Novelty Interventions to Enhance Broad Cognitive Abilities and Prevent Dementia: Synergistic Approaches for the Facilitation of Positive Plastic Change

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Abstract

Process based cognitive trainings (PCTs) and novelty interventions are two traditional approaches aiming to prevent cognitive decline and dementia. However, both have their limitations. PCTs improve performance only in cognitive tests similar to the training tasks with inconsistent transfer effects on dissimilar tests. We argue that this learning specificity is due to a low training task variability. Novelty interventions are characterized by a high task variability but do not target specific processing demands affected in aging and dementia. To overcome the limitations of both approaches, we developed a process based novelty intervention using a card and board game based training approach. Here, we use highly variable tasks, which overlap in targeted processing demands (“overlapping variability” framework). An other nontraditional training approach combines cognitively with physically challenging tasks to induce multimechanistic effects, which might even interact positively. Initial results of both synergistic approaches indicate their potential to enhance broad cognitive abilities and prevent dementia.

Keywords

challenging mental activity, novelty intervention, process based cognitive training, process based novelty intervention, physically demanding novelty intervention, learning specificity, variability of practice, executive control, dementia

1 INTRODUCTION

As the world population ages, costs of dementia are expected to double within the next 40 years (Hurd et al., 2013). Effective interventions to prevent dementia are urgently sought after. Currently, no preventive or curative pharmacological therapy for dementia exists (Daviglus et al., 2011; Plassman et al., 2010); however, a vast and steadily growing literature suggests cognitive health benefits from engaging in mentally challenging activities (see, e.g., Verghese et al., 2003; Wang et al., 2013) and physical activities (see, e.g., Smith et al., 2010; Sofi et al., 2011; Weuve et al., 2004). Here, we review interventional studies on mentally challenging activities, excluding studies on pure physical activities such as aerobic (Kramer et al., 1999; Smith et al., 2010) and resistance exercise (Nagamatsu et al., 2012). We conclude that currently used cognitive interventions, namely, *novelty interventions* and *process-based cognitive trainings* (PCTs), did not tap specific processes or showed only inconsistent transfer effects on cognitive tests dissimilar to the training tasks, respectively. Addressing these limitations, the rationale for a synergistic *process-based novelty intervention* is presented, followed by initial results that indicate improvement in executive control. Finally, the rationale and cognitive effects of *physically demanding novelty interventions* are depicted.

2 EFFECTS OF CHALLENGING MENTAL ACTIVITIES

Evidence from prospective observational studies suggests that the risk for dementia is reduced in individuals who engaged in challenging mental activities over the whole lifespan (see Stern and Munn, 2010, and Valenzuela and Sachdev, 2006, for a meta-analysis and a systematic review). Individuals who were raised with multiple languages (Bialystok et al., 2007; Craik et al., 2010; Perquin et al., 2013), acquired a high educational level and a high occupational status (Valenzuela and Sachdev, 2006), or engaged in mentally challenging leisure activities (e.g., playing board games and musical instruments, Verghese et al., 2003) showed a better cognitive development (see Wang et al., 2012, for a recent review).

At the same time, observational studies have the downside that causal attributions cannot be made, as attribution of effects to nonmeasured confounding variables and reverse causality (cognitive impairments lead to reduced activities) cannot be excluded (see Eriksson Sörman et al., 2013). Experimental studies, on the other hand, allow for the causal interpretation of effects. Furthermore, their interventional nature enables the evaluation of theory-driven interventions, for example, cognitive training instead of unspecific mental activities.

Two approaches within cognitive interventions seem most promising and will be outlined in more detail in the succeeding text: novelty intervention and process-based cognitive training (PCT).

Novelty intervention is defined as a program which enables participants to engage in difficult, novel tasks offering a high variability but generally not targeting

specific processes. Thus, it induces a mismatch of functional organismic supply and task demands (see Lövdén et al., 2010) in multiple unspecific processes. Often, these interventions are intrinsically motivating, related to real life and implemented in a social context (e.g., Carlson et al., 2008; Cheng et al., 2013; Klusmann et al., 2010; Mortimer et al., 2012). *Cognitive leisure activity* (Stern and Munn, 2010), *complex mental activity* (Valenzuela et al., 2007; Wilson, 2011), and *engagement intervention* (Park et al., 2007) depict similar concepts.

Based on Gates and Valenzuela (2010), we define PCT as a repeated practice on standardized and theory-driven tasks. Similar to novelty interventions, PCTs induce a supply demand mismatch but not in unspecific but in specifically targeted processes. This mismatch is not maintained by introducing novel tasks but by the adaptation of difficulty to participants' performance in repeatedly practiced tasks. Similar concepts include cognitive exercise (Gates and Valenzuela, 2010) or process training (Lustig et al., 2009).

2.1 Novelty interventions

Experimental animal studies on the effect of environmental enrichment (see van Praag et al., 2000, for a review and Li et al., 2013) and observational studies in humans suggest the importance of novelty for brain health (Angevaren et al., 2007; Eskes et al., 2010; Fritsch et al., 2005). For example, Fritsch et al. (2005) tested the role of novelty-seeking activities from ages 20 to 60 in predicting Alzheimer's disease (AD) using a case-control study design. By running a factor analysis on 16 activities, a novelty-seeking factor was extracted, composed of indicators such as the frequency of learning new skills, taking up new hobbies or learning about a new subject. More frequent engagement in novelty-seeking activities significantly reduced the odds ratio for AD even after adjusting for other predictive factors such as age, education, and occupational status (odds ratio = 0.25; 97.5% CI: 0.139–0.443; $p < 0.001$).

These studies stimulated interventional studies on beneficial cognitive effects of exposure to novelty. For example, Klusmann et al. (2010) compared healthy older adults unfamiliar with computers who were randomized to a 6-month computer course (75 sessions; 90 min each) or to a passive control group. The computer course was composed of novel tasks such as writing, playing, calculating, e-mailing, drawing, image editing, or videotaping, to name just a few. Participants who attended the computer course significantly improved in tests of episodic memory and executive function, compared with the control group. Various other interventions exposing participants to novel, multifaceted mental tasks such as playing strategy video games (Basak et al., 2008; Glass et al., 2013) and multiple other kinds of video games (Oei and Patterson, 2013); a diverse range of cognitive and perceptual motor activities (Tranter and Koutstaal, 2008); convergent and divergent problem solving in groups (Stine-Morrow et al., 2008); volunteering to help children with reading achievement, classroom behavior, and library support (Carlson et al., 2008); participating in individualized piano instruction (Bugos et al., 2007); and engaging in

group discussion (Mortimer et al., 2012) showed beneficial effects on cognitive outcomes. On the contrary, there are also a few studies failing to find any effect from action and strategy video gaming (Boot et al., 2008, 2013). In contrast to the studies mentioned earlier, Cheng et al. (2013) investigated the potential to improve cognition in people with dementia rather than in healthy individuals. Participants in the intervention group played the Chinese tile-based game *mahjong* for 1 h, 3 days a week for 3 months, while the active control group was engaged in simple handicraft for the same duration. Six months after treatment completion, the mahjong group differed by 4.5 points (95% confidence interval: 2.0–6.9; $d=0.48$) on the Mini-Mental State Examination from the active control group. To our knowledge, no experimental study investigated the effects of a pure novelty intervention on incidence of dementia. Thus, conclusions as to whether these cognitive benefits translate to a delay of dementia onset cannot be drawn. Taken together, novelty interventions showed promising and rather consistent effects on cognitive outcomes, indicating enhancement of cognitive ability. Nevertheless, the tasks used in novelty interventions did not tackle specific processes affected in aging and dementia, such as executive control processes (see Fig. 1). PCT addresses this issue.

2.2 Process-based cognitive trainings

A recent meta-analysis from Hindin and Zelinski (2012) reliably showed improvements of PCTs on untrained cognitive test performance. These beneficial effects were found for different types of PCT such as visual (Wolinsky et al., 2013) and auditory processes (Zelinski et al., 2011) and higher-order process training such as task switching (Karch and Kray, 2009) and working memory training (Jaeggi et al., 2008; Klingberg et al., 2005). However, the crucial question is whether those improvements in assessed outcomes represented improvements in a broad cognitive ability or only the acquisition of task-specific skills (e.g., stimulus response mappings or strategies). There is an ongoing debate on this decisive question without consensus as of yet (see, e.g., Hulme and Melby-Lervåg, 2012; Li et al., 2008; Lövdén et al., 2013; Melby-Lervåg and Hulme, 2012; Redick et al., 2013; Schmiedek et al., 2010; Shipstead et al., 2010, 2012). In the following, we explain why this question is still open to debate despite a vast amount of studies.

Conclusively answering the ability/skill question is hindered because of methodological aspects. In the following, these aspects are shortly addressed before study results are reviewed. Next to the lack of appropriate control conditions (e.g., Schmiedek et al., 2010), outcome abilities were frequently not assessed by *multiple tests of the targeted cognitive ability* (e.g., Jaeggi et al., 2008, and see, e.g., Shipstead et al., 2012, for the same argument). Maybe the most important methodological aspect is that the *cognitive tests shared peripheral task characteristics with the training tasks* (e.g., Dahlin et al., 2008a). Thus, not only improvements in the targeted processes may have contributed to the effects but also lower-order processes not representing the broad cognitive ability (see, e.g., Shipstead et al., 2012). The similarity between training and transfer measure is rather subjective, and judgments are

FIGURE 1

Traditional cognitive intervention approaches. Novelty interventions or PCTs depict the most promising traditional cognitive interventions. Novelty interventions are challenging through difficult novel tasks, include a high variability of tasks, but target only unspecific cognitive processes, thus leading to broad transfer but only small improvements in unspecific abilities. PCT is challenging primarily through task difficulty adaptation to participants' performance, targets specific processes, but traditionally implements only a small variability of training tasks, thus leading to large effects on trained tasks but only very limited transfer on the cognitive ability level. Limitations of traditional approaches are depicted in italic and bold letters.

difficult as a thorough description of the training tasks as well as an analysis of the relation between the training and transfer tasks was often missing (e.g., [Shatil, 2013](#), and see [Lövdén et al., 2013](#), for the same argument). Finally, the *measurement of neurofunctional and neurostructural outcomes* could reveal whether the performance improvements in cognitive tests were mediated by the targeted processes. This field is still in its infancy and does not show consistent patterns which allow conclusive interpretations (see [Buschkuhl et al., 2012](#), for a review).

Several studies addressed at least some of the mentioned methodological aspects. While some results suggested cognitive ability enhancement by improvements in *multiple outcomes tapping the same cognitive ability* (Smith et al., 2009; Wolinsky et al., 2013), others did not (Borness et al., 2013; Colom et al., 2010; Li et al., 2008; Redick et al., 2013; Schneiders et al., 2011, 2012; Stephenson and Halpern, 2013; Thompson et al., 2013). A similar mixed picture arises from studies that assessed *cognitive tests substantially dissimilar to the training task*. While some studies found positive effects (Brehmer et al., 2011; Jaeggi et al., 2008, 2010; Karbach and Kray, 2009; Klingberg et al., 2002, 2005; Schweizer et al., 2011, 2013; Zhao et al., 2011), others did not (Ball et al., 2002; Barnes et al., 2013; Bergman Nutley et al., 2011; Borness et al., 2013; Brehmer et al., 2012; Buschkuehl et al., 2008; Dahlin et al., 2008b; Jaeggi et al., 2011; Li et al., 2008; Redick et al., 2013; Thompson et al., 2013).

A study by Schmiedek et al. (2010) used both *multiple tests for a single cognitive ability* and *outcomes with task characteristics substantially different to the training tasks*. The large sample size even allowed the use of latent difference score models to extract latent factors representing broad cognitive abilities. Only the lack of an active control group hindered interpretation of results. The intervention group, in contrast to a passive control group, engaged in 100 days of processing speed, episodic memory, and working memory training and showed small improvements on broad cognitive abilities such as fluid intelligence and episodic memory in younger adults. In older adults, however, improvements were only found on a latent factor, which was based on tests with a high overlap of training and test task characteristics. Improvements in latent factors, which were based on dissimilar tests, were not significant, indicating that in older adults, improvements were limited to task-specific skills (see Dahlin et al. (2008a) for similar differential age-related transfer effects). Even a more pessimistic view arises with respect to a recent working memory training study, which used *appropriate control groups*, *multiple assessments for each cognitive ability*, and *cognitive tests dissimilar to the training tasks* (Redick et al., 2013). No differential effect was found as a function of treatment group.

A strategy avoiding the earlier-mentioned methodological problems with regard to the ability/skill debate is the direct measurement of incidents of dementia. To our knowledge, only one recent study published results regarding this outcome (Unverzagt et al., 2012). In this study, which comprised more than 2,800 participants, none of the three short-term cognitive interventions (including one PCT) were able to reduce the hazard ratio (HR) for dementia during the 5 years of follow-up, compared to a passive control group (nonadjusted HR: 0.9; 95% CI: 0.65 1.24 and adjusted HR: 1.00; 95% CI: 0.71 1.40 of all interventions combined).

2.3 Conclusion

Overall, observational (e.g., Fritsch et al., 2005) and experimental studies (e.g., Klusmann et al., 2010) have shown beneficial effects of exposure to novelty on cognitive functions with only a few exceptions (e.g., Boot et al., 2013). In contrast to

PCT, the training tasks applied in novelty interventions have no obvious similarity to cognitive outcome tests, allowing a straightforward interpretation of results. However, to our knowledge, no study investigated the effect of novelty interventions on the incidence of dementia. Furthermore, novelty interventions provided rather unspecific processing demands, thus not tackling specific processes, which are particularly prone to deterioration in aging and dementia (see Fig. 1). It seems reasonable that interventions targeting these specific processes might be more effective.

PCT aims to address this issue by targeting perceptual (e.g., Mahncke et al., 2006a) and higher-order cognitive abilities such as working memory (e.g., Buschkuhl et al., 2008) or task switching (e.g., Karbach and Kray, 2009). Regarding the efficacy of PCTs, we conclude that several methodological issues leave room for different interpretations of observed effects (see also Shipstead et al., 2012). There is abundant evidence that PCTs improve task-specific skills, but most decisively, it seems that the potential for improvement exists even on the level of broad cognitive abilities (e.g., Jaeggi et al., 2010; Wolinsky et al., 2013). However, this potential seems to be exploited only to a very limited degree with current training programs, especially in older adults (see Fig. 1, Schmiedek et al., 2010, and Dahlin et al., 2008a). Therefore, new synergistic training approaches are needed, which enable both the targeting of specific processes shown to deteriorate in aging and dementia and a generalization to the level of broad cognitive abilities rather than task-specific skills.

3 RATIONALE AND EVIDENCE FOR SYNERGISTIC APPROACHES

Beneficial effects of traditional interventions such as novelty interventions and PCTs may be improved by two synergistic approaches: the combination of novelty interventions with (1) a process-based or (2) a physically demanding element. First, the process-based novelty interventions aim to overcome limited effects on broad cognitive abilities while enabling process specificity. Second, the previously discussed generalization effects of novelty interventions might be enhanced by additive or synergistic effects of an integrated physical activity component.

3.1 Process-based novelty interventions

In the following, we propose a new cognitive intervention approach, which targets specific processes while overcoming learning specificity, that is, only cognitive tests that were similar to the training tasks improved consistently (see Fig. 2). After we discuss the processes that are worth targeting to delay the onset of dementia, we point to the overarching phenomenon of learning specificity in various fields of learning. Furthermore, we present results demonstrating that high task variability counteracted this phenomenon. The differential neuronal underpinning of learning effects induced by variable and constant practice protocols will be outlined before we review how the concept of task variability is implemented in currently used PCTs. Finally, we

FIGURE 2

Process-based novelty interventions. In contrast to previous process-based approaches, the new approach targets a specific process, for example, executive control, by using a high variability of training tasks with overlapping processing demands (“overlapping variability” framework). It thus enables broad transfer on specific cognitive abilities. Strengths of this synergistic approach are depicted in bold letters.

present the “overlapping variability” framework of effective cognitive interventions and its implementation in our newly developed process-based novelty intervention using card and board games.

3.1.1 Tackling specific processes

Executive control (Park et al., 2002) on the behavioral level and the dorsolateral prefrontal cortex (dlPFC) on the neuronal level are particularly affected by the aging process (Raz et al., 2005). Next to memory impairment, decline in executive control is a core symptom of dementia. In line, synaptic integrity is affected in the frontal lobe of individuals with high AD pathology (Arnold et al., 2013). Interestingly, disrupted synapse integrity was only found in individuals suffering from dementia symptoms but not in those with resilient cognition despite high AD pathology (Arnold et al., 2013). Furthermore, increased neural density and cortical thickness in the dlPFC seem to mediate the mental activity-induced protective effect on dementia (Valenzuela et al., 2011). Those studies indicate that improving executive control and its underlying neural substrate can delay the onset of dementia even in the presence of AD pathology. We want to stress that other processes such as visual (Unverzagt et al., 2012; Willis et al., 2006; Wolinsky et al., 2013), auditory (Mahncke et al., 2006a,b; Smith et al., 2009; Zelinski et al., 2011), and memory processes (Jennings and Jacoby, 2003; Lustig and Flegal, 2008) might be additional potential targets for the prevention of dementia.

3.1.2 Overcoming learning specificity

As reviewed in the previous section, PCT not only addressed the issue of process specificity but also led to learning specificity. This indicated that improvement in an underlying ability did not or only to a limited extent occur. In line with Green and Bavelier (2012), we propose an “overlapping variability” framework (see Fig. 2) to induce changes on the cognitive ability level. According to that framework,

plastic changes can be induced in broad cognitive abilities by variable practice regimes, which overlap in the targeted processing demands while excluding overlap in demands on lower-order processes. That means that the targeted processing level on which the different tasks overlap is the one where plastic changes take place but only if all lower-order processes are varied. The framework that we outline in the following section can be applied to a wide range of processes including perceptual and motor processes.

3.1.2.1 Learning specificity as an overarching learning principle

The phenomenon of learning specificity is encountered beyond PCT. Examples range from auditory learning ([Lively et al., 1993](#)), visual learning ([Ahissar and Hochstein, 1997](#)), motor learning ([Proteau, 1992](#)), avoidance learning ([Adolph, 2000](#)), and knowledge acquisition ([Barnett and Ceci, 2002](#)). Interestingly, learning specificity is so strong that even contextual factors that normally go along with impaired cognitive performance, for example, alcohol intoxication, can improve memory performance, if learning and recall occur in the same intoxicated state ([Goodwin et al., 1969](#)): intoxicated participants who drank ~270 ml of 80-proof vodka showed better performance in recalling items in contrast to sober participants, when both had learned those in an intoxicated state. Taken together, specific task characteristics, states, and contexts in which learning occurs have a strong impact on transfer tasks (see also [Green and Bavelier, 2012](#)).

3.1.2.2 Variability of practice enhances generalization

Beginning already in the 1970s, research in motor, verbal, and perceptual learning revealed that learning specificity can be overcome by using a variable practice protocol (see [Schmidt and Bjork, 1992](#), for a review). Although variable practice, in contrast to constant practice, generally decreased the rate of training task improvements, it increased performance on transfer tasks.

Regarding perceptual learning, for example, [Lively et al. \(1993\)](#) demonstrated that Japanese listeners were able to improve in an identification task between the English consonants /r/ and /l/ presented by a single speaker. However, if an unfamiliar speaker presented the words, they performed significantly worse, indicating learning specificity for the single speaker. In another experiment, words were presented not by a single but by five different speakers during learning. Participants successfully learned to differentiate /r/ and /l/ words. Decisively, if the words were produced by yet another novel speaker, a decline in identification performance was not evident at all.

Further evidence for transfer after variable practice comes from observational studies ([Angevaeren et al., 2007](#); [Eskes et al., 2010](#)). For example, [Eskes et al. \(2010\)](#) found that a higher amount of different mental activities, but not a higher frequency of engagement in activities, was associated with better overall cognitive function. We might speculate that different mental activities have shared processing demands, which are improved by these activities and allow transfer to novel tasks.

What is the differential neuronal underpinning between these specific and generalizing effects?

3.1.2.3 Neural underpinning of variable and constant practice effects

It is logical that improvement in higher-order processes induces transfer on other tasks, while improvement in lower-order processes is very specific to the task (see psycho-anatomy logic, [Ahissar and Hochstein, 2004](#)). As variable practice leads to enhanced transfer of learning, higher-order processes should be responsible. Decades after the first findings on variable practice effects on transfer tasks ([Schmidt, 1975](#)), neural mechanisms underlying this phenomenon were revealed ([Ahissar and Hochstein, 2004](#); [Kantak et al., 2010](#)). Indeed, results suggest that plastic brain changes of variable and constant practice occur at different hierarchical processing levels. [Kantak et al. \(2010\)](#) discovered in a motor learning paradigm that retention performance after variable practice was affected by repetitive transcranial magnetic stimulation (rTMS)-induced interference in the dlPFC, but not by rTMS interference in the primary motor cortex. This indicates that effects of variable practice were attributable to higher-order processing, which are assumed to be dependent on the dlPFC. In contrast, interference in the primary motor cortex was exclusively detrimental for retention performance after constant practice, indicating reliance on lower-order processes in constant practice learning. This finding fits well with behavioral and physiological studies in the visual domain, suggesting that initial training involves high-order brain areas ([Ahissar and Hochstein, 1997, 2004](#)); with increased expertise and task difficulty, neural substrates of learning shift to lower-order areas, even including the primary visual cortex ([Schoups et al., 2001](#)).

Furthermore, we argue that investigations of the neural processing in multilingualism shed some light on the role of task-overlapping higher-order processes as a function of the variability of practice. Speech acquisition in early and late bilinguals might be regarded as a model for variable and constant training regimes, respectively. Technically speaking, early bilinguals were exposed to a variable training protocol in early childhood, while late bilinguals initially learned only a single language (constant practice protocol) before they learned the second language later in life. According to transfer and higher-order effects of variable practice, early bilinguals should create an overlapping higher-order processing system for multiple languages enabling them to integrate and learn novel languages faster. Late bilinguals should develop a network that processes language information on a lower order and should thus not be able to integrate a newly learned language. In fact, a functional magnetic resonance imaging study demonstrated that early bilinguals represented both languages in a shared, overlapping brain area ([Kim et al., 1997](#)), while in late bilinguals, the two languages were represented by adjacent but distinct areas (see also [Bloch et al., 2009](#), for further evidence supporting this notion). Furthermore, the organization of the shared network seemed to facilitate transfer to novel languages, as it was repeatedly shown that bilinguals learn a novel language faster than monolinguals (see [Cenoz, 2003](#), for a review). Taken together, variable practice with shared processing demands seems not only to induce plastic changes in

higher rather than lower processing networks but also to induce task-invariant higher-order processing capabilities. These processing networks could then be utilized also by subsequent novel tasks. On the behavioral level, this seems to be reflected by transfer effects on tasks never encountered before. On the other hand, constant or repeated practice on the same task appears to redistribute the involved processes from higher- to lower-order networks (e.g., [Kantak et al., 2010](#)), thus enabling fast learning and highly efficient processing of these tasks but without transfer to dissimilar ones ([Schmidt and Bjork, 1992](#)). What can be deduced from these studies to the training of executive control?

As mentioned earlier, we conclude that the training of a variety of tasks rather than the constant practice of a single task yielded better transfer to subsequent untrained tasks. This seems to be accompanied by higher-order processing networks able to efficiently process demands of a wide variety of tasks. With regard to executive control, we propose that training of variable tasks tapping overlapping executive control processes enhances a shared frontoparietal control network, thus leading to an improvement even in dissimilar tasks, which tap these task-invariant processing capabilities (see [Duncan, 2010](#), proposing the existence of such a common frontoparietal processing network). On the other hand, repeated practice on a single or a limited amount of executive control tasks will induce initial plastic changes in higher-order processes followed by a shift to plastic changes in increasingly lower-order processing levels. This may be reflected by fast improvements on the training task but with only very limited transfer to dissimilar tasks.

3.1.3 Variability in process-based cognitive trainings

But how is variability of practice implemented in current training programs targeting executive control processes? With regard to the phenomena of learning specificity in repeated practice of the same task, it is astonishing that current PCT studies used interventions that included only a very limited amount of task paradigms. For example, some studies used only a single task paradigm ([Jaeggi et al., 2008, 2010](#); [Schweizer et al., 2011, 2013](#)) or two task paradigms only varying in task content ([Dahlin et al., 2008b](#)). Others used three task paradigms ([Buschkuhl et al., 2008](#); [Olesen et al., 2003](#); [Schmiedek et al., 2010](#)), four task paradigms ([Brehmer et al., 2012](#); [Klingberg et al., 2005](#)), or five task paradigms ([Thorell et al., 2009](#)). Furthermore, not only the limited amount of tasks but also the similarity of them may limit generalization of effects. For example, in the study by [Thorell et al. \(2009\)](#) which found strong effects on near-transfer outcomes with mixed effects and generally smaller effect sizes on far-transfer measures the training program focused on visuospatial working memory trained with five different exercises. However, for all exercises, stimuli were presented with constant presentation times and interstimulus intervals and the participant had to accomplish the same general task, namely, to remember location and order of the stimuli.

Two studies mentioned explicitly to have used variable tasks to increase generalization of the effects ([Dahlin et al., 2008a](#); [Karchach and Kray, 2009](#)). [Karchach and Kray \(2009\)](#) even manipulated variability systematically. Conditions included a

task-switching training with and without task variability. However, [Karch and Kray \(2009\)](#) did not induce variability by novel task-switching paradigms but by novel dimensions between which participants had to switch. That is, the constant task-switching group had to switch only between the dimensions “transportation” and “number,” while the variable training group also needed to switch between several additional dimensions such as “plant” and “color” or “animal” and “direction.” The variable training group outperformed the nonvariable conditions in the near-transfer outcome. In this outcome test, exactly the same task as during the training sessions was administered but with novel, untrained switching dimensions. There was no differential group effect between the variable and constant task-switching conditions in far-transfer measures of intelligence, working memory, or interference. We assume that variability of task paradigms rather than of stimulus dimensions is decisive for far transfer. A rule of thumb may be that the variation level must be equal to the transfer level. For example, varying speakers in an identification task may induce transfer on new speakers in this identification task. Varying stimuli dimensions in a task paradigm may induce transfer on new stimuli dimensions in this paradigm. That means that a variation in task paradigms within a specific ability is needed to induce a “farer” transfer on a new paradigm within this specific ability.

A study by [Dahlin et al. \(2008a\)](#) supports this idea: their 5-week training intervention (45 min, three sessions/week) consisted of a single running span paradigm with five different kinds of stimuli and a keep-track task. A numerical n-back task and a Stroop task were assessed as a near- and far-transfer measure, respectively. fMRI served to investigate neuroplastic changes mediating transfer effects. Despite the fact that the Stroop and the training task activated a shared frontoparietal network at the baseline assessment, no transfer effect was found. Only the similar near-transfer n-back task improved as a function of training group. Strikingly, this near-transfer effect was only evident in young adults, while no improvement was found in older adults. As a number running span task was part of the training, the training and the near-transfer task were identical regarding the kind of stimuli used and differed slightly only by the response format (recalling the last four numbers as soon as the presentation list ended vs. indicating whether each presented item matched an item that appeared three items back). The similarity of training and near-transfer task and the absence of transfer effects to the far-transfer Stroop task suggest that plastic brain changes occurred at a lower-order level only. Indeed, pre-post changes in the fMRI revealed a pattern of activation redistribution from higher- to lower-order brain areas during the training task: while the activation in striatal, temporal, and occipital areas increased, frontal and parietal activation decreased. The striatal activation also increased during the near-transfer n-back task and was interpreted as the mediating area for the transfer effect. Those results allow different interpretations, but clearly, the higher-order frontoparietal network did not mediate the near-transfer effects.

Taken together, the variation of stimulus dimensions improved performance on the near-transfer but not the far-transfer outcome measures, indicating some generalization effect, however only on that level where variation took place. This interpretation is in line with the shift from higher- to lower-order processing in a

training task after 5 weeks of a repeated practice protocol (see [Buschkuehl et al., 2012](#), for a comprehensive review of training-induced neuronal effects).

In conclusion, repeated practice of a single task leads to a shift from higher-order to lower-order processing (see [Ahissar and Hochstein, 2004](#), concluding the same in the perceptual domain), whereas generalization seems to be promoted by high task variability (see [Schmidt and Bjork, 1992](#), concluding the same for motor and verbal learning). On that background, it seems surprising that previous training programs aiming to improve working memory, shifting, or inhibition applied only a very limited amount of tasks, which shared most task characteristics. We suggest that enhancing variability of training tasks (not only of stimuli material but also of task paradigms) while targeting specific executive control processes enhances generalization on the cognitive ability level (see [Fig. 2](#)).

3.1.4 “Overlapping variability” framework

Process-based novelty interventions implement three components necessary to induce far-transfer effects on broad cognitive abilities (see [Fig. 2](#)). According to the framework by [Lövdén et al. \(2010\)](#), a prolonged mismatch between functional supply and environmental demands is a prerequisite to induce plastic change. This component is part of almost all PCTs. In contrast to the common procedure to induce challenge by difficulty adaptation in repeated tasks, we suggest to use primarily novel tasks of appropriate difficulty to achieve this aim. This method enables the application of the “overlapping variability” framework, which comprises the other two training components of this approach: First, high task variability represents a prerequisite for generalization and improvements on the ability level (see also [Green and Bavelier, 2012](#)). This component is usually not found in current PCTs, but implemented in novelty interventions. Second, specific processes should be targeted based on knowledge regarding their neuronal basis and their age- and dementia-related changes. Novelty interventions are currently not emphasizing this component, in contrast to PCTs. Hence, the combination of variable tasks with a targeted approach, which makes use of overlapping processing demands of superficially dissimilar tasks, is the main difference of this new approach from traditional PCTs and novelty interventions (see [Figs. 1 and 2](#)). We want to stress that the “overlapping variability” framework contrasts with multidomain trainings (see, e.g., [Cheng et al., 2012](#)) as in process-based novelty interventions, only a common processing demand is targeted and not several independent processes such as episodic memory, reasoning, and visuospatial ability. Though we focused on executive control processes, this framework can be applied to several other ones ranging from perceptual to motor and language processes.

3.1.5 Nourishing intrinsic motivation

As detailed earlier, challenge and task variability seem to be two decisive factors for healthy brain development and prevention of dementia. Exposure to novelty inherently goes along with both. Interestingly, the same concepts are a key point in [Ryan and Deci’s \(2000: p. 70\)](#) definition of one of the most influential concepts in psychology: intrinsic motivation “the inherent tendency to seek out novelty

and challenges, to extend and exercise one's capacities, to explore, and to learn [...]. From the time of birth, children, in their healthiest states, are active, inquisitive, curious, and playful." From an evolutionary perspective, there should be an unconditional predisposition to strive for factors that increase fitness. Moreover, [Ryan and Deci \(2000\)](#) not only stressed the natural tendency of humans to strive for challenge and variability but also proposed its value for cognitive development and psychological well-being.

Therefore, novelty interventions seem to fit well to nourish intrinsic motivation by providing an environment which comprises the basic ingredients to elicit feelings of interest and curiosity. In which way is intrinsic motivation functional for interventions? First, intrinsic motivation determines the environment people choose (guiding function), allowing long-term adherence to interventions. Second, the motivation-associated psychological states such as interest and curiosity have been shown to go hand in hand with the activation of the neuromodulatory control system – a central regulatory system for the facilitation of plastic brain changes (plasticity facilitation function; see, e.g., [Bao et al., 2001](#), for the role of dopamine). For example, it has been shown that curiosity is associated with activation of caudate regions, which are innervated by dopaminergic neurons and part of the neuromodulatory control system. Curiosity during learning was associated with improved recall one to two weeks later, indicating its plasticity facilitating effect ([Kang et al., 2009](#)).

3.1.6 Implementation in a novel game-based intervention: Results from a pilot study

This novel intervention aimed to implement the “overlapping variability” framework, which was embedded in a socially meaningful context. We used card and board games as the vehicle for the development of variable and challenging tasks while tapping shared executive control processes based on the unity/diversity framework of [Miyake et al. \(2000\)](#).

After thorough cognitive task analyses, we included a total of 15 games including self-developed and off-the-shelf games tapping all components of executive control. While some games stressed a single executive control component, others involved all components to a similar degree. We selected games with a minimal amount of rules, allowing for a quick start of the game and restricting the amount of strategies which can be used to accomplish the task. For optimally nourishing intrinsic motivation, not only challenge and novelty were provided but also a socially meaningful context, which allows the fulfillment of the need for relatedness ([Ryan and Deci, 2000](#)).

In a single-blinded randomized controlled pilot study, we tested this intervention to enhance cognitive functions in community-dwelling older adults. Participants ($N=17$) were randomized to a gaming group ($n=9$; 7 females; mean age = 70.4) and a control group ($n=8$; 6 females; mean age = 69.8). The groups did not differ significantly in age, gender, or years of higher education, $ps > 0.80$. The 5-week training protocol (three times per week) emphasized variability of practice by playing three games in every 2 h training session. In every other session, two already-introduced games (~30 min each) and one game never played before (~1 h) were

applied. That means every game was played not more than three times and 2 h in total. Overall, participants completed 30 training hours within 15 sessions.

Outcome measures were selected on the basis of the methodological prerequisites for the assessment of broad abilities rather than task-specific skills (see Section 2.2). Aiming to assess multiple measures of executive control dissimilar to the training tasks, three computerized tests assessing inhibition (flanker task, Stahl et al., 2013), switching (Stahl et al., 2013), and updating (Oberauer et al., 2000) were applied. Additionally, two complex executive control tests, namely, the Standard Progressive Matrices (Raven et al., 1990) and the Culture Fair Test 20-R (Weiß, 2006), were used. The primary outcome operationalizing executive control was calculated by averaging the standardized single-test scores. Despite the small sample size, linear mixed effect modeling revealed a marginally significant Group $\times$ Session interaction effect, $F(1,15)=4.39$, $p=0.054$, net effect size, 0.53 SD (see Fig. 3), indicating performance improvement in the intervention group compared to the passive control group. While the gaming group improved performance in executive control (0.46 SD, $p=0.04$), performance in the passive control group did not change (-0.06 SD; $p=0.70$). The use of a passive rather than an active control group limits the interpretation of effects. Nevertheless, a marginally significant improvement of the gaming group, in contrast to the control group, in a broad measure of executive control composed of tests dissimilar to the training tasks was revealed. The result indicates improvement in executive control, that is, a broad cognitive ability, overcoming often observed learning specificity.

FIGURE 3

Intervention effect. Change of executive control (standardized) from pre- to posttraining as a function of intervention group in a pilot study of a process-based novelty intervention using card and board games. While the waiting-list control group (dark triangles) remained stable, the intervention group (white squares) significantly improved, resulting in a marginally significant group $\times$ time interaction. Arrows represent standard errors. Statistically significant effects are marked by asterisks: * $p < 0.05$.

3.2 Physically demanding novelty interventions

In the following, we present a rationale for the combination of novelty interventions with a physical activity component, which is based on two arguments: First, the combination might induce multimechanistic effects appropriate for a multicausal disease such as dementia. Second, both components may interact in a way that we term “guided plasticity facilitation”. Thus, this extended novelty interventions might induce additive or synergistic effects by the integration of a physical activity component.

3.2.1 Tackling multiple mechanisms

Dementia is a multicausal disease (see [Olde Rikkert et al., 2006](#), for a review). For optimal prevention, it is plausible to tackle different pathological mechanisms by multiple approaches ([Gillette-Guyonnet et al., 2009](#)). Physical and cognitive activities have shown differential effects on disease progression in animal models (e.g., [Wolf et al., 2006](#)). Furthermore, these multiple pathogenic mechanisms and, hence, the preventive interventions may be dependent upon person-specific characteristics. Indeed, there is evidence that cognitive effects of physical, social, or cognitive activity interact with such characteristics, including genetic polymorphisms such as APOE genotype ([Head et al., 2012](#); [Luck et al., 2013](#); [Niti et al., 2008](#)), brain-derived neurotrophic factor (BDNF) Val66Met polymorphism ([Erickson et al., 2013](#); [Kim et al., 2011](#)) and dopamine-related genes ([Bellander et al., 2011](#); [Brehmer et al., 2009](#); [Pieramico et al., 2012](#)) as well as baseline levels of growth factors such as VEGF ([Voss et al., 2013](#)), gender (see, e.g., [Baker et al., 2010](#); [Kåreholt et al., 2011](#)), or personality traits such as neuroticism ([Wang et al., 2009](#)). If, for example, one population profits most from physical activity due to a certain BDNF polymorphism ([Erickson et al., 2013](#); [Kim et al., 2011](#)), APOE genotype ([Head et al., 2012](#); [Luck et al., 2013](#); [Niti et al., 2008](#)), or gender ([Baker et al., 2010](#); [Kåreholt et al., 2011](#)), a second population profits most from social activity due to personality traits (see [Wang et al., 2009](#)) or gender ([Wang et al., 2013](#)) and a third population benefits most from cognitive activity due to dopamine-related polymorphisms ([Bellander et al., 2011](#); [Brehmer et al., 2009](#)), the averaged effect across all populations would be best in a combined intervention of all the three types of activity. Such a combination of activity types is given in certain leisure activities such as dancing or Tai Chi.

3.2.2 Guided plasticity facilitation

In addition to addressing various potential mechanisms by a combination of physical and cognitive activity, there is increasing evidence that the combination of both exercise types may have synergistic effects (see [Kraft, 2012](#), for a review). While physical exercise may “facilitate plasticity,” cognitive activity may “guide” the plastic changes (see [Fig. 4](#)). Exercise-induced plasticity facilitation was shown by enhanced precursor cell proliferation in the hippocampus ([Fabel et al., 2009](#)) and increased synaptic plasticity such as long-term potentiation ([Van Praag et al., 1999](#)). BDNF

FIGURE 4

Guided plasticity facilitation framework.

seems to be one potential mediator of plasticity facilitation effects of exercise as exercise induces BDNF production (e.g., [Neeper et al., 1995](#); [Rasmussen et al., 2009](#)). BDNF, in turn, is known for its potential to increase synaptic transmission, synaptic plasticity, and synaptic growth (see [Lu et al., 2013](#), for a recent review). Indeed, the learning and memory-enhancing effects of exercise were shown to disappear after blockage of the BDNF-binding receptor TrkB ([Vaynman et al., 2004](#)).

Cognitive activity, on the other hand, may “guide” this facilitated plastic potential by (1) a survival-promoting effect on exercise-induced newborn cells ([Fabel et al., 2009](#)) and (2) the regulation of synaptic change by time-dependent neural activity (see [Hebb, 1949](#)). For example, [Trachtenberg et al. \(2002\)](#) demonstrated experience-dependent synaptic plasticity. Experience-induced neural activity seems to guide elimination and formation of synapses. Neurofunctional plastic changes were induced after PCT (see [Buschkuehl et al., 2012](#), for a review), which may be partly attributable to the experience-dependent synaptic turnover. Cognitive activity-induced plasticity was shown on not only the neurofunctional (see also [Elbert et al., 1995](#)) but also the neurostructural level (see, e.g., [Draganski et al., 2004, 2006](#); [Maguire et al., 2000](#); [Takeuchi et al., 2011](#); [Woollett and Maguire, 2011](#)). Overall, cognitive activity has consistently revealed plasticity-inducing effects by synaptic change and neurofunctional and neurostructural change.

[Kempermann et al. \(2010\)](#) argued that these “guiding” and “facilitation” effects of cognitive and physical activity would be beneficial from an evolutionary point of view given the frequent coincidence of the necessity for learning and physical activity. For example, acquisition of new spatial representations is inherently bound to physical activity (disregarding video gaming).

Not only plasticity but also stability of the central nervous system is crucial for its function ([Koleske, 2013](#)). It thus seems apparent that effects of physical activity on plasticity facilitation would be dysfunctional if they were not restricted to a certain time frame. In line with this notion, studies repeatedly reported an increase of peripheral BDNF during and within one hour after an acute bout of physical exercise followed by a reduction below baseline, indicating increased BDNF production and utilization after exercise (see [Knaepen et al., 2010](#), for a review). Therefore, facilitation of plastic mechanisms, for example, mediated by BDNF, might be most pronounced during or right after physical exercise. Indeed, [Winter et al. \(2007\)](#) demonstrated in humans that verbal learning and memory were improved after an acute bout of physical exercise, compared to a period of rest. Performance parameters of learning and memory were associated with peripheral BDNF and various

catecholamine levels supporting their effect-mediating role. In line with this result, [Roig et al. \(2012\)](#) found that an acute bout of 20 min intense cycling immediately before and after a motor task, compared with a period of rest, improved retention of a learned motor skill 24 h and 7 days after practice. Interestingly, the effect of an acute bout of exercise after the motor task, in contrast to before practice, had even larger effect on retention 7 days after motor practice. Taken together, the timing of physical activity in relation to cognitive activity seems to be crucial in the “guided plasticity facilitation” framework (see [Fig. 4](#)).

3.2.3 Evidence

There is a growing evidence from observational studies indicating that engaging in a number of different types of activities ranging from cognitive to physical and social activities is able to reduce cognitive decline ([Chan et al., 2005](#); [Lee et al., 2009](#); [Wang et al., 2013](#)) or dementia incidence ([Karp et al., 2006](#); [Paillard-Borg et al., 2009](#); [Verghese et al., 2003](#); [Wang et al., 2002](#)). Interestingly, beneficial effects of leisure activity types on cognition follow a dose response relationship ([Wang et al., 2013](#)). For example, cognition declined over a 2-year period in participants engaged in low levels in all three activity types, while cognition was stable in participants who engaged in high levels in one activity type, and engagement in multiple activities even predicted cognitive improvement. In this, the different types of activities had differential effects on several cognitive domains. This result supports the rationale that multidomain interventions induce multimechanistic effects; thus, they may be best suited to address a multicausal disease. [Karp et al. \(2006\)](#) demonstrated that even dementia risk could be reduced by engaging in physical, social, or cognitive leisure activities and that the strongest effect was present in individuals who engaged in more than one type of activity. A dose response pattern of the number of different activity types including physical, cognitive, and social activity for dementia risk was also found in a study by [Paillard-Borg et al. \(2009\)](#): high engagement in no or only one type of activity served as the reference group. High engagement in two types of activities reduced the risk by 34%, and high engagement in all three types of activities reduced the risk even by 49%. The combination of multiple lifestyle activities is decisive for prevention of cognitive decline and dementia and should be further investigated (see also [Lee et al., 2009](#)). One leisure activity that is a good model for an integrative physical, cognitive, social, and emotional approach is dancing. In an observational study, [Kattenstroth et al. \(2010\)](#) demonstrated that long-time amateur dancers outperformed age-, education-, and gender-matched controls in reaction times, motor behavior, and cognitive performance, exhibiting the potential of this challenging, multicomponent activity.

However, as mentioned earlier, observational studies cannot exclude other interpretations of effects. So what does experimental evidence tell us about the effectiveness of a combined physical and cognitive approach?

Several interventional studies investigated the effect of combined physical and cognitive interventions on cognition ([Barnes et al., 2013](#); [Fabre et al., 2002](#); [Legault et al., 2011](#); [Oswald et al., 2006](#); [Shatil, 2013](#)). Apart from the first two studies,

which showed better effects of the combined approach (Fabre et al., 2002; Oswald et al., 2006), the more recent studies could not show additional or synergistic effects of the combination of both interventions (Barnes et al., 2013; Legault et al., 2011; Shatil, 2013). Those studies investigated the effect of combined interventions, but each component was separated in time from each other. As depicted in the rationale for the guided plasticity facilitation framework, simultaneous cognitive and physical activities might be crucial for interaction effects, explaining the negative findings.

Physically demanding novelty interventions provide simultaneous cognitive and physical activity (see Fig. 5). Indeed, there are several interventional studies which found beneficial effects on cognition for such a multimodal approach. For example, consistent and large improvements in cognitive outcomes were found in older adults allocated to a dancing intervention (Kattenstroth, Kalisch, Holt, Tegenthoff, and Dinse, 2013), mind body exercises like Tai Chi (Mortimer et al., 2012), theater play (Noice and Noice, 2009; Noice et al., 2004), or “exergaming” (Anderson-Hanley et al., 2012; Maillot et al., 2012), that is, physical exercise carried out in a mentally stimulating and motivating virtual reality environment. Mixed results, showing improvements in some cognitive tests but not others, were found by Pieramico et al. (2012) for a 1-year multimodal training program consisting of various activities and by Coubard et al. (2011) for a dancing intervention.

After a 6-month dancing intervention, elderly adults significantly improved in cognitive outcomes, such as attention and memory functions, compared to participants of an inactive control group (Kattenstroth, Kalisch, Holt, Tegenthoff, and Dinse, 2013). Noice et al. (2004) compared the outcome of a 7-session theater course for healthy older adults not only to the one of an inactive control group but also to an active visual arts control group. The mentally and physically challenging theater course resulted in an enhancement in problem solving compared to both control groups and an improvement in episodic memory when compared to the inactive

FIGURE 5

Physically demanding novelty interventions. Dancing, Tai Chi, cybercycling, and theater arts depict examples of this combined physical cognitive approach. In contrast to traditional novelty interventions, they include physical demands in addition to highly variable, novel tasks and thus enhance the transfer to unspecific cognitive based abilities.

control group. Similar effects were found for the same intervention with older adults in retirement homes (Noice and Noice, 2009). Compared to physical training only, greater improvements were yielded by cybercycling, that is, cycling within a mentally challenging virtual reality environment (Anderson-Hanley et al., 2012), and by Tai Chi (Mortimer et al., 2012).

Finally, there is even initial experimental evidence that long-term Tai Chi training decreases the incidence of dementia, evaluated with the Clinical Dementia Rating (Lam et al., 2011, 2012). However, this study had some limitations with respect to dropout rates, operationalization of dementia incidence, and baseline differences between groups. Therefore, caution is necessary in the interpretation of results.

To sum up, the evidence for physically demanding novelty interventions such as dancing, Tai Chi, theater play, or exergaming is promising. To elucidate whether the combination of activities is decisive, further research is needed comparing physically demanding novelty interventions with pure physical and novelty interventions. Also, more research investigating the potential for dementia prevention must follow.

4 CONCLUSIONS

Observational and experimental studies suggest that novelty interventions are effective behavioral means to delay cognitive decline (e.g., Eskes et al., 2010; Klusmann et al., 2010) and the onset of dementia (e.g., Fritsch et al., 2005). However, this approach is rather unspecific, that is, it does not tackle specific processes shown to deteriorate in aging and dementia (see Fig. 1). PCT addresses this problem and has shown transfer effects on untrained cognitive tests. Crucially, however, consistent effects were only shown for cognitive tests sharing superficial training task characteristics, suggesting learning specificity with only limited transfer to broad cognitive abilities (see Fig. 1, e.g., Redick et al., 2013; Barnes et al., 2013). Based on a growing literature on biological and behavioral effects of variable practice, in contrast to constant practice, we propose in line with Green and Bavelier (2012) that low task variability of currently available PCTs is partly responsible for limited transfer (compare Figs. 1 and 2). A process-based novelty intervention, using variable card and board games in a socially meaningful context, addressed this issue and showed initial evidence for an enhancement in the broad cognitive ability of executive control (see Fig. 3). Furthermore, rather small transfer effects of novelty interventions might be enhanced by engaging in novel challenging mental activities which also comprise physical demands such as dancing or Tai Chi (see Fig. 5). A mechanism of action of this multimodal approach may be guided plasticity facilitation (see Fig. 4).

With respect to current evidence, we suggest four principles that behavioral interventions for the prevention of dementia should implement:

- **Challenge:** The training tasks should induce a mismatch of supply and demand (see Lövdén et al., 2010).
- **“Overlapping variability”:** The training tasks should have a high task variability but a low variability in targeted processes. In other words, tasks should overlap in

the targeted processing demands while relying on a diverse set of nontargeted lower-order processing demands (see Fig. 2 and Green and Bavelier, 2012).

- Multimodality: The training tasks should implement cognitive and physical demands (see, e.g., Kempermann et al., 2010; Kraft, 2012) in temporal proximity (see Roig et al., 2012).
- Meaningfulness: The training tasks and setting should provide elements that match the human tendency to seek for novelty while fulfilling basic needs of autonomy, relatedness, and competence (Ryan and Deci, 2000). Thus, an engaging and personally meaningful environment necessary for long-term adherence should be provided (see, e.g., Carlson et al., 2008; Park et al., 2007; Lautenschlager and Cox, 2013).

Novelty interventions are specifically powerful with regard to these four principles as they induce a mismatch of supply and demand, go along with high variability, and provoke interest and curiosity, that is, nourish intrinsic motivation (see Fig. 1). For even more beneficial effects, this approach may be implemented in a process-based or a physically demanding approach (see Figs. 2 and 5).

According to a recent National Institute of Health consensus and state-of-the-science statement prepared by independent panels of public representatives and health professionals, no intervention can be recommended to delay dementia, as “the evidence is inadequate to conclude that any are effective” (Daviglus et al., 2010, p. 12). We propose that no single type of activity such as cognitive or physical activity should be considered as a prevention technique. The focus should rather lie on a style of activity engagement, a composition of activities, or underlying effective factors such as novelty, variability, process overlap, and challenge. This is crucial as activities interact to produce their beneficial effects, which is clearly demonstrated by variable and constant practice protocols. Therefore, we propose that recommendations for single-activity types are inherently flawed. We come to an alternate conclusion for dementia prevention in recommending a lifestyle composed of both physical demands and novel challenging mental activities integrated in a socially meaningful context. This conclusion is based on the earlier-mentioned findings of novelty interventions and on the ratio of their potential costs and benefits: (1) potential emotional and financial benefits through dementia prevention are high on both a personal and a societal level, and (2) costs for engagement in such activities are with exceptions rather low.

For future interventional studies, we suggest that they should assess the most important outcome of interventions, which is the incidence of dementia. To accomplish this aim with clinically meaningful results, we are convinced that long-term intervention with high adherence is key (see Unverzagt et al., 2012). Therefore, interventions should be personally meaningful to participants (see, e.g., Carlson et al., 2008; Lautenschlager and Cox, 2013) while nourishing intrinsic motivation. Thus, in the coming years, structured programs for the prevention of dementia might be experimentally validated allowing for widespread public recommendations and implementation in the health-care system (see Dehnel, 2013).

Acknowledgments

We thank Lisa Dommes for her ideas and her engagement in the development of the game based novelty intervention; Julia Günzer, Manuela Rappel, and Sarah Köhler for their contribution in the organization and execution of the earlier mentioned game based pilot study; Andreas Fritz, Johannes Moog, Alexandra König, Friedrich Meixner, Ferdinand Pittino, and Tanja Dolpp for administering the training sessions; Dana Fischer, Julia Berger, and Susan Leutloff for their contributions in data collection and data analysis; Lisa Gabriel, Isabell Ehrmann, Anna Gässler, Christa Selig, and Julia Fischerkeller for selecting the outcome tests and administering the test sessions; and Florian Schmitz for providing expert advice regarding the assessment of executive control and for providing the computerized inhibition and switching tasks. We also thank Steven Jaeger for proofreading and Laura Loy for her ideas and helpful comments on the chapter.

References

- Adolph, K.E., 2000. Specificity of learning: why infants fall over a veritable cliff. *Psychol. Sci.* 11, 290–295.
- Ahissar, M., Hochstein, S., 1997. Task difficulty and the specificity of perceptual learning. *Nature* 387, 401–406.
- Ahissar, M., Hochstein, S., 2004. The reverse hierarchy theory of visual perceptual learning. *Trends Cogn. Sci.* 8, 457–464.
- Anderson Hanley, C., Arciero, P.J., Brickman, A.M., Nimon, J.P., Okuma, N., Westen, S.C., Merz, M.E., Pence, B.D., Woods, J.A., Kramer, A.F., Zimmerman, E.A., 2012. Exergaming and older adult cognition: A cluster randomized clinical trial. *Am. J. Prev. Med.* 42, 109–119.
- Anglevarren, M., Vanhees, L., Wendel Vos, W., Verhaar, H., Aufdemkampe, G., Aleman, A., Verschuren, W., 2007. Intensity, but not duration, of physical activities is related to cognitive function. *Eur. J. Cardiovasc. Prev. Rehabil.* 14, 825–830.
- Arnold, S.E., Louneva, N., Cao, K., Wang, L. S., Han, L. Y., Wolk, D.A., Negash, S., Leurgans, S.E., Schneider, J.A., Buchman, A.S., 2013. Cellular, synaptic, and biochemical features of resilient cognition in Alzheimer's disease. *Neurobiol. Aging* 34, 157–168.
- Baker, L., Frank, L., Foster Schubert, K., Green, P., Wilkinson, C., McTiernan, A., Plymate, S., Fishel, M., Watson, G., Cholerton, B., 2010. Effects of aerobic exercise on mild cognitive impairment: A controlled trial. *Arch. Neurol.* 67, 71–79.
- Ball, K., Berch, D., Helmers, K., Jobe, J., Leveck, M., Marsiske, M., Morris, J., Rebok, G., Smith, D., Tennstedt, S., 2002. Effects of cognitive training interventions with older adults: a randomized controlled trial. *JAMA* 288, 2271–2281.
- Bao, S., Chan, V.T., Merzenich, M.M., 2001. Cortical remodelling induced by activity of ventral tegmental dopamine neurons. *Nature* 412, 79–83.
- Barnes, D.E., Santos Modesitt, W., Poelke, G., Kramer, A.F., Castro, C., Middleton, L.E., Yaffe, K., 2013. The Mental Activity and eXercise (MAX) Trial: a randomized controlled trial to enhance cognitive function in older adults. *JAMA Intern. Med.* 173, 797–804.
- Barnett, S.M., Ceci, S.J., 2002. When and where do we apply what we learn?: A taxonomy for far transfer. *Psychol. Bull.* 128, 612–637.
- Basak, C., Boot, W.R., Voss, M.W., Kramer, A.F., 2008. Can training in a real time strategy video game attenuate cognitive decline in older adults? *Psychol. Aging* 23, 765–777.

- Bellander, M., Brehmer, Y., Westerberg, H., Karlsson, S., Fürth, D., Bergman, O., Eriksson, E., Bäckman, L., 2011. Preliminary evidence that allelic variation in the LMX1A gene influences training related working memory improvement. *Neuropsychologia* 49, 1938–1942.
- Bergman Nutley, S., Söderqvist, S., Bryde, S., Thorell, L.B., Humphreys, K., Klingberg, T., 2011. Gains in fluid intelligence after training non verbal reasoning in 4 year old children: A controlled, randomized study. *Dev. Sci.* 14, 591–601.
- Bialystok, E., Craik, F.I., Freedman, M., 2007. Bilingualism as a protection against the onset of symptoms of dementia. *Neuropsychologia* 45, 459–464.
- Bloch, C., Kaiser, A., Kuenzli, E., Zappatore, D., Haller, S., Franceschini, R., Luedi, G., Radue, E. W., Nitsch, C., 2009. The age of second language acquisition determines the variability in activation elicited by narration in three languages in Broca's and Wernicke's area. *Neuropsychologia* 47, 625–633.
- Boot, W.R., Kramer, A.F., Simons, D.J., Fabiani, M., Gratton, G., 2008. The effects of video game playing on attention, memory, and executive control. *Acta Psychol.* 129, 387–398.
- Boot, W.R., Champion, M., Blakely, D.P., Wright, T., Souders, D.J., Charness, N., 2013. Video games as a means to reduce age related cognitive decline: attitudes, compliance, and effectiveness. *Front. Psychol.* 4, 1–9.
- Borness, C., Proudfoot, J., Crawford, J., Valenzuela, M., 2013. Putting brain training to the test in the workplace: A randomized, blinded, multisite, active controlled trial. *PLoS ONE* 8, e59982.
- Brehmer, Y., Westerberg, H., Bellander, M., Fürth, D., Karlsson, S., Bäckman, L., 2009. Working memory plasticity modulated by dopamine transporter genotype. *Neurosci. Lett.* 467, 117–120.
- Brehmer, Y., Rieckmann, A., Bellander, M., Westerberg, H., Fischer, H., Bäckman, L., 2011. Neural correlates of training related working memory gains in old age. *Neuroimage* 58, 1110–1120.
- Brehmer, Y., Westerberg, H., Bäckman, L., 2012. Working memory training in younger and older adults: training gains, transfer, and maintenance. *Front. Hum. Neurosci.* 6, 1–7.
- Bugos, J., Perlstein, W., McCrae, C., Brophy, T., Bedenbaugh, P., 2007. Individualized piano instruction enhances executive functioning and working memory in older adults. *Aging Ment. Health* 11, 464–471.
- Buschkuhl, M., Jaeggi, S.M., Hutchison, S., Perrig Chiello, P., Däpp, C., Müller, M., Breil, F., Hoppeler, H., Perrig, W.J., 2008. Impact of working memory training on memory performance in old old adults. *Psychol. Aging* 23, 743–753.
- Buschkuhl, M., Jaeggi, S.M., Jonides, J., 2012. Neuronal effects following working memory training. *Dev. Cogn. Neurosci.* 1, 167–179, Supplement.
- Carlson, M., Saczynski, J., Rebok, G., Seeman, T., Glass, T., McGill, S., Tielsch, J., Frick, K., Hill, J., Fried, L., 2008. Exploring the effects of an “everyday” activity program on executive function and memory in older adults: Experience Corps®. *The Gerontologist* 48, 793–801.
- Cenoz, J., 2003. The additive effect of bilingualism on third language acquisition: A review. *Int. J. Biling.* 7, 71–87.
- Chan, A.S., Ho, Y. C., Cheung, M. C., Albert, M.S., Chiu, H.F.K., Lam, L.C.W., 2005. Association between mind body and cardiovascular exercises and memory in older adults. *J. Am. Geriatr. Soc.* 53, 1754–1760.

- Cheng, Y., Wu, W., Feng, W., Wang, J., Chen, Y., Shen, Y., Li, Q., Zhang, X., Li, C., 2012. The effects of multi domain versus single domain cognitive training in non demented older people: a randomized controlled trial. *BMC Med.* 10, 1–30.
- Cheng, S. T., Chow, P.K., Song, Y. Q., Yu, E., Chan, A., Lee, T., Lam, J.H., 2013. Mental and physical activities delay cognitive decline in older persons with dementia. *Am. J. Geriatr. Psychiatry* 10, 1–13.
- Colom, R., Quiroga, M.Á., Shih, P.C., Martínez, K., Burgaleta, M., Martínez Molina, A., Román, F.J., Requena, L., Ramírez, I., 2010. Improvement in working memory is not related to increased intelligence scores. *Intelligence* 38, 497–505.
- Coubard, O.A., Duretz, S., Lefebvre, V., Lapalus, P., Ferrufino, L., 2011. Practice of contemporary dance improves cognitive flexibility in aging. *Front. Aging Neurosci.* 3, 1–12.
- Craik, F.I., Bialystok, E., Freedman, M., 2010. Delaying the onset of Alzheimer disease: Bilingualism as a form of cognitive reserve. *Neurology* 75, 1726–1729.
- Dahlin, E., Neely, A.S., Larsson, A., Backman, L., Nyberg, L., 2008a. Transfer of learning after updating training mediated by the striatum. *Science* 320, 1510–1512.
- Dahlin, E., Nyberg, L., Bäckman, L., Neely, A.S., 2008b. Plasticity of executive functioning in young and older adults: Immediate training gains, transfer, and long term maintenance. *Psychol. Aging* 23, 720–730.
- Daviglus, M.L., Plassman, B.L., Pirzada, A., Bell, C.C., Bowen, P.E., Burke, J.R., Connolly Jr., E.S., Dunbar Jacob, J.M., Granieri, E.C., McGarry, K., 2011. Risk factors and preventive interventions for Alzheimer disease: State of the science. *Arch. Neurol.* 68, 1185–1190.
- Daviglus, M.L., Bell, C.C., Berrettini, W., Bowen, P.E., Connolly, E.S., Cox, N.J., Dunbar Jacob, J.M., Granieri, E.C., Hunt, G., McGarry, K., Patel, D., Potosky, A.L., Sanders Bush, E., Silberberg, D., Trevisan, M., 2010. National Institutes of Health State of the Science conference statement: preventing alzheimer's disease and cognitive decline. *NIH Consens. State Sci. Statements* 27, 1–30.
- Dehnell, T., 2013. The European Dementia Prevention Initiative. *Lancet Neurol.* 12, 227–228.
- Draganski, B., Gaser, C., Busch, V., Schuierer, G., Bogdahn, U., May, A., 2004. Neuroplasticity: changes in grey matter induced by training. *Nature* 427, 311–312.
- Draganski, B., Gaser, C., Kempermann, G., Kuhn, H.G., Winkler, J., Buchel, C., May, A., 2006. Temporal and spatial dynamics of brain structure changes during extensive learning. *J. Neurosci.* 26, 6314–6317.
- Duncan, J., 2010. The multiple demand (MD) system of the primate brain: mental programs for intelligent behaviour. *Trends Cogn. Sci.* 14, 172–179.
- Elbert, T., Pantev, C., Wienbruch, C., Rockstroh, B., Taub, E., 1995. Increased cortical representation of the fingers of the left hand in string players. *Science* 270, 305–307.
- Erickson, K.I., Banducci, S.E., Weinstein, A.M., MacDonald, A.W., Ferrell, R.E., Halder, I., Flory, J.D., Manuck, S.B., 2013. The brain derived neurotrophic factor Val66Met polymorphism moderates an effect of physical activity on working memory performance. *Psychol. Sci.* 24, 1770–1779.
- Eriksson Sörman, D., Sundström, A., Rönnlund, M., Adolfsson, R., Nilsson, L. G., 2013. Leisure activity in old age and risk of dementia: A 15 year prospective study. *J. Gerontol. Ser. B Psychol. Sci. Soc. Sci.* 68, 1–9.
- Eskes, G., Longman, S., Brown, A., McMorris, C., Langdon, K., Hogan, D., Poulin, M., 2010. Contribution of physical fitness, cerebrovascular reserve and cognitive stimulation to cognitive function in post menopausal women. *Front. Aging Neurosci.* 2, 1–7.

- Fabel, K., Wolf, S., Ehninger, D., Babu, H., Leal Galicia, P., Kempermann, G., 2009. Additive effects of physical exercise and environmental enrichment on adult hippocampal neurogenesis in mice. *Front. Neurosci.* 3, 1–7.
- Fabre, C., Chamari, K., Mucci, P., Masse Biron, J., Prefaut, C., 2002. Improvement of cognitive function by mental and/or individualized aerobic training in healthy elderly subjects. *Int. J. Sports Med.* 23, 415–421.
- Fritsch, T., Smyth, K.A., Debanne, S.M., Petot, G.J., Friedland, R.P., 2005. Participation in novelty seeking leisure activities and Alzheimer's disease. *J. Geriatr. Psychiatry Neurol.* 18, 134–141.
- Gates, N.J., Valenzuela, M., 2010. Cognitive exercise and its role in cognitive function in older adults. *Curr. Psychiatry Rep.* 12, 20–27.
- Gillette Guyonnet, S., Andrieu, S., Dantoine, T., Dartigues, J. F., Touchon, J., Vellas, B., 2009. Commentary on “A roadmap for the prevention of dementia II. Leon Thal Symposium 2008”. The Multidomain Alzheimer Preventive Trial (MAPT): A new approach to the prevention of Alzheimer's disease. *Alzheimers Dement.* 5, 114–121.
- Glass, B.D., Maddox, W.T., Love, B.C., 2013. Real time strategy game training: emergence of a cognitive flexibility trait. *PLoS ONE* 8, e70350.
- Goodwin, D.W., Powell, B., Bremer, D., Hoine, H., Stern, J., 1969. Alcohol and recall: State dependent effects in man. *Science* 163, 1358–1360.
- Green, C., Bavelier, D., 2012. Learning, attentional control, and action video games. *Curr. Biol.* 22, R197–R206.
- Head, D., Bugg, J.M., Goate, A.M., Fagan, A.M., Mintun, M.A., Benzinger, T., Holtzman, D.M., Morris, J.C., 2012. Exercise engagement as a moderator of the effects of APOE genotype on amyloid deposition. *Arch. Neurol.* 69, 636–643.
- Hebb, D.O., 1949. *The Organization of Behavior: A Neuropsychological Theory*. Wiley and Sons, New York.
- Hindin, S.B., Zelinski, E.M., 2012. Extended practice and aerobic exercise interventions benefit untrained cognitive outcomes in older adults: A meta analysis. *J. Am. Geriatr. Soc.* 60, 136–141.
- Hulme, C., Melby Lervåg, M., 2012. Current evidence does not support the claims made for CogMed working memory training. *J. Appl. Res. Mem. Cogn.* 1, 197–200.
- Hurd, M.D., Martorell, P., Delavande, A., Mullen, K.J., Langa, K.M., 2013. Monetary costs of dementia in the United States. *N. Engl. J. Med.* 368, 1326–1334.
- Jaeggi, S.M., Buschkuhl, M., Jonides, J., Perrig, W.J., 2008. Improving fluid intelligence with training on working memory. *Proc. Natl. Acad. Sci.* 105, 6829–6833.
- Jaeggi, S.M., Studer Luethi, B., Buschkuhl, M., Su, Y.F., Jonides, J., Perrig, W.J., 2010. The relationship between n back performance and matrix reasoning – implications for training and transfer. *Intelligence* 38, 625–635.
- Jaeggi, S.M., Buschkuhl, M., Jonides, J., Shah, P., 2011. Short and long term benefits of cognitive training. *Proc. Natl. Acad. Sci.* 108, 10081–10086.
- Jennings, J.M., Jacoby, L.L., 2003. Improving memory in older adults: training recollection. *Neuropsychol. Rehabil.* 13, 417–440.
- Kang, M.J., Hsu, M., Krajchich, I.M., Loewenstein, G., McClure, S.M., Wang, J.T. y., Camerer, C.F., 2009. The wick in the candle of learning: epistemic curiosity activates reward circuitry and enhances memory. *Psychol. Sci.* 20, 963–973.
- Kantak, S.S., Sullivan, K.J., Fisher, B.E., Knowlton, B.J., Winstein, C.J., 2010. Neural substrates of motor memory consolidation depend on practice structure. *Nat. Neurosci.* 13, 923–925.

- Karbach, J., Kray, J., 2009. How useful is executive control training? Age differences in near and far transfer of task switching training. *Dev. Sci.* 12, 978–990.
- Kåreholt, I., Lennartsson, C., Gatz, M., Parker, M.G., 2011. Baseline leisure time activity and cognition more than two decades later. *Int. J. Geriatr. Psychiatry* 26, 65–74.
- Karp, A., Paillard Borg, S., Wang, H. X., Silverstein, M., Winblad, B., Fratiglioni, L., 2006. Mental, physical and social components in leisure activities equally contribute to decrease dementia risk. *Dement. Geriatr. Cogn. Disord.* 21, 65–73.
- Kattenstroth, J. C., Kolankowska, I., Kalisch, T., Dinse, H.R., 2010. Superior sensory, motor, and cognitive performance in elderly individuals with multi year dancing activities. *Front. Aging Neurosci.* 2, 1–9.
- Kattenstroth, J. C., Kalisch, T., Holt, S., Tegenthoff, M., Dinse, H.R., 2013. Six months of dance intervention enhances postural, sensorimotor, and cognitive performance in elderly without affecting cardio respiratory functions. *Front. Aging Neurosci.* 5, 1–16.
- Kempermann, G., Fabel, K., Ehninger, D., Babu, H., Leal Galicia, P., Garthe, A., Wolf, S., 2010. Why and how physical activity promotes experience induced brain plasticity. *Front. Neurosci.* 4, 1–9.
- Kim, K.H., Relkin, N.R., Lee, K. M., Hirsch, J., 1997. Distinct cortical areas associated with native and second languages. *Nature* 388, 171–174.
- Kim, J.M., Stewart, R., Bae, K.Y., Kim, S.W., Yang, S.J., Park, K.H., Shin, I.S., Yoon, J.S., 2011. Role of BDNF val66met polymorphism on the association between physical activity and incident dementia. *Neurobiol. Aging* 32, 551.e5–551.e12.
- Klingberg, T., Forssberg, H., Westerberg, H., 2002. Training of working memory in children with ADHD. *J. Clin. Exp. Neuropsychol.* 24, 781–791.
- Klingberg, T., Fernell, E., Olesen, P., Johnson, M., Gustafsson, P., Dahlström, K., Gillberg, C., Forssberg, H., Westerberg, H., 2005. Computerized training of working memory in children with ADHD a randomized, controlled trial. *J. Am. Acad. Child Adolesc. Psychiatry* 44, 177–186.
- Klusmann, V., Evers, A., Schwarzer, R., Schlattmann, P., Reischies, F., Heuser, I., Dimeo, F., 2010. Complex mental and physical activity in older women and cognitive performance: a 6 month randomized controlled trial. *J. Gerontol. Ser. A* 65, 680–688.
- Knaepen, K., Goekint, M., Heyman, E.M., Meeusen, R., 2010. Neuroplasticity—Exercise induced response of peripheral brain derived neurotrophic factor: a systematic review of experimental studies in human subjects. *Sports Med.* 40, 765–801.
- Koleske, A.J., 2013. Molecular mechanisms of dendrite stability. *Nat. Rev. Neurosci.* 14, 536–550.
- Kraft, E., 2012. Cognitive function, physical activity, and aging: possible biological links and implications for multimodal interventions. *Aging Neuropsychol. Cognit.* 19, 248–263.
- Kramer, A.F., Hahn, S., Cohen, N.J., Banich, M.T., McAuley, E., Harrison, C.R., Chason, J., Vakil, E., Bardell, L., Boileau, R.A., Colcombe, A., 1999. Ageing, fitness and neurocognitive function. *Nature* 400, 418–419.
- Lam, L.C.W., Chau, R.C.M., Wong, B.M.L., Fung, A.W.T., Lui, V.W.C., Tam, C.C.W., Leung, G.T.Y., Kwok, T.C.Y., Chiu, H.F.K., Ng, S., Chan, W.M., 2011. Interim follow up of a randomized controlled trial comparing Chinese style mind body (Tai Chi) and stretching exercises on cognitive function in subjects at risk of progressive cognitive decline. *Int. J. Geriatr. Psychiatry* 26, 733–740.
- Lam, L.C.W., Chau, R.C.M., Wong, B.M.L., Fung, A.W.T., Tam, C.W.C., Leung, G.T.Y., Kwok, T.C.Y., Leung, T.Y.S., Ng, S.P., Chan, W.M., 2012. A 1 year randomized

- controlled trial comparing mind body exercise (Tai Chi) with stretching and toning exercise on cognitive function in older chinese adults at risk of cognitive decline. *J. Am. Med. Dir. Assoc.* 13, 568.e15–568.e20.
- Lautenschlager, N.T., Cox, K.L., 2013. Can participation in mental and physical activity protect cognition in old age? Comment on “The Mental Activity and eXercise (MAX) Trial: a randomized controlled trial to enhance cognitive function in older adults” Can mental and physical activity protect cognition. *JAMA Int. Med.* 173, 805–806.
- Lee, Y., Kim, J., Back, J.H., 2009. The influence of multiple lifestyle behaviors on cognitive function in older persons living in the community. *Prev. Med.* 48, 86–90.
- Legault, C., Jennings, J., Katula, J., Dagenbach, D., Gaussoin, S., Sink, K., Rapp, S., Rejeski, W., Shumaker, S., Espeland, M., 2011. Designing clinical trials for assessing the effects of cognitive training and physical activity interventions on cognitive outcomes: The Seniors Health and Activity Research Program Pilot (SHARP P) Study, a randomized controlled trial. *BMC Geriatr.* 11, 1–14.
- Li, S., Schmiedek, F., Huxhold, O., Röcke, C., Smith, J., Lindenberger, U., 2008. Working memory plasticity in old age: practice gain, transfer, and maintenance. *Psychol. Aging* 23, 731–742.
- Li, S., Jin, M., Zhang, D., Yang, T., Koeglsperger, T., Fu, H., Selkoe, Dennis J., 2013. Environmental novelty activates β_2 adrenergic signaling to prevent the impairment of hippocampal LTP by A β oligomers. *Neuron* 77, 929–941.
- Lively, S.E., Logan, J.S., Pisoni, D.B., 1993. Training Japanese listeners to identify English/r/ and/l/. II: The role of phonetic environment and talker variability in learning new perceptual categories. *J. Acoustic. Soc. Am.* 94, 1242–1255.
- Lövdén, M., Bäckman, L., Lindenberger, U., Schaefer, S., Schmiedek, F., 2010. A theoretical framework for the study of adult cognitive plasticity. *Psychol. Bull.* 136, 659–676.
- Lövdén, M., Xu, W., Wang, H. X., 2013. Lifestyle change and the prevention of cognitive decline and dementia: what is the evidence? *Curr. Opin. Psychiat.* 26, 239–243.
- Lu, B., Nagappan, G., Guan, X., Nathan, P.J., Wren, P., 2013. BDNF based synaptic repair as a disease modifying strategy for neurodegenerative diseases. *Nat. Rev. Neurosci.* 14, 401–416.
- Luck, T., Riedel Heller, S.G., Lupp, M., Wiese, B., Köhler, M., Jessen, F., Bickel, H., Weyerer, S., Pentzek, M., König, H. H., Prokein, J., Ernst, A., Wagner, M., Mösch, E., Werle, J., Fuchs, A., Brettschneider, C., Scherer, M., Maier, W., 2013. Apolipoprotein E epsilon 4 genotype and a physically active lifestyle in late life: analysis of gene environment interaction for the risk of dementia and Alzheimer’s disease dementia. *Psychol. Med. FirstView*, 1–11.
- Lustig, C., Flegal, K., 2008. Targeting latent function: Encouraging effective encoding for successful memory training and transfer. *Psychol. Aging* 23, 754–764.
- Lustig, C., Shah, P., Seidler, R., Reuter Lorenz, P.A., 2009. Aging, training, and the brain: a review and future directions. *Neuropsychol. Rev.* 19, 504–522.
- Maguire, E., Gadian, D., Johnsrude, I., Good, C., Ashburner, J., Frackowiak, R., Frith, C., 2000. Navigation related structural change in the hippocampi of taxi drivers. *Proc. Natl. Acad. Sci. U. S. A.* 97, 4398–4403.
- Mahncke, H.W., Bronstone, A., Merzenich, M.M., 2006a. Brain plasticity and functional losses in the aged: scientific bases for a novel intervention. *Prog. Brain Res.* 157, 81–109.
- Mahncke, H.W., Connor, B.B., Appelman, J., Ahsanuddin, O.N., Hardy, J.L., Wood, R.A., Joyce, N.M., Boniske, T., Atkins, S.M., Merzenich, M.M., 2006b. Memory enhancement

- in healthy older adults using a brain plasticity based training program: a randomized, controlled study. *Proc. Natl. Acad. Sci.* 103, 12523–12528.
- Maillot, P., Perrot, A., Hartley, A., 2012. Effects of interactive physical activity video game training on physical and cognitive function in older adults. *Psychol. Aging* 27, 589–600.
- Melby Lervåg, M., Hulme, C., 2012. Is working memory training effective? A meta analytic review. *Dev. Psychol.* 49, 270–291.
- Miyake, A., Friedman, N.P., Emerson, M.J., Witzki, A.H., Howerter, A., Wager, T.D., 2000. The unity and diversity of executive functions and their contributions to complex. *Cogn. Psychol.* 41, 49–100.
- Mortimer, J.A., Ding, D., Borenstein, A.R., DeCarli, C., Guo, Q., Wu, Y., Zhao, Q., Chu, S., 2012. Changes in brain volume and cognition in a randomized trial of exercise and social interaction in a community based sample of non demented Chinese elders. *J. Alzheimers Dis.* 30, 757–766.
- Nagamatsu, L.S., Handy, T.C., Hsu, C.L., Voss, M., Liu Ambrose, T., 2012. Resistance training promotes cognitive and functional brain plasticity in seniors with probable mild cognitive impairment. *Arch. Intern. Med.* 172, 666–668.
- Neeper, S.A., Gomez Pinilla, F., Choi, J., Cotman, C., 1995. Exercise and brain neurotrophins. *Nature* 373, 109.
- Niti, M., Yap, K.B., Kua, E.H., Tan, C.H., Ng, T.P., 2008. Physical, social and productive leisure activities, cognitive decline and interaction with APOE 4 genotype in Chinese older adults. *Int. Psychogeriatr.* 20, 237–251.
- Noice, H., Noice, T., 2009. An arts intervention for older adults living in subsidized retirement homes. *Neuropsychol. Dev. Cogn.* 16, 56–79.
- Noice, H., Noice, T., Staines, G., 2004. A short term intervention to enhance cognitive and affective functioning in older adults. *J. Aging Health* 16, 562–585.
- Oberauer, K., Süß, H. M., Schulze, R., Wilhelm, O., Wittmann, W.W., 2000. Working memory capacity: facets of a cognitive ability construct. *Personal. Individ. Differ.* 29, 1017–1045.
- Oei, A.C., Patterson, M.D., 2013. Enhancing cognition with video games: a multiple game training study. *PLoS ONE* 8, e58546.
- Olde Rikkert, M.G., van der Flier, W.M., de Leeuw, F.E., Verbeek, M., Jansen, R.W., Verhey, F., Scheltens, P., 2006. Multiple diagnostic tests are needed to assess multiple causes of dementia. *JAMA Neurol.* 63, 144–146.
- Olesen, P., Westerberg, H., Klingberg, T., 2003. Increased prefrontal and parietal activity after training of working memory. *Nat. Neurosci.* 7, 75–79.
- Oswald, W., Gunzelmann, T., Rupprecht, R., Hagen, B., 2006. Differential effects of single versus combined cognitive and physical training with older adults: the SimA study in a 5 year perspective. *Eur. J. Ageing* 3, 179–192.
- Paillard Borg, S., Fratiglioni, L., Winblad, B., Wang, H.X., 2009. Leisure Activities in Late Life in Relation to Dementia Risk: Principal Component Analysis. *Dement. Geriatr. Cogn. Disord.* 28, 136–144.
- Park, D.C., Lautenschlager, G., Hedden, T., Davidson, N.S., Smith, A.D., Smith, P.K., 2002. Models of visuospatial and verbal memory across the adult life span. *Psychol. Aging* 17, 299–320.
- Park, D., Gutches, A., Meade, M., Stine Morrow, E., 2007. Improving cognitive function in older adults: nontraditional approaches. *J. Gerontol. Ser. B Psychol. Sci. Soc. Sci.* 62, 45–52.

- Perquin, M., Vaillant, M., Schuller, A. M., Pastore, J., Dartigues, J. F., Lair, M. L., Diederich, N., 2013. Lifelong exposure to multilingualism: New evidence to support cognitive reserve hypothesis. *PLoS ONE* 8, e62030.
- Pieramico, V., Esposito, R., Sensi, F., Cilli, F., Mantini, D., Mattei, P.A., Frazzini, V., Ciavardelli, D., Gatta, V., Ferretti, A., 2012. Combination training in aging individuals modifies functional connectivity and cognition, and is potentially affected by dopamine related genes. *PLoS ONE* 7, e43901.
- Plassman, B.L., Williams, J.W., Burke, J.R., Holsinger, T., Benjamin, S., 2010. Systematic review: factors associated with risk for and possible prevention of cognitive decline in later life. *Ann. Intern. Med.* 153, 182–193.
- Proteau, L., 1992. On the specificity of learning and the role of visual information for movement control. *Adv. Psychol.* 85, 67–103.
- Rasmussen, P., Brassard, P., Adser, H., Pedersen, M.V., Leick, L., Hart, E., Secher, N.H., Pedersen, B.K., Pilegaard, H., 2009. Evidence for a release of brain derived neurotrophic factor from the brain during exercise. *Exp. Physiol.* 94, 1062–1069.
- Raven, J.C., Raven, J., Court, J.H., 1990. Standard progressive matrices. Oxford Psychologists Press, Oxford, UK.
- Raz, N., Lindenberger, U., Rodrigue, K., Kennedy, K., Head, D., Williamson, A., Dahle, C., Gerstorf, D., Acker, J., 2005. Regional brain changes in aging healthy adults: general trends, individual differences and modifiers. *Cereb. Cortex* 15, 1676–1689.
- Redick, T.S., Shipstead, Z., Harrison, T.L., Hicks, K.L., Fried, D.E., Hambrick, D.Z., Kane, M.J., Engle, R.W., 2013. No evidence of intelligence improvement after working memory training: a randomized, placebo controlled study. *J. Exp. Psychol. General* 142, 359–379.
- Roig, M., Skriver, K., Lundbye Jensen, J., Kiens, B., Nielsen, J.B., 2012. A single bout of exercise improves motor memory. *PLoS ONE* 7, e44594.
- Ryan, R.M., Deci, E.L., 2000. Self determination theory and the facilitation of intrinsic motivation, social development, and well being. *Am. Psychol.* 55, 68–78.
- Schmidt, R.A., 1975. A schema theory of discrete motor skill learning. *Psychol. Rev.* 82, 225–260.
- Schmidt, R.A., Bjork, R.A., 1992. New conceptualizations of practice: Common principles in three paradigms suggest new concepts for training. *Psychol. Sci.* 3, 207–217.
- Schmiedek, F., Lövdén, M., Lindenberger, U., 2010. Hundred days of cognitive training enhance broad cognitive abilities in adulthood: findings from the COGITO study. *Front. Aging Neurosci.* 2, 1–10.
- Schneiders, J., Opitz, B., Krick, C.M., Mecklinger, A., 2011. Separating intra modal and across modal training effects in visual working memory: an fMRI investigation. *Cereb. Cortex* 21, 2555–2564.
- Schneiders, J., Opitz, B., Tang, H., Deng, Y., Xie, C., Li, H., Mecklinger, A., 2012. The impact of auditory working memory training on the fronto parietal working memory network. *Front. Hum. Neurosci.* 6, 1–14.
- Schoups, A., Vogels, R., Qian, N., Orban, G., 2001. Practising orientation identification improves orientation coding in V1 neurons. *Nature* 412, 549–553.
- Schweizer, S., Hampshire, A., Dalgleish, T., 2011. Extending brain training to the affective domain: increasing cognitive and affective executive control through emotional working memory training. *PLoS ONE* 6, e24372.

- Schweizer, S., Grahn, J.A., Hampshire, A., Mobbs, D., Dalgleish, T., 2013. Training the emotional brain: improving affective control through emotional working memory training. *J. Neurosci.* 33, 5301–5311.
- Shatil, E., 2013. Does combined cognitive training and physical activity training enhance cognitive abilities more than either alone? A four condition randomized controlled trial among healthy older adults. *Neuroscience* 5, 1–12.
- Shipstead, Z., Redick, T., Engle, R., 2010. Does working memory training generalize? *Psychol. Belg.* 50 (3), 245–276.
- Shipstead, Z., Redick, T., Engle, R., 2012. Is working memory training effective? *Psychol. Bull.* 138, 628–654.
- Smith, G.E., Housen, P., Yaffe, K., Ruff, R., Kennison, R.F., Mahncke, H.W., Zelinski, E.M., 2009. A cognitive training program based on principles of brain plasticity: Results from the Improvement in Memory with Plasticity based Adaptive Cognitive Training (IMPACT) study. *J. Am. Geriatr. Soc.* 57, 594–603.
- Smith, P.J., Blumenthal, J.A., Hoffman, B.M., Cooper, H., Strauman, T.A., Welsh Bohmer, K., Browndyke, J.N., Sherwood, A., 2010. Aerobic exercise and neurocognitive performance: a meta analytic review of randomized controlled trials. *Psychosom. Med.* 72, 239–252.
- Sofi, F., Valecchi, D., Bacci, D., Abbate, R., Gensini, G.F., Casini, A., Macchi, C., 2011. Physical activity and risk of cognitive decline: a meta analysis of prospective studies. *J. Intern. Med.* 269, 107–117.
- Stahl, C., Voss, A., Schmitz, F., Nuszbaum, M., Tuescher, O., Lieb, K., Klauer, C., 2013. Behavioral components of impulsivity. *J. Exp. Psychol. General.* No Pagination Specified.
- Stephenson, C.L., Halpern, D.F., 2013. Improved matrix reasoning is limited to training on tasks with a visuospatial component. *Intelligence* 41, 341–357.
- Stern, C., Munn, Z., 2010. Cognitive leisure activities and their role in preventing dementia: a systematic review. *Int. J. Evid. Based Healthc.* 8, 2–17.
- Stine Morrow, E.A.L., Parisi, J.M., Morrow, D.G., Park, D.C., 2008. The effects of an engaged lifestyle on cognitive vitality: A field experiment. *Psychol. Aging* 23, 778–786.
- Takeuchi, H., Taki, Y., Sassa, Y., Hashizume, H., Sekiguchi, A., Fukushima, A., Kawashima, R., 2011. Working memory training using mental calculation impacts regional gray matter of the frontal and parietal regions. *PLoS ONE* 6, e23175.
- Thompson, T.W., Waskom, M.L., Garel, K. L.A., Cardenas Iniguez, C., Reynolds, G.O., Winter, R., Chang, P., Pollard, K., Lala, N., Alvarez, G.A., Gabrieli, J.D.E., 2013. Failure of working memory training to enhance cognition or intelligence. *PLoS ONE* 8, e63614.
- Thorell, L., Lindqvist, S., Bergman Nutley, S., Bohlin, G., Klingberg, T., 2009. Training and transfer effects of executive functions in preschool children. *Dev. Sci.* 12, 106–113.
- Trachtenberg, J.T., Chen, B.E., Knott, G.W., Feng, G., Sanes, J.R., Welker, E., Svoboda, K., 2002. Long term in vivo imaging of experience dependent synaptic plasticity in adult cortex. *Nature* 420, 788–794.
- Tranter, L.J., Koutstaal, W., 2008. Age and flexible thinking: an experimental demonstration of the beneficial effects of increased cognitively stimulating activity on fluid intelligence in healthy older adults. *Aging Neuropsychol. Cognit.* 15, 184–207.
- Unverzagt, F.W., Guey, L.T., Jones, R.N., Marsiske, M., King, J.W., Wadley, V.G., Crowe, M., Rebok, G.W., Tennstedt, S.L., 2012. ACTIVE cognitive training and rates of incident dementia. *J. Int. Neuropsychol. Soc.* 18, 669–677.

- Valenzuela, M.J., Sachdev, P., 2006. Brain reserve and dementia: a systematic review. *Psychol. Med.* 36, 441–454.
- Valenzuela, M.J., Breakspear, M., Sachdev, P., 2007. Complex mental activity and the aging brain: molecular, cellular and cortical network mechanisms. *Brain Res. Rev.* 56, 198–213.
- Valenzuela, M.J., Matthews, F.E., Brayne, C., Ince, P., Halliday, G., Kril, J.J., Dalton, M.A., Richardson, K., Forster, G., Sachdev, P.S., 2011. Multiple biological pathways link cognitive lifestyle to protection from dementia. *Biol. Psychiatry* 71, 783–791.
- Van Praag, H., Christie, B., Sejnowski, T., Gage, F., 1999. Running enhances neurogenesis, learning, and long term potentiation in mice. *Proc. Natl. Acad. Sci. U. S. A.* 96, 13427–13431.
- van Praag, H., Kempermann, G., Gage, F.H., 2000. Neural consequences of environmental enrichment. *Nat. Rev. Neurosci.* 1, 191–198.
- Vaynman, S., Ying, Z., Gomez Pinilla, F., 2004. Hippocampal BDNF mediates the efficacy of exercise on synaptic plasticity and cognition. *Eur. J. Neurosci.* 20, 2580–2590.
- Verghese, J., Lipton, R., Katz, M., Hall, C., Derby, C., Kuslansky, G., Ambrose, A., Sliwinski, M., Buschke, H., 2003. Leisure activities and the risk of dementia in the elderly. *N. Engl. J. Med.* 348, 2508–2516.
- Voss, M.W., Erickson, K.I., Prakash, R.S., Chaddock, L., Kim, J.S., Alves, H., Szabo, A., White, S.M., Wójcicki, T.R., Mailey, E.L., 2013. Neurobiological markers of exercise related brain plasticity in older adults. *Brain Behav. Immun.* 28, 90–99.
- Wang, H. X., Karp, A., Winblad, B., Fratiglioni, L., 2002. Late life engagement in social and leisure activities is associated with a decreased risk of dementia: a longitudinal study from the Kungsholmen Project. *Am. J. Epidemiol.* 155, 1081–1087.
- Wang, H. X., Karp, A., Herlitz, A., Crowe, M., Kåreholt, I., Winblad, B., Fratiglioni, L., 2009. Personality and lifestyle in relation to dementia incidence. *Neurology* 72, 253–259.
- Wang, H. X., Xu, W., Pei, J. J., 2012. Leisure activities, cognition and dementia. *Biochim. Biophys. Acta* 1822, 482–491.
- Wang, H. X., Jin, Y., Hendrie, H.C., Liang, C., Yang, L., Cheng, Y., Unverzagt, F.W., Ma, F., Hall, K.S., Murrell, J.R., Li, P., Bian, J., Pei, J. J., Gao, S., 2013. Late life leisure activities and risk of cognitive decline. *J. Gerontol. A: Biol. Med. Sci.* 68, 205–213.
- Weiß, R.H., 2006. Grundintelligenztest Skala 2 (CFT 20 R), Göttingen, Hogrefe.
- Weuve, J., Kang, J.H., Manson, J.E., Breteler, M.M.B., Ware, J.H., Grodstein, F., 2004. Physical activity, including walking, and cognitive function in older women. *JAMA* 292, 1454–1461.
- Willis, S., Tennstedt, S., Marsiske, M., Ball, K., Elias, J., Koepke, K., Morris, J., Rebok, G., Unverzagt, F., Stoddard, A., 2006. Long term effects of cognitive training on everyday functional outcomes in older adults. *JAMA* 296, 2805–2814.
- Wilson, R.S., 2011. Mental stimulation and brain health: complex, challenging activities can support cognitive health in older adults. *Generations* 35, 58–62.
- Winter, B., Breitenstein, C., Mooren, F.C., Voelker, K., Fobker, M., Lechtermann, A., Krueger, K., Fromme, A., Korsukewitz, C., Floel, A., 2007. High impact running improves learning. *Neurobiol. Learn. Mem.* 87, 597–609.
- Wolf, S., Kronenberg, G., Lehmann, K., Blankenship, A., Overall, R., Staufenbiel, M., Kempermann, G., 2006. Cognitive and physical activity differently modulate disease progression in the amyloid precursor protein (APP) 23 model of Alzheimer's disease. *Biol. Psychiatry* 60, 1314–1323.

- Wolinsky, F.D., Vander Weg, M.W., Howren, M.B., Jones, M.P., Dotson, M.M., 2013. A randomized controlled trial of cognitive training Beneficial effects of traditional interventions such as novelty interventions and PCTs may be improved by two novel synergistic approaches: the combination of novelty interventions with 1) a process based or 2) a physically demanding element . using a visual speed of processing intervention in middle aged and older adults. *PLoS ONE* 8, e61624.
- Woollett, K., Maguire, E.A., 2011. Acquiring the knowledge of london's layout drives structural brain changes. *Curr. Biol.* 21, 2109–2114.
- Zelinski, E.M., Spina, L.M., Yaffe, K., Ruff, R., Kennison, R.F., Mahncke, H.W., Smith, G.E., 2011. Improvement in memory with plasticity based adaptive cognitive training: results of the 3 month follow up. *J. Am. Geriatr. Soc.* 59, 258–265.
- Zhao, X., Wang, Y., Liu, D., Zhou, R., 2011. Effect of updating training on fluid intelligence in children. *Chin. Sci. Bull.* 56, 2202–2205.