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Taking control! Structural and behavioural plasticity in response to gamebased inhibition training in older adults

Simone Kühn^{a,e,*}, Robert C. Lorenz^b, Markus Weichenberger^a, Maxi Becker^e, Marten Haesner^c, Julie O'Sullivan^c, Anika Steinert^c, Elisabeth Steinhagen-Thiessen^c, Susanne Brandhorst^d, Thomas Bremer^d, Jürgen Gallinat^e

^a Max Planck Institute for Human Development, Center for Lifespan Psychology, Lentzeallee 94, 14195 Berlin, Germany

^b Charité University Medicine, St. Hedwig-Krankenhaus, Clinic for Psychiatry and Psychotherapy, Große Hamburger Straße 5-11, 10115 Berlin, Germany

^c Charité University Medicine, Geriatrics Research Group, Reinickendorfer Str. 61, 13347 Berlin, Germany

^d University of Applied Sciences, Department of Game Design, Wilhelminenhofstraße 75, 12459 Berlin, Germany

e University Clinic Hamburg-Eppendorf, Clinic and Policlinic for Psychiatry and Psychotherapy, Martinistraße 52, 20246 Hamburg, Germany

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ABSTRACT

While previous attempts to train self-control in humans have frequently failed, we set out to train response inhibition using computer-game elements. We trained older adults with a newly developed game-based inhibition training on a tablet for two months and compared them to an active and passive control group. Behavioural effects reflected in shorter stop signal response times that were observed only in the inhibitiontraining group. This was accompanied by structural growth in cortical thickness of right inferior frontal gyrus (rIFG) triangularis, a brain region that has been associated with response inhibition. The structural plasticity effect was positively associated with time spent on the training-task and predicted the final percentage of successful inhibition trials in the stop task. The data provide evidence for successful trainability of inhibition when game-based training is employed. The results extend our knowledge on game-based cognitive training effects in older age and may foster treatment research in psychiatric diseases related to impulse control.

Introduction

Self-control is at the heart of human nature and frequently diminished in older age and psychiatric disease. Self-control interrupts the normal flow from intention to action. This ability to prevent and override unwanted thoughts, behaviours or emotions is integral to our functioning in daily life (Muraven et al., 1999), e.g. in traffic when you see that another car swerves into your blind spot just as you are about to switch lanes and you need to hit the brakes, or when trying to be polite during a conversation with a friend and not checking the mobile phone although you hear that a text message has just arrived. In experimental psychology, self-control is usually conceptualized under the construct of inhibition and frequently assessed using behavioural tasks like the stop signal task (Logan and Burkell, 1986). The stop signal task consists of a primary motor task, e.g. responding to a white arrow with a button press. If, however, a stop signal is presented (e.g. colour change to red), the participants are instructed to stop the ongoing motor response. The duration of the inhibition process can be derived from the reaction time data, a measure that has been termed

stop signal reaction time (SSRT).

In the literature inhibition has been associated with a consistent network of brain regions comprising most prominently the prefrontal cortex, in particular the right inferior frontal gyrus (rIFG, Aron et al., 2014). The rIFG is reliably activated during inhibition (for a metaanalysis see Swick et al. (2011)), and disruption of its integrity via lesions (Aron et al., 2003) or by means of transcranial magnetic stimulation (Verbruggen et al., 2010) result in substantial increases in SSRT.

Within the scope of the present study, we set out to train externally triggered inhibition. Interestingly, compared to the wealth of knowledge obtained on the training of various executive functions such as working memory (Klingberg, 2010; Kühn et al., 2012a), the literature on training of inhibitory control is relatively sparse. In two early studies, no effect of inhibition training was found (Logan and Burkell, 1986; Cohen and Poldrack, 2008) and several meta-analyses and large scale studies on the training of executive functions show mixed evidence for training effects and little or no evidence for transfer effects (Owen et al., 2010; Melby-Lervåg and Hulme, 2013). The lack of

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^{*} Corresponding author at: University Clinic Hamburg-Eppendorf, Clinic and Policlinic for Psychiatry and Psychotherapy, Martinistraße 52, 20246 Hamburg, Germany. *E-mail address:* skuehn@uke.de (S. Kühn).

research in this area can most likely be attributed to the fact that inhibition is widely regarded as "untrainable" (Gray et al., 2003). However, recent findings from cognitive neuroscience provide evidence for the existence of training effects. One study used an adaptive stop task design over a training period of three weeks showing decreases in rIFG activation during implementation of control, and increases in lateral prefrontal cortex during the cue phase (Berkman et al., 2014). The authors argue that transfer effects in the domain of inhibition might be difficult to find, because particular contingencies of the cue stimuli are learned, which are highly task specific. Recently, several authors have suggested that training with video games results in surprisingly wide transfer effects (Cardoso-Leite and Bavelier, 2014). In a previous study, we have been able to demonstrate structural changes in a brain network involved in spatial navigation after a twomonth training period with a platform game that places high demands on 3D orientation (Super Mario 64), accompanied by changes in an untrained orientation task (Kühn et al., 2013).

Based on this prior evidence, we set out to design a video game-like training task that encompassed elements of response inhibition. Throughout the training intervention, difficulty level was increased by introducing faster switches between the inhibition stimuli and more items that required inhibition. We predicted structural increases in rIFG, based on the abovementioned evidence linking response inhibition to the integrity of rIFG, in particular in rIFG orbitalis and triangularis based on a previous meta-analysis on inhibition tasks (Kühn et al., 2013) and behavioural effects in a classical stop signal task. We selected cortical thickness as the parameter of interest since it has previously been suggested to be a more sensitive parameter with a higher signal-to-noise ratio compared to voxel-based morphometry (Dickerson et al., 2008; Hutton et al., 2009; Salat et al., 2004). Moreover, cortical thickness measures have been considered to be more easily interpretable than the probabilistic grey matter volumes in VBM (Lehmann et al., 2011). Since older age has been associated with a decrease in the capacity to inhibit (Kramer et al., 1994), most likely associated with the widely described age-related decline in the frontal lobe (Fjell et al., 2009), we selected a sample of adults aged 60 and above, where a realistic need to train self-control can be expected.

Materials & methods

Participants

Fifty three healthy participants (mean age=69 years, SD=4.2, range 62-78, 27 females) were recruited from the student body of the Senior University, Berlin and by means of flyers and internet advertisements. The advertisement did mention that we were recruiting for a cognitive training study but did not specify which training effects we expected. Moreover participants were randomly assigned to the different groups ruling self-selection effects out. The sample size was based on estimates from a previous study with a similar design and similar outcome measures (Kühn et al., 2014). Based on this previous study with an effect size of 0.65 we aimed for recruiting 17 participants per group to achieve a power of 0.80 and alpha error of 0.05. After complete description of the study, the participants' informed written consent was obtained. The local ethics committee of the Charité University Clinic, Germany, approved of the study. Cognitive status was assessed with the Mini Mental State Examination (MMSE, Folstein et al., 1975). All participants reached a MMSE score of 25 or higher (mean MMSE score=28.45, SD=1.14; range 25-30) indicating they were cognitively intact. An exclusion criterion was previous experience with a tablet computer. According to personal interviews (Mini-International Neuropsychiatric Interview) participants were free of mental disorders. In addition, exclusion criteria for all participants were abnormalities in MRI, general medical disorders and neurological diseases. The participants received a financial compensation for the testing sessions, but not for the training itself (Table 1).

Training procedure

The participants were randomly assigned to one of three groups. The inhibition game group (n=20, mean age=69.6, SD=4.5, 11 females) played an inhibition game on a tablet (Samsung Galaxy Tab 3) over a period of eight weeks. The active control group was introduced to a tablet-based cognitive training platform (n=15, mean age=68.4, SD = 4.7, 7 females) that ran on the same model. This group was included to control for the fact that participants in the inhibition-training group also received a novel technical device to interact with. The passive control group (n=18, mean age=69.6, SD=3.5, 9 females) was not given a tablet and had no task but underwent the same testing procedure as the two other groups.

Both training groups were asked to train the game or with the cognitive training platform for approximately 15 min a day. However, we intentionally compensated the participants only for the sessions in which they came to the lab for testing. Our previous research, in which we used a similar procedure, suggests that the perceived fun while engaging in an intervention is positively associated with brain plasticity (Kühn et al., 2014) and we speculate that enforcing longer training sessions and therewith forcing participants to engage longer than they feel like, may impair motivation and therewith the hypothesized training effects.

Inhibition game

The inhibition game (developed using the Unity platform) consisted of target objects (mostly specific types of food, 35 items in total) that appeared on a buffet at the top of the screen and a plate that was displayed at the bottom of the screen (Fig. 1) (the game "Schiff Ahoi" can be downloaded via https://mpibox.mpib-berlin.mpg.de/f/ 06bf74aad2/). At the beginning of the game, the task was fairly simple, namely to move the target items from the buffet onto the plate as quickly as possible by means of swiping gestures. A timer to the left of the plate displayed how much time participants had left to displace the items (on each trial, the timer started at 1 min 30 s and ran down to 0). Successful placement of the target item onto the plate coincided with a pleasant, while unsuccessful placement coincided with an unpleasant sound. Also, after an item had been swiped away from the buffet, a new one appeared after a short delay to ensure that participants were constantly encouraged to speed up their performance and translocate as many objects as possible. Once participants were familiar with the basic task, inhibition items were introduced and displayed on the red napkin (with the label "NEIN", "no" in German) located to left of the plate. Participants were specifically instructed not to drag the inhibition items onto the plate, if they appeared on the buffet. Likewise, incorrect selection or translocation of an inhibition item coincided with an unpleasant sound. The display of the inhibition items on the napkin stayed visible during game play, so that participants did not need to memorize the items, however with growing number of inhibition items this is what participants reported doing. To increase the general tendency to respond, more than one target item appeared on the buffet and the items disappeared after a short time, therewith withdrawing a chance to collect another item. Moreover inhibition items were less frequently presented compared with target items (about 25% inhibition items, 75% target items). Inhibition items were frequently exchanged between different trials, in order to prevent training of specific S-R associations and to promote cognitive flexibility. Moreover, task difficulty was gradually increased: participants started out with non-food objects as inhibition items, and then advanced to food items that became more and more difficult to discriminate from the target items in terms of food group, colour etc. Additionally, the number of inhibition items that needed to be avoided was increased from one up to twenty to make the task even more difficult. Moreover, inhibition items did not exclusively occur as inhibition items, but also appeared as target items in other trials.

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