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Cognitive Flexibility Training in Healthy Aging.

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SUMMARY

Despite the neurocognitive deterioration that is generally associated with increased age, recent studies suggest that it is possible to stave off or slow down this decline and enhance mental functioning using cognitive training. The aim of this thesis was to determine whether frequent use of a cognitive flexibility training can be an effective way to maintain or enhance cognitive and subjective functioning in healthy older adults. In this final chapter, I will first summarize our most important findings regarding these questions. Following this, I will critically reflect on this study and on training studies in general, and discuss the implications and directions for future interventions.

At the outset of this project, a myriad of cognitive training studies was developing, promising far-reaching results, yet without being backed by guidelines on what makes up an effective intervention for older adults. We therefore reviewed the available training literature before 2012 to create an overview (**Chapter 2**) of the specific elements that show the greatest evidence of beneficial effects. We noted several methodological limitations in the current literature, such as the absence of control groups and short training times. Additionally, we argued that executive functions should be an essential ingredient of training, as they are crucial in guiding and monitoring performance in daily life and are susceptible to deterioration with increasing age. Promising avenues were discussed in training shifting, updating, and inhibition. We especially emphasized the addition of aspects of cognitive flexibility, particularly evident in task switching, given the enhancement of untrained functions (far transfer) demonstrated in the literature.

Additionally, a few relatively uninvestigated issues seemed particularly relevant to training in the aging population. First, including decision learning in training studies offers potential for improved outcome optimization, given the age-related behavioral differences and activation patterns in decision making and decision learning. Second, both integrating novel items into training sessions and creating interventions around novel skill learning were suggested to lead to benefits in functioning, by preparing the neuronal system for learning as well as develop new connections. Third, we advised an increased focus on training memory strategies, including considerable practice and individual choice, to investigate whether transfer of learning specific memory techniques might help older adults cope with situations on a daily basis. Fourth, the issue of individual variation in the population of older adults was raised, which can be addressed by creating adaptive training programs as well as identifying predictors of trainability.

We incorporated most of the above-mentioned aspects into our own intervention, the Training Project Amsterdam Seniors and Stroke (TAPASS), a randomized controlled trial, of which cognitive effects are detailed in **Chapter 3**. This study consisted of three programs, all including playing a combination of short computer

games for 30 minutes a day for 12 weeks. Games for the first two interventions were diverse, cognitively stimulating, and adaptive. The third intervention, a mock training, was meant as an active control. Additionally, the first intervention required participants to switch between games of different domains (working memory, reasoning and attention) every three minutes, thus instigating and capitalizing on the need for flexibility. The second intervention required a switch every ten minutes, controlling for the elements of adaptibility and the diversity in games themselves. The mock training allowed participants to only play visually attractive games, demanding minimal cognitive stimulation and offering minimal adaptability. Cognitive effects were measured at four time points: before training, after 6 weeks of training, after 12 weeks of training, and 4 weeks post-training. Although most training gain was seen in the two interventions, all three conditions equally improved on measures of task switching, reasoning, planning, working memory, and psychomotor speed, all of which were further increased post-training. No benefit or disadvantage was found for individual characteristics. As we found no evidence for training-specific improvement, we interpreted these time-based increases as effects of motivation, expectancy and test familiarity, rather than an enhancement of underlying mechanisms of functioning due to specific elements of the training. Given these results, we further underscore the usage of both passive and active control groups in training research, as well as using parallel tests to limit retest effects.

Apart from the cognitive effects, we also examined how the training affected subjective mental functioning (**Chapter 4**). Effects were measured before and after training on subjective cognitive failures and executive dysfunctioning, everyday functioning, quality of life, depressive symptoms, and anxiety. Both subjective cognitive failures and executive dysfunctioning were also assessed 4 weeks post-training and were additionally rated by participants' proxies. No changes were seen immediately after training. Amelioration of subjective executive dysfunctioning and cognitive failures was seen at 4 weeks post-training, but with minimal effect sizes and equal improvement in all groups. Participants' self-ratings for cognitive failures were significantly lower on both time points than those of their proxies, but proxies noted no changes over time. Several limitations notwithstanding, we concluded that computerized cognitive flexibility training was not advantageous for subjective mental functioning.

Individual variation within a group can lead to over- or underestimation of an intervention's merit: a training might be especially advantageous for one, yet not for another. As striatal dopaminergic activity is strongly associated with age-related decline, we included spontaneous eye blink rate, an indirect measure of dopaminergic function, to predict executive functioning and trainability in older adults (**Chapter 5**). Eye blink rate was measured before and after training by requiring participants to focus on a fixation cross and recording their blinks for 5 minutes. Blink rate per minute was used to predict working memory updating, response inhibition and switching, as well as training improvement and transfer in the two interventions and the mock training. Eye blink rate significantly predicted performance of both measures of updating, but not of inhibition and switching. Eye blink rate also predicted transfer of the two interventions on one of the updating tasks, but not on any other tasks or on training gain. These results provide initial albeit modest hints at possibilities in predicting working memory performance using eye blink rate in older adults, although further research is warranted to thoroughly interpret this relationship.

Conclusion

To summarize, we concluded that our computerized cognitive flexibility training, based fully on the elements shown in previous research to be most effective, did not provide any further benefit to cognitive or subjective mental functioning in healthy elderly adults, beyond a non-flexible training or a mock training. Limited evidence could be found of individual differences predicting performance on cognitive tasks or on the training. Caution is advised in interpreting the (positive) conclusions of many earlier studies, given their methodological limitations.