. Since all different lines were randomly assigned to each run, no counterbalancing was needed for the training days of the random group.

Table 2: Counterbalancing in blocked practice

	Day 1	Day 2	Day 3
Order 1	1:1	2:3	1:2
Order 2	1:2	1:1	2:3
Order 3	2:3	1:2	1:1

Retention On DR, each participant performed a retention test consisting of two runs, i.e. a blocked and a random retention, involving 36 trials for each run (24 move trials, 12 no-move trials). These two runs were counterbalanced for all participants.

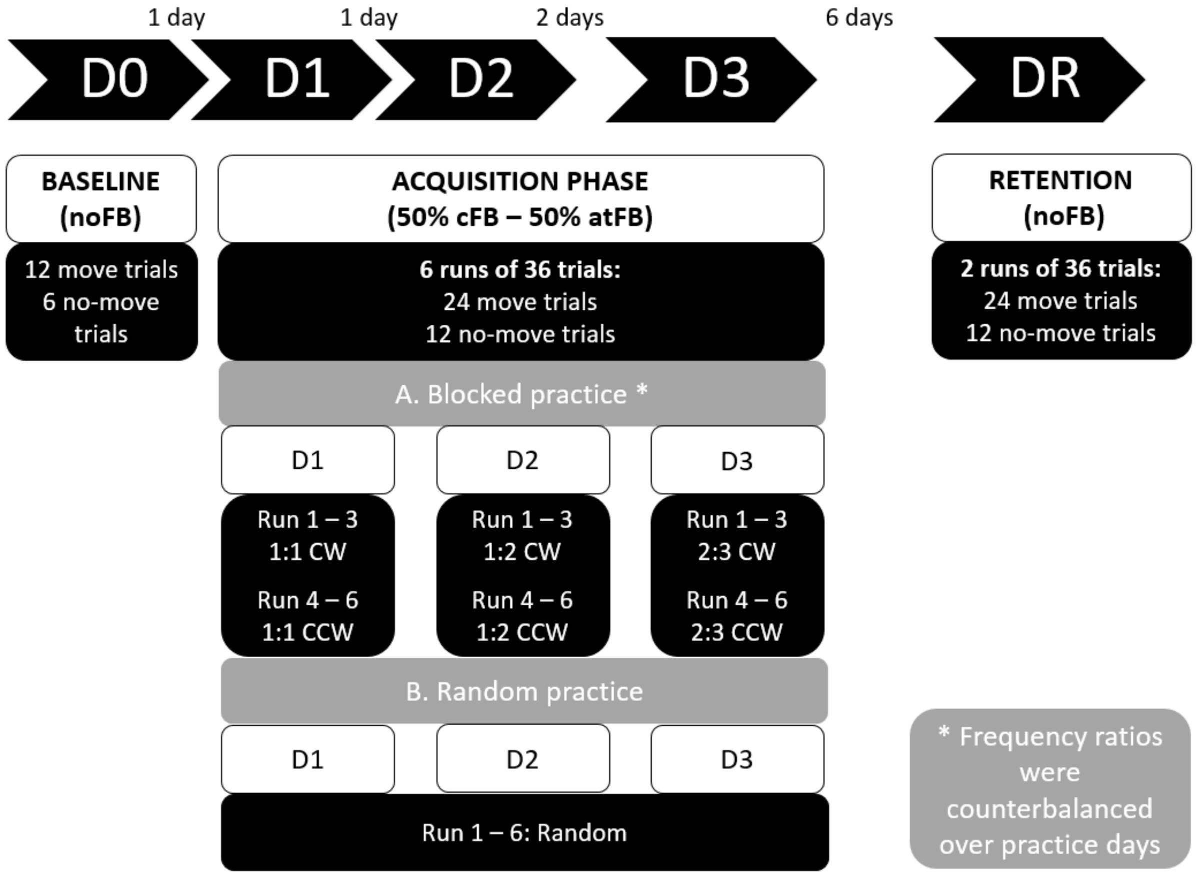

Figure 6: Behavioural design *This figure provides an overall view of the behavioural design including the composition of the different trials. On D0, a baseline assessment, composed of both move and no-move trials, without feedback (noFB) was conducted. Consecutively, the acquisition phase, consisting of three training days (D1, D2 & D3) is presented. Each training day incorporates 6 runs of 24 move and 12 no-move trials with continuous feedback (cFB) in 50% of the trials and after-trial feedback (atFB) in the other half of trials. Whereas only one frequency ratio per day was presented to the subjects in the blocked group, the random group practiced all frequency ratios within one day in a randomised order. For blocked practice, the first three runs demanded a clockwise (CW) rotation, in contrast to the last three runs that asked for a counterclockwise (CCW) rotation of both dials. The order of presentation of the frequency ratios in the blocked group was counterbalanced, giving three possible orders in total. Finally, retention was conducted 6 days later without any feedback.*

3.4 Imaging procedure

MRI data were obtained in Gasthuisberg, i.e. the university hospital of Leuven, using a Phillips Achieva 3 Tesla scanner. For all participants, both structural and functional scans were obtained. To start with, a three-dimensional T_1-weighted scan of seven minutes was performed to capture the anatomical characteristics of the brain (magnetization prepared rapid gradient echo, time repetition/time echo (TR/TE) = 9.6ms/4.6ms; 0.98mm x 0.98mm x 1.2mm voxel size; field of view (FOV) = 192x250x250; 160 coronal slices). During each training day, six functional MRI (fMRI) runs of nine minutes consisting of 36 trials each were conducted. In contrast to the training days, DR incorporated only two retention runs, both composed of 36 trials. The above mentioned functional runs consisted of 41 ascending gradient echo planar images (EPI) for T_2-weighted functional images (TR/TE = 3000ms/30ms; flip angle = 90°; 54 parallel axial slices with a slice thickness of 2.5 mm; inter-slice gap = 0.2 mm; in-plane resolution = 2.5 x 2.5 mm; 82x84 matrix).

3.5 Analysis

3.5.1 Behavioural analysis

Dependent Measures

Labview (8.5) software (National Instruments, Austin, Texas, USA) was used for both recording and analysing the behavioural data. The exact coordinates of the target line and the cursor of the subject were sampled at 100 Hz. Afterwards, Matlab R2011b and Microsoft Excel 2013 were used for a further offline analysis of the obtained data. The average track deviation (ATrD) was used as a measure of error score. By using the perpendicular distance between the blue target line and the subject's track, the track deviation was measured at each point in time for every specific trial and then averaged. In this way, the ATrD (i.e. error scores) for each point in time could be measured. Thus, a small error score, i.e. minimal distance between the cursor and target line, indicates good performance. Consecutively, data of coordination directions, i.e. CW and CCW, were collapsed within each frequency ratio since the different coordination directions were not of interest in this study. Since we aimed to look at a global learning effect, the three different frequency ratios were collapsed as well (for a more profound investigation of different frequency ratios, consult Pauwels L. et al., 2014 and 2015). Afterwards, data points of the baseline assessment were averaged, leading to one composite score for all data points per frequency ratio. The same was repeated for the retention test. With regards to the acquisition phase, average scores were calculated across every set of three data points, giving a sum of 12 data points for the acquisition phase per frequency ratio.

Statistical analysis

The statistical analysis was performed using the statistical package for the social sciences (SPSS). One participant showed very poor results due to the usage of an incorrect mirror in the actual scanner on D1. This issue resulted in an erroneous mirroring of the task image. Therefore, the behavioural data from this subject were excluded from the statistical analysis. Because of the small number of participants within every group, the use of non-parametrical testing was mandatory. Both the effect of age and CI were of interest. In order to make a comparison between age groups on the one hand and practice groups, i.e. CI, on the other hand, a Mann-Whitney U test was performed for baseline, acquisition and retention phases separately. With regard to the acquisition phase, the 12 data points were averaged according to either age or practice group to enable the execution of this test. Furthermore, a Friedman test was conducted in order to assess behavioural performance gains during acquisition within the different subgroups.

3.5.2 Imaging analysis

The imaging data were processed using the FMRIB Software Library (FSL 5.1), using both a first and higher-level analysis. Prior to entering the data into the statistical model, images were reoriented and the brain extraction tool (BET) was applied to make sure that only relevant brain voxels in the T_1 image were included. In the first level analysis MCFLIRT motion correction was utilized in order to reorient the images to the middle volume as an initial template image (Jenkinson, Bannister, Brady, & Smith, 2002). Regressors of the move and no-move trials were defined for the execution phase (9sec) for all types of feedback. The EPI's were aggregated with the obtained T_1 image and a FSL template (MNI). Consecutively, all runs from one training day were collapsed for each participant during higher level analysis. Afterwards, different comparisons were investigated by contrasting a specific condition to its respective baseline, i.e. no-move condition. More specifically, the task-related activation was explored at first. This was done for the acquisition phase within both younger and older adults. Afterwards, for the acquisition and retention phases, the CI effect was separately investigated within each age group as well as in the overall sample, i.e. collapsing younger and older subgroups. At last, the effect of age during the acquisition and retention phases was of interest in this study. For an overview of the effects of interest, see figure 7.

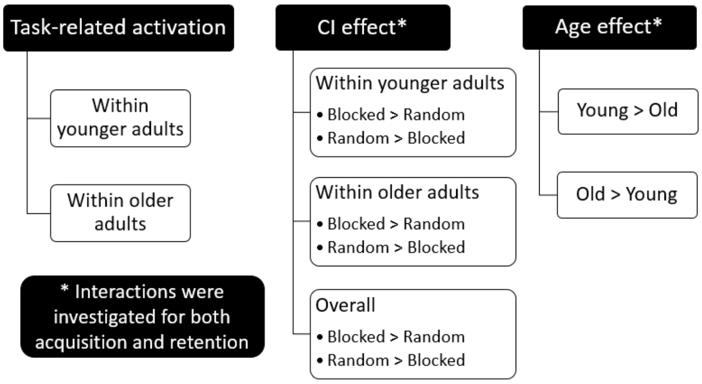

Figure 7: Effects of interest *This schedule provides an overview of the different effects that were investigated. First, the task-related activations were investigated for both younger and older adults during the acquisition phase. Second, the effect of CI was examined within younger adults, older adults and in the overall sample. For both the acquisition and retention phase, the blocked and random groups were contrasted in order to see which brain regions were activated more during blocked compared to random practice (Blocked > Random), as well as the extra activations during random compared to blocked practice (Random > Blocked). Third, the effect of age, i.e. brain areas activated more in younger compared to older adults and vice versa, was considered for both the acquisition and retention phase.*

4. RESULTS

4.1 Behavioural data

With respect to the statistical analysis of the behavioural data, the effect of CI and the effect of age on performance were investigated for baseline, acquisition and retention phases. Moreover, performance change over time during the acquisition phase was examined for all groups. An overview of results can be seen in table 3 together with a visualisation of results in figure 8.

4.1.1 CI effect

Regarding the CI effect in the overall sample, results did not show a significant difference between the blocked and random groups for baseline assessment (U=45, p=1), meaning that performance of blocked and random groups did not differ at this stage. With respect to the acquisition and retention phase, a trend towards significance was demonstrated (acquisition: U=22, p=0.06; retention: U=24, p=0.086). This finding demonstrates that the random and blocked groups tend to exhibit varying results during training. More specifically, the random group seemed to perform poorer during training, though better during retention compared to the blocked group. Hence, the random group exhibited a better retrieval of the task at the retention phase although they encountered more difficulties in performance during the acquisition phase compared to the blocked group.

Likewise, the CI effect was also investigated within each age group. For the younger subjects, there was no significant difference in performance between the blocked and random practice group in neither baseline (U=7, p=0.251) nor retention (U=9, p=0.465). Nevertheless, CI did have a significant effect on performance during the acquisition phase (U=3, p=0.047), indicating that the random group encounters more difficulties with the task. When examining the results of the older subjects, performance at baseline assessment (U=6, p=0.327) and acquisition phase (U=8, p=0.624) were not significantly affected by CI. Although there was no significant difference between the blocked and random group during retention (U=4, p=0.142), a trend towards a superior performance of the random group was exhibited.

Moreover, a Friedman test across all subjects for the acquisition phase revealed a significant difference between the different data points in time (X^2 =111.823, p<0.001), representing an improvement in performance over time during training. Also within each of the four different groups, a significant gain in performance was detected, i.e. YB (X^2 =31.8, p=0.001), YR (X^2 =33.4, p<0.001), OB (X^2 =31.8, p=0.049) and OR (X^2 =34.785, p<0.001), implicating that all groups significantly enhanced their performance during the acquisition phase.

4.1.2 Aging

With regard to baseline, no significant difference was found between performance of the younger and older participants (U=36, p=0.462), indicating that both age groups performed almost equally during baseline assessment. In order to investigate the effect of age on the acquisition phase, the 12 data points of training were averaged and as such reduced to one point. A Mann-Whitney U test on this measure revealed a trend towards significance (U=22, p=0.060), indicating that elderly performed poorer during training compared to their younger counterparts. At last, a comparison of performance at retention across age groups revealed no significant effect of age (U=42, p=0.806), illustrating that both age groups performed almost at a same level during the retention phase.

Table 3: Overview of the performed statistical analysis

	Timing of interest	**Statistical test**	**P-value**
Overall effect of CI	Baseline assessment	U = 45.000	1.000
	Acquisition phase	U = 22.000	0.060
	Retention	U = 24.000	0.086
Effect of CI within younger adults	Baseline assessment	U = 7.000	0.251
	Acquisition phase	U = 3.000	**0.047**
	Retention	U = 9.000	0.465
Effect of CI within older adults	Baseline assessment	U = 6.000	0.327
	Acquisition phase	U = 8,000	0.624
	Retention	U = 4.000	0.142
Overall effect of time	Acquisition phase	X^2 = 111.823	**< 0.001**
Effect of time within the YB group	Acquisition phase	X^2 = 31.800	**0.001**
Effect of time within the YR group	Acquisition phase	X^2 = 33.400	**< 0.001**
Effect of time within the OB group	Acquisition phase	X^2 = 19.731	**0.049**
Effect of time within the OR group	Acquisition phase	X^2 = 34.785	**< 0.001**
Effect of age	Baseline assessment	U = 36.000	0.462
	Acquisition phase	U = 22.000	0.060
	Retention	U = 42.000	0.806

Note: the p-value of a significant result is marked in bold

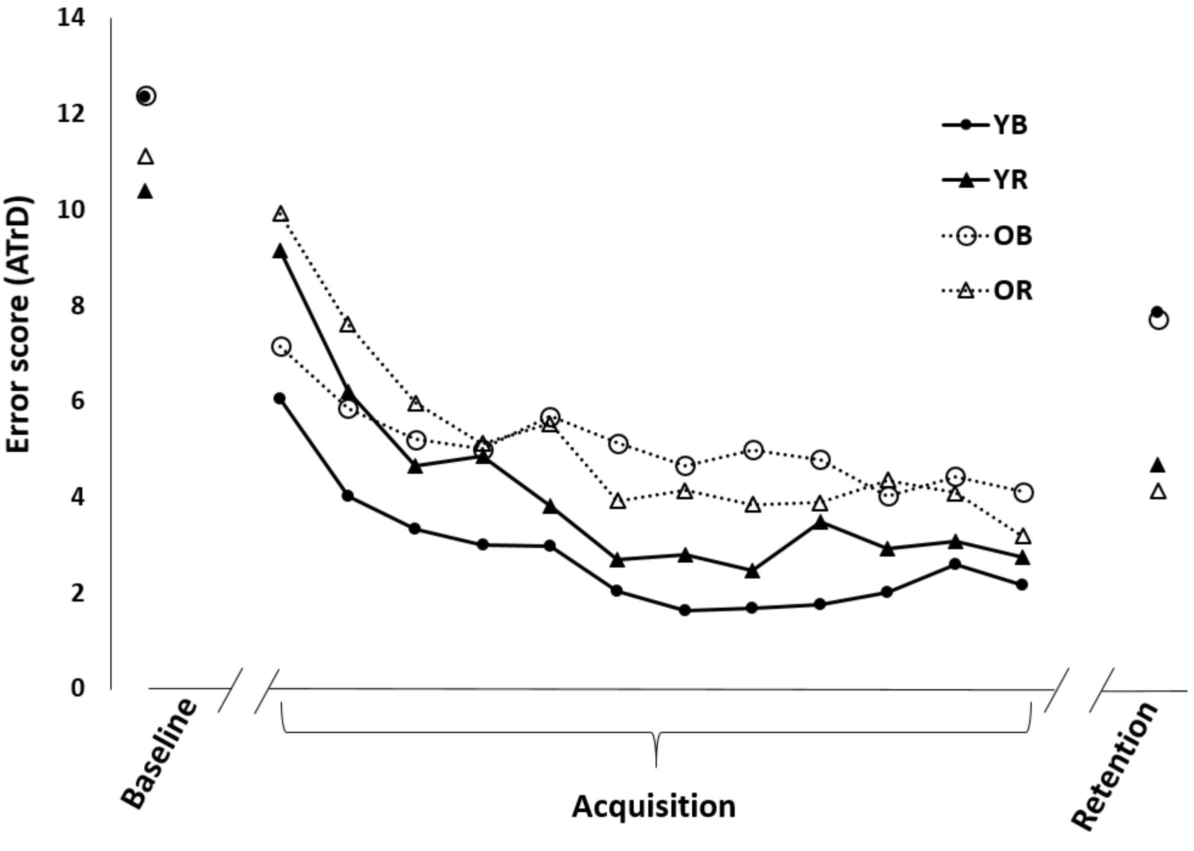

Figure 8: Behavioural results *The error score (ATrD, i.e. average track deviation) during baseline, acquisition phase and retention is presented as a measure of performance for the four subgroups of interest, with lower scores representing a better task performance. Since non-parametrical tests were performed, median scores are presented. Whereas the full black lines represent younger adults, the dotted lines embody the older adults. Blocked and random practice groups are visualised by a circle or triangle respectively.*

4.2 Imaging data

In this section, the neural activations observed during task acquisition and retention will be presented. An overview of the activated regions, together with their coordinates and Z-values can be found in table 4 to table 11.

4.2.1 Acquisition

Main task-related activation

Within both age groups, the activations related to the task execution during the acquisition phase were explored (figure 9). An overview of the most important activated regions per age group can be found in table 4 and 5. In general, most task-related activations were found to be similar in younger and older adults. As such they both recruited bilateral cerebellum, various motor regions (bilateral primary motor cortex (M1), bilateral secondary motor area (SMA) and premotor cortex (PMC)), bilateral primary sensory cortex (S1), insular cortex as well as subcortical areas (bilateral thalamus, right caudate and left pallidum). Concentrating on the younger participants, task executions also relied on other parietal regions (bilateral parietal operculum/secondary sensory cortex (S2) and right superior parietal lobe), together with frontal areas (inferior frontal cortex, frontal pole and middle frontal gyrus) and the subcortical putamen, caudate and pallidum bilaterally. On the contrary, a strong recruitment of multiple frontal areas (right frontal pole and inferior frontal gyrus) along with right lateral occipital cortex extending to the middle temporal gurus was observed within the older participants. Besides these most prominent activations, a wide diversity of other regions was less profoundly engaged within the elderly. Hence, when comparing the age groups, there was a clear discrepancy in the amount of activation with the elderly showing a more widespread neural recruitment.

Table 4: Overview of task-related activations within the younger adults during the acquisition phase.

MAIN TASK-RELATED ACTIVATIONS WITHIN YOUNGER ADULTS					
Brain region	**Left (L) / right (R)**	**Coordinates**			**Z-value**
		x	**y**	**z**	
Cerebellum (VIII)	R	16	-44	-20	10.3
	L	-20	-46	-24	9.7
S1	R	46	-24	44	7.7
	L	-46	-20	48	10.8
M1	R	36	-18	46	10
	L	-44	-16	52	9.6
PMC	R	30	-10	56	10.3
	L	-28	-8	56	9
Parietal operculum/S2	R	56	-26	18	8.1
	L	-46	-28	18	7.4
Inferior frontal cortex	R	50	10	6	9.5
Frontal pole & middle frontal gyrus	R	46	48	6	7.5
SMA	R	4	-2	56	10.2
	L	-4	-8	60	9.8
Superior parietal lobe	R	14	-62	56	7.9
Insula	R	40	6	2	8.5
	L	-36	16	6	8.9
Thalamus	R	12	-22	2	7.5
	L	-18	-24	10	7.8
Pallidum	R	20	-2	-2	6.3
	L	-14	-2	-2	6.7
Caudate	R	8	8	0	5.2
	L	-8	6	0	5.9
Putamen	R	26	0	10	8.8
	L	-26	-4	10	7.9

Table 5: Overview of task-related activations within the older adults during the acquisition phase.

MAIN TASK-RELATED ACTIVATIONS WITHIN OLDER ADULTS					
Brain region	**Left (L) / right (R)**	**Coordinates**			**Z-value**
		x	**y**	**z**	
M1	R	2	-22	52	11.6
	L	-40	-20	56	9,8
PMC	R	32	-18	62	8,8
	L	-36	-18	60	8.9
SMA	R	4	-12	64	9.5
	L	-2	-10	62	9.4
Cerebellum (VIII)	R	8	-66	-36	10.9
	L	-2	-72	-38	11.9
Lateral occipital & middle temporal gyrus	R	54	-60	2	8.2
Frontal pole	R	44	46	4	8.9
Inferior frontal gyrus	R	58	12	8	9
Insula	R	32	18	6	8.4
	L	-40	12	-2	7.9
Thalamus	R	14	-18	4	7.6
	L	-14	-20	4	7.6
Caudate	R	14	6	14	4.8
Pallidum	L	-14	-4	-8	5.4
S1	R	38	-22	44	10.3
	L	-44	-18	50	11

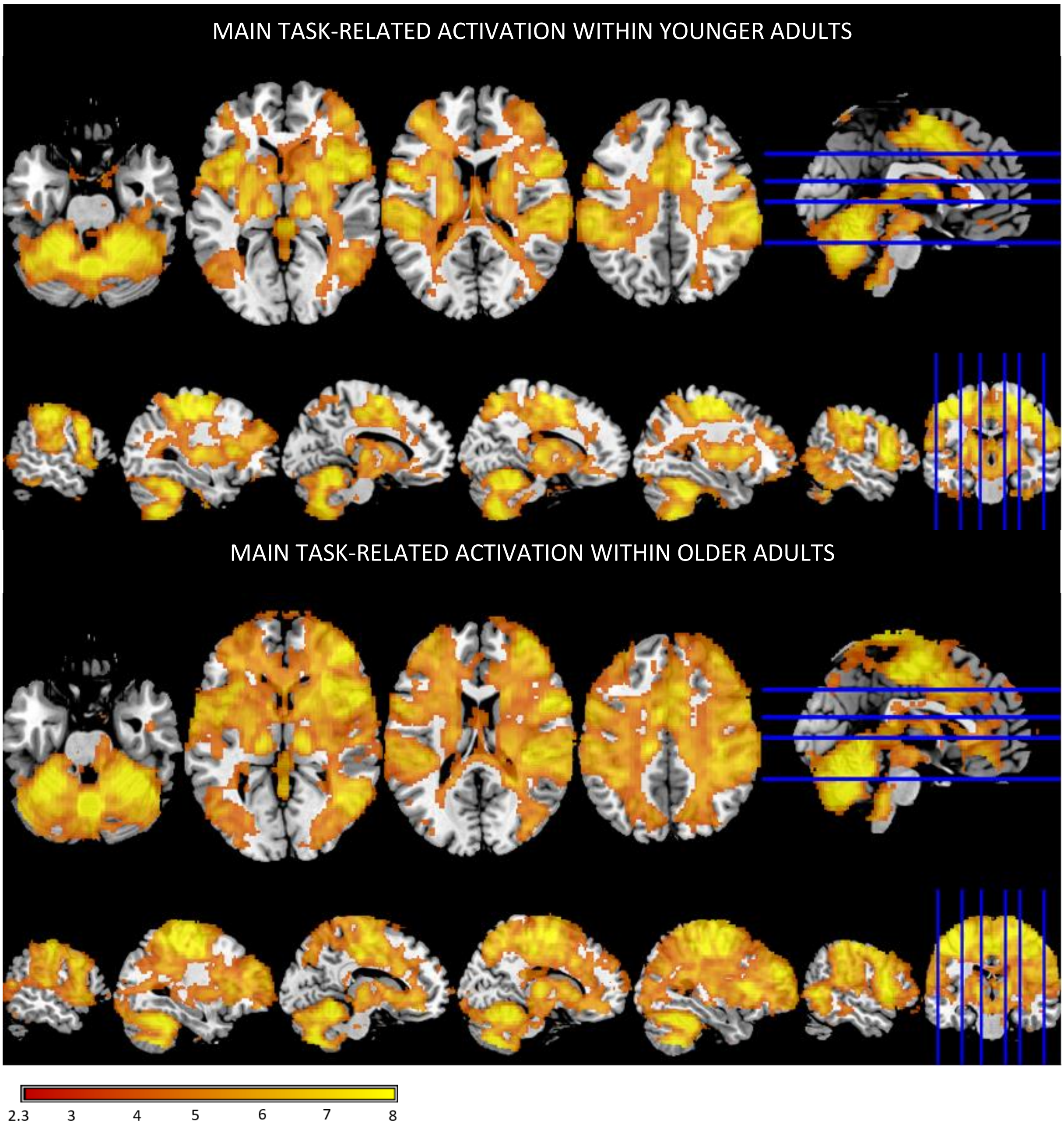

Figure 9: Task-related activation *The neural activation during task execution in the acquisition phase for both younger and older adults is shown in this figure. Axial as well as sagittal slices are presented for both age groups. The colour bar represents the threshold for activation, with the minimum set on Z-value 2.3 and maximum on 8.*

CI effect

The CI effect was examined within younger adults, within older adults and in the overall sample (table 6, 7 and 8 respectively).

Within the *younger adults*, the blocked group, as opposed to the random group, showed higher activation of different motor regions (bilateral M1, bilateral SMA and left PMC). Besides the motor regions in this comparison, neural recruitment also expanded to the left cerebellum, right S1 and parietal regions (right superior parietal cortex and left inferior parietal lobule), left lateral occipital cortex, right temporo-occipital cortex, left cingulate gyrus, right middle as well as inferior temporal gyrus and superior frontal gyrus together with the frontal pole. On the other hand, the random group, as compared to the blocked group, showed higher activations in the right S2, right insula and right parietal along with the frontal operculum as well as activity of the left SMA, left superior frontal cortex and right caudate. These results are summarized in table 6.

When focusing on the *older adults* (table 7), as compared to younger adults, a greater neural recruitment was observed across practice groups. As such, an enrolment of a large variety of brain regions was detected in the blocked group in contrast to the random group. More specifically, the blocked group activated the right cerebellum, various sensorimotor areas (bilateral M1 and S1, right PMC, left SMA together with the mid cingulate cortex and right S2 and parietal operculum), numerous regions in the temporal cortex (bilateral middle and left inferior temporal cortex), right visual cortex, left middle and inferior frontal cortex, left caudate, right parahippocampal cortex and the right hippocampus. Random practice, in contrast to blocked practice, showed a higher activation of the left cerebellum, sensorimotor areas (right PMC, bilateral M1, left S1 and left inferior parietal cortex) and right middle and inferior frontal cortex.

At last, when *combining both age groups*, various brain regions showed higher activations in blocked compared to random practice, i.e. different left-sided sensorimotor areas (S1, M1, SMA and PMC), right hippocampus, right cerebellum, frontal cortices (bilateral middle, bilateral inferior and left superior frontal cortex), bilateral middle temporal gyrus, anterior cingulate cortex and cingulate gyrus, left precuneus, bilateral frontal pole and bilateral visual cortex. Inversely, the random group activated multiple sensorimotor regions (right M1, right PMC, bilateral SMA, bilateral S1, left inferior parietal cortex as well as right parietal operculum and S2), frontal areas (right middle and inferior frontal cortex) and the left cerebellum. For an overview of the activations across both age groups, consult table 8.

Table 6: Overview of the most prominent neural activations within younger adults when comparing the practice groups.

CI EFFECT WITHIN YOUNGER ADULTS DURING THE ACQUISITION PHASE						
	Brain region	**Left (L) / right (R)**	**Coordinates**			**Z-value**
			x	**y**	**z**	
Blocked > Random	Cerebellum (VIII)	L	-18	-56	-56	5.3
	M1	R	40	-10	48	5.9
		L	-22	-26	48	5.6
	Superior parietal cortex	R	34	-38	46	4.9
	S1	R	48	-24	48	6
	SMA	R	2	-4	62	5
		L	-6	-6	62	5.4
	superior frontal gyrus & frontal pole	R	8	58	30	3.9
	Temporoccipital cortex	R	52	-54	12	5.9
	Cingulate gyrus & paracingulate gyrus	L	-2	44	4	5.4
	Lateral occipital cortex & inferior parietal lobule	L	-40	-68	24	5.3
	PMC	L	-16	-10	60	5.5
	Middle and inferior temporal gyrus	R	56	-2	-34	6.1
Random > Blocked	SMA & superior frontal cortex	L	-4	34	42	3.8
	S2	R	52	0	10	4.3
	Caudate	R	14	16	16	3.3
	Frontal operculum & insula	R	38	12	8	4.3
	Parietal operculum	R	52	-18	10	4.6

Table 7: Overview of the most prominent neural activations within older adults when comparing the practice groups.

CI EFFECT WITHIN OLDER ADULTS DURING THE ACQUISITION PHASE						
	Brain region	**Left (L) / right (R)**	**Coordinates**			**Z-value**
			x	**y**	**z**	
Blocked > Random	Cerebellum (VII & VIII)	R	34	-56	-48	4.5
	M1	R	18	-28	60	3.9
		L	-48	-4	56	5.1
	PMC	R	36	-24	70	4.2
	S1	R	28	-28	46	5.8
		L	-44	-28	56	4.1
	SMA & mid cingulate cortex	L	-4	-10	42	4.5
	Visual cortex	R	6	-94	22	5.9
	S2/Parietal operculum	R	58	-22	22	5.3
	Caudate	L	-12	8	12	3.9
	Middle temporal cortex	R	-54	-6	-24	4.4
		L	56	2	-20	3.8
	Inferior temporal cortex	L	-54	-14	-26	3.9
	Middle and inferior frontal cortex	L	-34	30	18	4.5
	Parahippocampal cortex	R	32	-4	-32	4.2
	Hippocampus	R	22	-12	-26	4.9
Random > Blocked	Cerebellum (VII & VIII)	L	-12	68	-38	5.2
	PMC	R	52	2	42	5.6
	M1	R	42	-16	62	4.6
		L	-34	-28	50	4.7
	S1	L	-40	-38	58	6.7
	Middle & inferior frontal cortex	R	38	20	26	4.5

Table 8: Overview of the most prominent neural activations in the overall sample when comparing the practice groups.

CI EFFECT ACROSS ALL SUBJECTS DURING THE ACQUISITION PHASE						
	Brain region	**Left (L) / right (R)**	**Coordinates**			**Z-value**
			x	**y**	**z**	
Blocked > Random	Cerebellum (VI)	R	24	-56	-28	3.6
	Hippocampus	R	22	-10	-26	6.6
	M1	L	-26	-22	60	3.9
	S1	L	-42	-24	56	5.6
	SMA extending to PMC	L	-6	-4	62	6.6
	Middle temporal gyrus	R	54	2	-32	5.9
		L	-48	2	-28	5.1
	Middle frontal cortex	L	-46	2	58	5.5
	Cingulate gyrus	-	0	-14	34	4.6
	Frontal Pole	R	54	36	-6	4.9
		L	-16	64	20	5.7
	Precuneus	L	-12	-52	40	4.8
	Inferior frontal cortex	R	54	32	-8	4.7
		L	-52	24	0	3.9
	Superior frontal cortex	L	-10	12	64	5
	Anterior cingulate cortex	-	0	42	4	5.8
	Visual cortex	R	6	-94	22	5.2
		L	-2	-98	18	4.3
Random > Blocked	Cerebellum	L	-20	-74	-42	3.7
	M1	R	50	2	40	6
	S1	R	60	-2	22	2.9
		L	-40	-40	56	6.5
	Inferior frontal cortex	R	42	12	22	3.8
	PMC	R	48	0	38	5.7
	Parietal operculum/S2	R	64	4	4	4.4
	Inferior parietal cortex	L	-46	-36	42	3.5
	Middle frontal cortex	R	34	12	30	3.5
	SMA	R	6	22	44	4.2
		L	-8	22	46	4

Age

When considering the effect of age, results showed that the elderly activated additional brain regions compared to their younger counterparts, i.e. the left cerebellum, various sensorimotor regions (left M1 and PMC, right SMA, left S1, right Parietal operculum/S2), right hippocampus, left precuneus, left cingulate and paracingulate gyrus, temporal areas (right middle and inferior temporal gyrus and right temporal pole), bilateral middle and inferior frontal gyrus as well as the left lateral occipital cortex extending to the inferior parietal lobule (table 9). On the contrary, no region showed higher activation in younger adults as compared to older adults.

Table 9: Overview of the main areas showing an effect of age group during the acquisition phase

EFFECT OF AGE DURING THE ACQUISITION PHASE						
	Brain region	**Left (L) / right (R)**	**Coordinates**			**Z-value**
			x	**y**	**z**	
Young > Old	-					
Old > Young	Cerebellum	L	-6	-56	-2	7.7
	Middle and inferior temporal gyrus	R	46	-6	-28	4.7
	Temporal pole	R	54	8	-2	4.5
	Parietal operculum/S2	R	40	-14	20	5.7
	PMC	L	-2	-16	62	6.2
	M1	L	-32	-16	44	6.2
	Hippocampus	R	38	-26	-10	6.6
	SMA	R	4	-12	66	6.2
	Cingulate & paracingulate gyrus	L	-8	42	0	6.2
	Precuneus	L	-2	-78	40	6.2
	S1	L	-34	-20	40	5.3
	Middle and inferior frontal gyrus	R	44	6	40	5.7
		L	-42	10	32	6
	Lateral occipital cortex & inferior parietal lobule	L	-54	-62	10	5.7

4.2.2 Retention

CI effect

For retention, a consistency in activation pattern could be recognized when exploring the CI effect within both younger and older adults and for the overall sample of subjects (table 10). As such, no brain region showed higher activation in blocked practice as compared to random practice in none of the three comparisons. Within the *younger adults*, the bilateral precuneus with extensions to the visual cortex, temporal areas (right superior temporal gyrus and bilateral temporal pole), frontal areas (right PMC extending to the superior and middle frontal cortex) and the right frontal and central operculum along with the superior parietal lobule exhibited higher activations in the random group as opposed to the blocked group. Furthermore, the random group of *older adults*, as compared to the blocked group, exhibited a greater activation of the left cerebellum, left precuneus, right putamen, right M1, parietal regions (right parietal operculum/S2, left superior parietal lobule), right middle temporal gyrus, bilateral middle frontal gyrus together with the left frontal pole and lateral occipital cortex extending to the inferior parietal lobule. Finally, when assessing the CI effect in the overall sample, the random group presented a higher recruitment of sensorimotor cortical structures (left M1, right PMC in combination with the middle frontal cortex and left S1), right insula, left cerebellum, bilateral precuneus, subcortical structures (left caudate and bilateral putamen), temporal structures (left temporal pole and operculum cortex as well as the superior temporal gyrus bilaterally) and left visual cortex.

Table 10: Overview of the brain regions showing a CI effect within younger adults, within older adults and for the overall sample of subjects during the retention phase.

CI EFFECT DURING THE RETENTION PHASE: Random > Blocked						
	Brain region	**Left (L) / right (R)**	**Coordinates**			**Z-value**
			x	**y**	**z**	
Within younger adults	Precuneus, extending to the visual cortex	R	14	-68	24	4
		L	-16	-70	24	3.4
	Superior temporal gyrus	R	50	-24	0	3
	Frontal & central operculum	R	38	12	10	3.2
	Temporal pole	R	48	14	-10	3
		L	-52	12	-6	3.7
	PMC & superior and middle frontal cortex	R	26	-6	64	3.6
	Superior parietal lobule	L	-12	-62	56	3.3
Within older adults	Cerebellum (VIII)	L	-26	-56	-48	4.1
	Precuneus	L	-8	-68	42	3.4
	Putamen	R	28	4	12	3.4
	Parietal operculum/S2/ventral premotor	R	64	-2	8	3.4
	M1	R	60	8	8	3.6
	Middle frontal gyrus	R	48	8	42	3.5
	Frontal pole & middle frontal gyrus	L	-30	40	32	3.6
	Middle temporal gyrus	R	60	-56	-2	3.1
	Lateral occipital cortex & inferior parietal lobule	L	-46	-72	18	3.2
	Superior parietal lobule	L	-2	-72	32	3.3
Overall sample	Precuneus	R	16	-62	22	4.9
		L	-18	-66	24	4.1
	PMC & middle frontal cortex	R	52	2	42	4.3
	Temporal pole & operculum cortex	L	-48	10	-6	3.9
	Superior temporal gyrus	R	52	-18	-6	3.2
		L	-54	-38	6	3.2
	Caudate	L	-14	12	10	3.5
	S1	L	-38	-38	56	3.9
	Putamen	R	24	0	10	3.3
		L	-26	0	12	3
	Visual cortex	L	-36	-80	-8	3.2
	Cerebellum	L	-26	-60	-44	3.1

Age

With respect to the effect of age, similar to our observation during the acquisition phase, the elderly displayed a greater neural recruitment compared to their younger counterparts. More specifically, a greater activation of the bilateral precuneus, right parahippocampal cortex, right insula, left thalamus, left cerebellum, right superior parietal lobule, bilateral middle temporal gyrus and bilateral superior and middle frontal cortex in conjunction with an activation of the right occipital pole extending to the lateral occipital cortex was observed. Inversely, no brain regions showed a higher activation in younger adults as compared to the older adults. These main activations related to the effect of age are presented in table 11.

Table 11: Overview of neural correlates that could be addressed to the effect of age in the retention phase.

EFFECT OF AGE DURING THE RETENTION PHASE						
	Brain region	**Left (L) / right (R)**	**Coordinates**			**Z-value**
			x	**y**	**z**	
Young > Old		-				
Old > Young	Precuneus	R	4	-60	56	4.5
		L	-6	-54	-52	3.5
	Parahippocampal cortex	R	32	-28	-20	3.7
	Insula	R	44	-6	12	3.9
	Superior & middle frontal cortex	R	42	4	40	4
		L	-16	28	62	3.9
	Middle temporal gyrus	R	60	-54	-2	3.4
		L	-56	-60	-2	3.4
	Superior parietal lobule	R	22	-54	66	4
	Cerebellum	L	-34	-46	-44	3.6
	Thalamus	L	-4	-2	4	3.5
	Occipital pole & lateral occipital cortex	R	34	-90	16	3.7

5. DISCUSSION

The purpose of this study was to investigate the CI effect within younger and older adults as well as to compare the CI effect across these age groups. Both the behavioural analysis and neural correlates of the CI effect were of interest. To this end, 10 younger and 10 older adults were trained a bimanual visuo-motor coordination task following either a random or a blocked practice schedule. Their skill learning was tested six days later on a retention day. As hypothesized a priori for both age groups, the random practice, as opposed to the blocked practice, tended to enhance motor skill retrieval despite a poorer performance during the acquisition phase. Furthermore, all subgroups expressed an improvement of performance over time during the acquisition phase, despite an overall poorer performance of older adults compared to younger adults. On the contrary, post-acquisition processes needed for retrieval did not seem to be affected by age. Although both age groups recruited various sensorimotor areas, cerebellum and subcortical structures during task execution, the older adults activated a more widespread neural network compared to their younger counterparts. This is in line with our expectations and the compensation related utilization of neural circuits hypothesis (CRUNCH) (Reuter-Lorenz & Cappell, 2008). With respect to the neural correlates of the CI effect during acquisition, random practice relied more on higher level cognitive cortices such as PMC, whereas the blocked group predominantly activated sensorimotor areas (M1, S1 and SMA). During retention, random practice, as opposed to blocked practice, demonstrated an additional activation of the higher order structures to retrieve memory and optimize the integration of sensory information (precuneus, cerebellum and hippocampus). When comparing both age groups, the elderly recruited additional non-motor areas enabling them to increase attention and feedback dependent performance. In the next section, the established behavioural and imaging results will be interpreted and discussed.

5.1 Behavioural data

5.1.1 CI effect

Acquisition

A main characteristic of CI is the detrimental effects of a random practice schedule, i.e. high CI, on performance during the acquisition phase in comparison to a blocked practice schedule, i.e. low CI (Shea & Morgan, 1979). When looking at our results of the CI effect on performance during training in the overall sample, random practice was more difficult compared with blocked practice. This result is in line with previous literature, indicating that random practice, as compared with blocked practice, is detrimental for performance during training (Cross et al., 2007; Lin et al., 2012; Pauwels et al., 2015, 2014). This can be explained by the fact that in random practice the extra difficulty incorporated in training, i.e. the constantly switching demands of the task, needs to be overcome (Guadagnoli & Lee, 2004). When dividing the overall sample into the different age groups, a clear discrepancy was seen. As such, within the younger adults, blocked practice was favourable over random practice during the acquisition phase. In contrast, within the older adults, blocked and random practice schedule did not induce inequality in performance during the acquisition phase, i.e. blocked practice did not outperform random practice. This might indicate that the CI effect does not stand ground within the aged population. However, this is not in line with our expectations and findings from previous studies (Lin et al., 2012; Pauwels et al., 2015). Therefore, it is important to consider the small sample size included within each age group, i.e. 10 younger adults and 10 older adults (among whom 9 had complete behavioural data). Hence, the low statistical power of this pilot study, particularly within the older group, might have contributed to the non-significant findings. This restrains us from drawing firm conclusions regarding the CI effect within the aged population.

When the acquisition phase was investigated in more details, all subgroups showed performance gains over time during training. This indicates that, despite of age and practice schedule, performance was ameliorated during the acquisition phase. Taking into account the small number of subjects within each subgroup, these results give a strong indication of an enhancement in task execution through training. Thus, on the one hand, both random and blocked practice schedules permit learning during training. On the other hand, these findings illustrate that both age groups accomplished to significantly lower their error scores and thus improve their performance.

Retention

The key message of the CI effect contains that performance during retention, known as a quantification of motor learning, benefits from a random practice schedule (Shea & Morgan, 1979). Hence, random practice, as opposed to blocked practice, leads to better retrieval of task performance. This is a robust phenomenon in the literature in younger adults (Cross et al., 2007; Pauwels et al., 2014; Shea & Morgan, 1979) and several studies point to a similar result in the elderly (Lin et al., 2010; Lin et al., 2012; Pauwels et al., 2015). Therefore, we also expected to find the advantage of random practice on skill retrieval in both age groups. When considering the overall sample of subjects, random practice, as opposed to blocked practice, seemed to have beneficial effects on the retention phase. However, this trend in favour of the random practice schedule disappeared when focussing on either the younger or the older adults separately. As such, the practice schedules did not promote performance differences within younger or older adults during the retention phase, despite a clear trend in the overall sample. Therefore, we argue that the small number of subjects might serve as the underlying cause for our inconclusive results.

5.1.2 Aging

Whereas the CI effect is well established within younger adults, the positive effect of high CI on motor learning within older adults is less convincing. Inclusion of both younger and older subjects in this study enabled us to make a comparison between the two age groups. We expected that the elderly would exhibit a poorer performance compared to the younger adults during baseline assessment as well as acquisition and retention phases (Seidler, 2006; Seidler et al., 2010; Swinnen, 1998; Voelcker-Rehage, 2008). With respect to baseline assessment, both younger and older adults showed similar performance. While younger adults often outperform their older counterparts on baseline assessment (Seidler, 2007a; Voelcker-Rehage, 2008), in this study they struggled as well to handle the complexity level incorporated in the task. As such, participants were only informed about the coordination direction and had no knowledge about the different frequency ratios and their corresponding bimanual coordination patterns that were demanded during baseline assessment. Hence, both age groups had to learn this novel skill implicitly during practice. Furthermore, no feedback was provided, restricting subjects from adjusting their movement during execution. This explains the absence of an effect of age group during the baseline assessment. In contrast, older adults struggled to keep up with their younger counterparts during the acquisition phase despite an improvement in performance within each subgroup. This is in line with the existing literature, showing that age has a detrimental effect on performance gains in complex tasks (Pauwels et al., 2015; Voelcker-Rehage, 2008). Nonetheless, our findings also support that elderly are able to learn a new skill and improve their performance by training (Seidler, 2007b). At last, similar to our results of baseline assessment, we did not find a significant effect of age group in the retention phase. This can easily be explained by the fact that the positive effect of a random compared to a blocked practice schedule is preserved within the elderly. More specifically, the blocked group of both younger and older adults performed very poor at retention, whereas the random group of both younger and older adults accomplished a better retrieval of the task. This may indicate that post-acquisition processes that serve as a basis for long-term memory are not affected by age (Seidler, 2007a). Therefore, results revealed no effect of age group within blocked and random practice and thus no difference between age groups during the retention phase.

5.2 Imaging data

5.2.1 Main task-related activations during the acquisition phase

Within both age groups, the main task-related activations during the acquisition phase were explored. The task activated mostly similar brain regions in the two age groups. As such, sensorimotor areas (S1, M1, PMC, SMA), subcortical regions (thalamus, pallidum, caudate), cerebellum, insular cortex and frontal areas (inferior frontal cortex and the frontal pole) were recruited bilaterally regardless of age. The bilateral activation of most of these regions can be explained by the bimanual nature of the task. For younger adults, our results are in line with several other studies demonstrating that execution of a bimanual task is mainly dependent on activation of the cerebellum, sensorimotor areas and subcortical structures (Aramaki, Osu, & Sadato, 2010; Christensen, Ehrsson, & Nielsen, 2013; Debaere, Wenderoth, Sunaert, Van Hecke, & Swinnen, 2004a, 2004b; Kraft et al., 2007; Swinnen & Wenderoth, 2004). Concerning the elderly, a study from Heuninckx et al. (2008) investigated the task-related activations in older adults performing ipsilateral movements of the right wrist and ankle. They also found a recruitment of predominantly sensorimotor areas, cerebellum and subcortical structures. Although other studies also investigated the neural correlates of motor learning in the aged population, they did not specifically report task-related activations within the aged population (Blais, Martin, Albaret, & Tallet, 2014; Coxon et al., 2010; Goble et al., 2010). Because of the great resemblance in activations across age groups, we could argue that the most important neural processes underlying the execution of a bimanual task are barely affected by age.

Nonetheless, overall the older adults displayed a more widespread activation pattern compared to the younger adults. Two different theories emerged to explain this disperse activation pattern within the aged population. Firstly, this activation could be due to dedifferentiation in the aging brain, which is a neural recruitment caused by the struggle that older adults encounter to recruit the specialized neural mechanisms needed for a good performance. Thus, in this hypothesis, the activation is not beneficial for task performance (Heuninckx et al., 2008; Ward, 2006). Secondly, the additional activations could represent an attempt of the aging brain to keep up with performance of the younger adults. Hence, the extra recruitment serves as a compensation mechanisms to counteract for age-related decline (Heitger et al., 2013; Heuninckx et al., 2008; Reuter-Lorenz & Cappell, 2008; Ward, 2006). The latter is confirmed by several studies demonstrating a positive relation between the additional neural recruitment and ameliorated task performance (Heitger et al., 2013; Heuninckx et al., 2008; Reuter-Lorenz & Cappell, 2008; Ward, 2006). Although these results highlight the ability of the older adults to compensate for age-related declines in motor function, behavioural data demonstrated a trend towards a significant effect of age group during the acquisition phase. Considering these results, we can argue that, in this complex bimanual task, the extra compensatory activation of the elderly is not sufficient to match the performance levels of the younger adults. This would support previous findings revealing that older adults are only able to compensate for age-related declines to a certain extend (Reuter-Lorenz & Cappell, 2008; Schneider-Garces et al., 2010). As such, with increasing task difficulty, the older adults will expand the activation of their compensatory network but this mechanism is limited. Thus, a ceiling will be reached for both behavioural and neural levels where the compensatory mechanisms fail to further increase. This explains why the neural compensation of the elderly might be insufficient in this difficult bimanual coordination task.

Furthermore, some small differences in the task-related activation pattern between the age groups were observed. Besides a large bulk of analogous activations, the younger adults showed a more extensive activation of various subcortical structures compared to the older adults. More specifically, they showed bilateral activation of both caudate and pallidum, whereas only the right caudate and left pallidum was activated within the older adults. Moreover, the bilateral activation of the putamen by the younger group was not seen in older adults. A study by Debaere et al. (2004) revealed that the basal ganglia, including the putamen and caudate, are crucial to consolidate motor programmes and thus to create a long-term memory of the task. Moreover, Albouy and colleagues (2013) stated that the putamen, also known as the sensorimotor part of the striatum, is involved in late learning with an important role in the formation of stimulus – response associations. The two studies mentioned above only serve as an example, with numerous other studies also pointing towards a role for the basal ganglia in optimizing learning (Boecker et al., 1998; Dreher & Grafman, 2002; Hikosaka, Nakamura, Sakai, & Nakahara, 2002). These findings might indicate that older adults encounter more difficulties during the task execution because of the less pronounced engagement of the subcortical basal ganglia structures. This hypothesis is supported by several studies. Coxon et al. (2010) reported that the elderly might struggle with flexibility of behaviour due to an inefficient enrolment of cortico – basal ganglia loops. Furthermore, King et al. (2013) reported that older adults were not able to compensate for their age-related degradations within the striatum in the acquisition phase of a complex motor sequence task. This neuroscientific evidence is also depicted in our behavioural results, showing a negative effect of age on performance during the acquisition phase. To summarize, literature points out that aging has detrimental effects on the basal ganglia structures, which could partially account for the poorer performance of older adults during the acquisition phase. Likewise, younger adults relied more on parietal regions compared to their older counterparts. The parietal cortex is known as the cortex specialized in processing sensory information. As such, somatosensory information of the sensory afferents will be processed to guide motor performance, especially when no feedback is provided (Beets et al., 2015; Debaere et al., 2004b). Ward (2006) also reported a greater activity of sensorimotor regions in younger compared to older adults, stating that these activations expand with training in younger adults, whereas they will diminish in older adults. Nonetheless, this is not in line with other literature, advocating a profounder engagement of sensory brain regions in older adults than younger adults (Goble et al., 2010; Heuninckx, Wenderoth, Debaere, Peeters, & Swinnen, 2005; Lin et al., 2012). The discrepancy between these studies could be due to the differences in task demands.

5.2.2 CI effect

Although a lot of research has been devoted to the neural substrates of motor learning, very few studies embody the neural substrates of the CI effect. Lage and contributors (2015) reviewed the neural correlates of different practice schedules, including 8 studies investigating CI. They concluded that during the acquisition phase, random practice, as opposed to blocked practice, leads to a more profound activation of neural structures mediating motor planning and execution, i.e. premotor areas, M1, DLPFC and posterior parietal cortex (PPC). The opposite is true for retention, where a decrement of activation is observed in those indicated regions (Lage et al., 2015). However, only studies in younger subjects were included in that review. The research group of Lin is, to the best of our knowledge, the only group that has investigated the neural correlates of CI within the aged population (Lin et al., 2016; Lin et al., 2012), signifying the innovative nature of this study. Here, the CI effect was explored within younger and older adults and in the overall sample of subjects.

Acquisition

Within the *younger adults*, the blocked group, compared to the random group, had predominantly greater activation in regions that have been previously associated with bimanual motor control, i.e. M1, S1, SMA and cerebellum (Debaere et al., 2004a, 2004b; Swinnen & Wenderoth, 2004). Furthermore, an activation of temporal areas was seen in this comparison, which might be attributed to the motor processing in the presence of visual feedback (Beets et al., 2015). When comparing random with blocked practice within younger adults, the caudate was found to be more activated in random practice. This subcortical structure is a part of the striatum that is important for a correct association between stimuli and related responses (Albouy et al., 2013). Furthermore, in a study by Dreher and Grafman (2002) the caudate was shown to be sensitive to the unpredictability of a task, supporting our findings of higher activation of this structure during random practice. Moreover, a higher activation of the insula together with the frontal and parietal operculum was observed. Karnath and Baier (2010) established that the right insula has a central role in the network devoted to the representation of the human body scheme. Furthermore, it connects the external visual information to the tactile internal information, enabling an incorporation of different sensory information sources (Karnath & Baier, 2010). Besides the insular cortex, frontal and inferior parietal cortices were also more activated in the random group. These are known as higher order processing cortices and are responsible for the attentional or preparatory processes related to the execution of the bimanual task. Hence, we argue that the CI benefits are partially a result of the continuous reconstruction of the task information in the higher level cortices (Cohen & Andersen, 2002; Hikosaka et al., 2002; Johansen-Berg & Matthews, 2002; Jueptner et al., 1997). Moreover, all these activations in random practice were observed in the right hemisphere, which is of great importance to detect and/or correct errors, especially with increasing attentional demands (Beets et al., 2015).

Within the *older adults*, comparing blocked versus random practice, a similar pattern as the one in younger adults was observed. This is a recruitment of brain regions typically involved in bimanual movements control (Bangert, Reuter-lorenz, Walsh, Anna, & Seidler, 2010; Goble et al., 2010; Heitger et al., 2013; Heuninckx et al., 2005). In addition, when comparing blocked to random practice, the activation of temporal areas as seen in the younger adults remains present. On top of these shared activations, a supplementary activation of the hippocampus was observed, which is possibly crucial in older adults for integrating information from diverse cortical areas into a coherent memory trace (Albouy et al., 2013). Furthermore, involvement of different frontal areas in this comparison points to the extensive need for cognition during task performance. Inversely, random practice, in contrast to blocked to practice, mainly relied on the cerebellum together with higher level frontal cortices. Thus, older adults relied on cognition in both comparisons. This penetration of cognitive related areas in motor performance of elderly, is extensively confirmed in literature (Goble et al., 2010; Heuninckx et al., 2005, 2008; Lin et al., 2012; Seidler et al., 2010). As such, the middle frontal cortex, i.e. the DLPFC, was found to be activated in both comparisons within the older adults. The DLPFC is already extensively investigated in literature and has been shown to be engaged in the working memory, serving as a top-down anticipatory control through online processing of movement in order to update motor plans (Albouy et al., 2013; Beets et al., 2015; Debaere et al., 2004b; Lin et al., 2012). More importantly, the DLPFC is also shown to be associated with unpredictability and extensively required during random practice (Lage et al., 2015; Ridderinkhof, Van Den Wildenberg, Segalowitz, & Carter, 2004). Although Lin et al. (2012) and Cross et al. (2007) reported a correlation between the activation of the DLPFC and behavioural benefit in random practice within the young group, we did not see this as one of the main activations within the younger group. To explain this conflicting finding, we need to consider the task of interest in these contradicting studies: whereas participants of the studies of Lin et al. and Cross et al. needed to perform a rather simple, unimanual serial reaction time task, our study demanded multiple complex bimanual coordination patterns. Thus, the task demands play a role in defining the activation pattern. Furthermore, Coxon et al. (2010) proposed an activation of the DLPFC by elderly because of an inefficient recruitment of cortico – basal ganglia loops.

At last, in the *overall sample*, the precuneus was activated during blocked as opposed to random practice. This brain regions, located in the posterior parietal cortex, serves as an integrative system that enables the processing of spatial coordinates of a movement with increasing attention when the complexity raises (Boecker et al., 1998).

Retention

During the retention phase, the blocked group did not exhibit additional neural recruitment compared to the random group in neither younger adults, nor older adults, nor within the overall sample. This was not in line with our expectations and previous literature stating that in blocked, as compared to random practice, less efficient processing occurs. (Lage et al., 2015; Lin et al., 2016). On the contrary, different brain regions demonstrated a higher activation during random as opposed to blocked practice. As such, in all the comparisons the precuneus was found to be activate. The precuneus is a key region in visual imagery memory recall (Fletcher et al., 1995). Since no feedback was provided during retention, participants needed to rely on their motor and spatial memory retrieval, emphasizing the importance of this brain region (Ogiso, Kobayashi, & Sugishita, 2000). Furthermore, the superior parietal lobule was found to be activated in both younger and older adults. This cortical area handles the spatial aspects of movement planning by converting sensory input into motor output via the dorsal PMC to M1 (Hardwick, Rottschy, Miall, & Eickhoff, 2013; Heuninckx et al., 2008). Along with these neural activations, both younger and older adults activated temporal as well as higher level cortices such as the DLPFC. As discussed above, these areas represent an enhanced active control of movement by cautiously integration sensory information (Coxon et al., 2010; Heuninckx et al., 2005; Schneider-Garces et al., 2010). As expected, this engagement of higher order structures is more pronounced in older adults because they need to compensate for the detrimental effects of aging on performance (Coxon et al., 2010; Heuninckx et al., 2008; Ward, 2006). Moreover, older adults were found to activate more brain regions compared to their younger counterparts. As such, they show a supplementary activation of the putamen and cerebellum. The former is involved in encoding, consolidation and retrieval of memory (Albouy et al., 2013; Jenkins, Brooks, Nixon, Frackowiak, & Passingham, 1994) and is associated with unpredictability of a task by scanning for events leading to an unpredicted reward (Dreher & Grafman, 2002). The latter is engaged in error-monitoring during bimanual coordination (Christensen et al., 2013; Debaere et al., 2004a; Witter & De Zeeuw, 2015). The cerebellum also presents as a key structure in motor timing (Dreher & Grafman, 2002) and internally generated movements (Naito et al., 2002). Furthermore, Puttemans and contributors (2005) reported that both the putamen and cerebellum are crucial for the development of a long-term motor memory for coordination tasks. These neural findings might explain the better retrieval performance of the random practice group. Taking into account these findings, we speculate that the random group exhibits a higher cerebellar activation due to a more profound attempt to internally plan the timing of the task. When looking at the overall sample, the presented interpretations remain relevant.

5.2.3 Aging

It is well established that older adults encounter more difficulties during the execution of a motor task compared to younger adults. This is a result of age-related decline in both the musculoskeletal and central nervous system (Ward, 2006). In order to compensate for this decrement in abilities, a distributed pattern of brain regions, including non-motor related areas, gets activated (Heuninckx et al., 2005; Ward, 2006). Goble et al. (2010) were the first to confirm this additional neural recruitment by elderly in a bimanual task. They reported a shift towards a more feedback dependent control of movement with involvement of SMA, higher order feedback processing areas and cognitive areas (Goble et al., 2010). These findings are supported by our results, also showing an involvement of motor, sensory and cognitive related brain areas. Furthermore, the hippocampus was more activated in the older adults, i.e. a structure that has found to be important in motor memory by triggering sleep-dependent performance gains (Albouy et al., 2013). Moreover, the precuneus was more activate in the older adults, implying the importance of spatial memory retrieval within the elderly (Ogiso et al., 2000). Likewise, the activation of the cerebellum stresses the importance of timing and the inner generation of movements to guide performance (Christensen et al., 2013; Dreher & Grafman, 2002; Naito et al., 2002). At last, the engagement of frontal regions illustrates the importance of attention to action (Jueptner et al., 1997) and action selection together with response inhibition (Ridderinkhof et al., 2004). The regions mentioned above were active during the acquisition and retention phases, suggesting that the older adults stick to the same strategy to compensate for their age-related decline.

5.3 Study limitations and future directions

Some precautions need to be made when interpreting the results of this study. Firstly, since this is a pilot study, only a low amount of subjects is incorporated which presents as the main limitation of this study. In total, twenty subjects participated in our study, i.e. 10 younger and 10 older adults. Taking into account that both younger and older adults were randomly assigned to either a blocked or a random practice groups, each subgroup represented five subjects. Therefore, we were obliged to use non-parametrical tests during the statistical analysis. Because of the relatively low power of this study, we were limited to speculations about the implications of our results. Secondly, MCFLIRT was applied on the imaging data in order to correct motion outliers. However, this technique is not able to fully correct for all movement artefacts. This is especially of importance within the elderly, because they presented with more movements during task performance resulting in activations at the border of the brain, mostly frontal. Therefore, some of the activations discussed could be attributed to motion artefacts. Hence, techniques such as tracking the movement of the subject’s head during scanning might serve as a solution for a more precise correction of movement artefacts. Thirdly, data of the different frequency ratios were collapsed prior to analysis. Although their implications on behavioural performance were already documented (Pauwels et al., 2015), we might have missed their possible differential influences on the neural correlates. Since differences between the frequency ratios were observed in the behavioural data, it might be interesting to investigate their neural implications as well.

Taking into account that literature concerning the neural correlates of CI is very scarce, this study provides some new interesting insights in the effect of different practice schedules on motor learning. Although we tried to tackle some of the gaps in the current literature, more powerful studies are needed to support and further interpret our findings. Furthermore, interactions between different areas still need to be exposed to gain a complete view of the underlying mechanism of CI. At last, the correlation of behavioural and neuroimaging data might give an insight on the neural activations associated with behavioural benefits.

6. CONCLUSION

To summarize, this study was conducted to gain some further insights regarding the CI effect during the learning of a bimanual task in younger and older adults on a behavioural and neuroimaging level. Behavioural results pointed towards a beneficial effect of a random compared to a blocked practice schedule on motor learning for both younger and older adults. Although age showed to have a detrimental effect on the performance level during the acquisition phase, post-acquisition processes seemed to be intact in the older subjects. Furthermore, each subgroup demonstrated a significant improvement in performance over time during the acquisition phase. With regard to the neural correlates, the main task-related activations together with the effect of age and CI during acquisition and retention phases were of interest. Our results of the main task-related activations supported literature, displaying neural recruitment of sensorimotor regions, cerebellum and subcortical structures such as caudate and thalamus. Although these activations were observed in both younger and older adults, a more widespread activation pattern was depicted in the older compared to the younger adults. This additional neural recruitment might have been used to compensate for age-related decline in motor performance. Furthermore, older adults relied more on higher order cortical areas, illustrating a profounder reliance on cognition during motor learning. Considering the effect of CI during the acquisition phase in younger adults, we found that blocked practice, as compared to random practice, mainly relied on sensorimotor areas and the cerebellum. These brain regions are previously shown to be involved in bimanual coordination. When comparing random with blocked practice, we demonstrated that higher order cortices were recruited due to the need for a continuous reconstruction of the task demands. For retention, younger adults in random practice, as opposed to blocked practice, enhanced their attentional resources and cognitive engagement. Considering the CI effect in older adults, as opposed to younger adults, an additional activation of a dispersed network was observed for the acquisition and retention phases. This illustrates their aim to match performance levels of their younger counterparts by increasing the activity of processes involved in feedback controlled movement, attention, internal movement generation and spatial memory retrieval. Although these results are promising, further investigation is needed to validate our findings. Keeping in mind the increasing number of elderly in our society, the results of this study could have major implications in the field of geriatrics as well as neuromotor rehabilitation.

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8. APPENDICES

8.1 Barrier-knock-down-task

Shea and Morgan (1979) were the first to explore the CI effect, a concept introduced in verbal learning by Battig (1966), in the learning of a motor skill using a barrier-knock-down-task. This task consisted of three coloured lights, indicating the commencement of the task, a tennis ball and six freely moveable barriers. Subjects were pressing down a start button prior to task execution. When one of the lights was lid, subjects needed to release the start button as soon as possible, grasp the tennis ball and knock down the moveable barriers in a specific order. Finally, the tennis ball needed to be returned to a specific position. The order in which the barriers had to be knocked down differed, resulting in 3 task variants each corresponding to a light in a specific colour. During the acquisition and retention phases, the same three task variants were presented in 3 sets composed of 18 trials. Retention, both in a random and blocked order, was performed 10 minutes and 10 days after training. Transfer was conducted immediately after retention and consisted of two new tasks variants with either low or high complexity. Performance was measured in milliseconds.

8.2 Populaire samenvatting

De vergrijzing van de bevolking is een alom bekend fenomeen. Zo verwacht men dat het aandeel ouderen in de wereldbevolking zal stijgen tot meer dan 20% in het jaar 2050. Aangezien het verouderingsproces gepaard gaat met een achteruitgang van verschillende systemen binnen het menselijk lichaam zoals bijvoorbeeld het evenwichtsvermogen en de motoriek, worden ouderen vaak hulpbehoevend. Tegen 2050 zou dit een overrompeling van de geriatrische afdelingen kunnen betekenen. Daarom gaat er momenteel veel onderzoek uit naar het onderliggend mechanisme van veroudering en manieren om dit proces af te zwakken/te vertragen. Zo is gebleken dat ouderen in staat zijn hun prestatieniveau aan de hand van training langer te behouden of zelfs te verbeteren.

In deze studie werd er dieper ingegaan op een aspect van motorisch leren, namelijk contextuele interferentie (CI). Dit kan gedefinieerd worden als de variabiliteit die aangeboden wordt binnen een trainingsschema. Zo spreekt men van hoge CI in een gerandomiseerd oefenschema, waarbij varianten van eenzelfde taak kriskras door elkaar worden aangeboden (ADBACDCB). Anderzijds bevat een geblokt oefenschema, waarbij dezelfde taakvarianten een voor een aangeboden worden (AABBCCDD), lage CI. Uit onderzoek, waarbij voornamelijk relatief eenvoudige taken aan jongeren aangeboden werden, bleek dat hoge CI (i.e. een gerandomiseerd oefenschema) een positief effect heeft op het motorisch leren ondanks de extra moeilijkheden die deze groep ondervindt tijdens de trainingsfase. Wij wilden nagaan of deze bevindingen konden doorgetrokken worden naar de uitvoering van een complexe taak enerzijds en naar ouderen anderzijds. Daarenboven waren we geïnteresseerd in de hersenactivatie die hiermee gepaard ging.

In dit onderzoek werden 10 jongeren en 10 ouderen geïncludeerd, die ad random in een geblokte of gerandomiseerde groep toegekend werden. Alle deelnemers leerden een complexe bimanuele taak gedurende drie trainingssessies gespreid over drie dagen. Vervolgens werd zes dagen later een retentie test afgenomen om na te gaan wat de proefpersonen geleerd hadden tijdens training. Deze taak werd uitgevoerd in een “magnetic resonance imaging” (MRI) scanner om op deze manier na te gaan welke hersengebieden proefpersonen activeren tijdens de uitvoering van de taak.

Uit onze resultaten kunnen we besluiten dat de voordelen van een gerandomiseerd oefenschema (hoge CI) lijken gegeneraliseerd te kunnen worden naar zowel een complexere taak als een oudere populatie. Verder bleken tijdens de taak zowel subcorticale gebieden als sensorische, motorische en cognitieve hersengebieden betrokken te zijn. Terwijl de geblokte groepen vooral vertrouwden op activatie van sensomotorische gebieden, speelden cognitieve gebieden een belangrijke rol bij de gerandomiseerde groepen. Dit impliceert dat hoge CI gepaard gaat met verhoogde aandacht en meer “denkwerk”. Wanneer men de twee leeftijdsgroepen vergelijkt, ziet men dat ouderen een groter en meer diffuus neuraal netwerk rekruteren. Deze extra activatie gebruiken ouderen om te compenseren voor de leeftijd gerelateerde achteruitgang in motorische functie waarmee ze te kampen krijgen. Ook hier gaat het voornamelijk om cognitieve gebieden. Door het kleine aantal geïncludeerde proefpersonen moeten we echter opletten bij het trekken van conclusies uit onze resultaten. Desalniettemin kan de bevestiging van deze resultaten een grote impact hebben op de omgang met ouderen en de neuromotorische revalidatie.

8.3 Richtlijnen voor auteurs

Richtlijnen voor auteurs voor publicatie binnen het journal Neurobiology of learning and memory:

https://www.elsevier.com/journals/neurobiology-of-learning-and-memory/1074-7427/guide-for-authors