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ORIGINAL ARTICLE

Playing Super Mario induces structural brain plasticity: gray matter changes resulting from training with a commercial video game

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Video gaming is a highly pervasive activity, providing a multitude of complex cognitive and motor demands. Gaming can be seen as an intense training of several skills. Associated cerebral structural plasticity induced has not been investigated so far. Comparing a control with a video gaming training group that was trained for 2 months for at least 30 min per day with a platformer game, we found significant gray matter (GM) increase in right hippocampal formation (HC), right dorsolateral prefrontal cortex (DLPFC) and bilateral cerebellum in the training group. The HC increase correlated with changes from egocentric to allocentric navigation strategy. GM increases in HC and DLPFC correlated with participants' desire for video gaming, evidence suggesting a predictive role of desire in volume change. Video game training augments GM in brain areas crucial for spatial navigation, strategic planning, working memory and motor performance going along with evidence for behavioral changes of navigation strategy. The presented video game training could therefore be used to counteract known risk factors for mental disease such as smaller hippocampus and prefrontal cortex volume in, for example, post-traumatic stress disorder, schizophrenia and neurodegenerative disease.

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INTRODUCTION

Video gaming has become more and more pervasive across the lifespan as well as across cultures. Nowadays, people spend a collective three billion hours per week playing video games worldwide.[1] It is predicted that the average young person will spend about 10 000 h gaming by age 21, twice the time it would take to earn a bachelor's degree.[2] This intense exposure is bound to have effects on neural structure and function. The growing evidence that video game experts outperform novices on multiple cognitive measures of attention and perception has increased interest in using video games for training purposes. There is evidence that as few as 10–20 h of video game exposure improves performance on attention demanding and perceptual tasks[3,4] as well as on tasks that require executive control.[5] The assumption underlying training studies is that the acquired skills on the trained task transfer to other untrained tasks and ideally to performance in day-to-day life situations. Compared with regular cognitive training,[6] the existing evidence that video game training has potential to elicit transfer effects is encouraging,[1,3–5] but not all studies have been successful in showing transfer effects.[2,7] A recent meta-analysis criticized several methodological short-comings, but comes to the conclusion that video game training holds great promise as one of the few training techniques to show transfer beyond the trained task.[3,4,8] If targeted video gaming would proof successful in changing brain structure it could be well suited as an intervention counteracting known risk factors for mental disease. It is highly likely that the acceptance and motivation of patients to engage in the video game training would be superior to other types of interventions.

Surprisingly, studies exploring the functional and structural neural correlates of frequent video gaming are scarce. We have recently collected cross-sectional data in adolescents where we investigated brain morphological correlates of current amount of video gaming. We found more gray matter (GM) volume in the left ventral striatum for frequent (>9 h per week) compared with infrequent video gamers (<9 h per week).[5,9] In another cross-sectional study on male adults, we observed a positive association between bilateral hippocampal formation (HC), in particular in entorhinal cortex, as well as occipital cortex, with the cumulative amount of video game hours over the lifetime.[6,10] Interestingly, the higher GM volume within the entorhinal cortex was significantly predicted by the game category gamers were primarily interested in. Platformer games (for example, Super Mario 64, Commander Keen, Sonic and Mega Man) and logic and puzzle games (for example, Tetris, Minesweeper and Professor Layton) as assessed by participants' self-reports, were the best predictors for increased GM volume within the entorhinal cortex. However, cross-sectional studies leave it impossible to determine whether observed structural differences are due to pre-existing differences or whether they represent the effects of intense training.

Therefore, longitudinal investigations of structural change are needed. In general, modifications of the brain's macrostructure by experience in adulthood have been shown in previous training studies using magnetic resonance imaging. The first study of this kind has reported changes in voxel-based morphometry (VBM) before and after 3 months of juggling training.[11] Others have focused on the effects of various interventions such as aerobic

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fitness, studying for exams, mnemonic and language training (for an overview see Lövden *et al.*[12]).

We theorized that a video game with a prominent navigation component, that is, the necessity to orient in a three-dimensional environment, and with orientation and strategic demands would have measurable plasticity effects on brain regions associated with these cognitive processes, namely the HC and the prefrontal cortex. To test this hypothesis, we examined structural changes after 2 months of daily video gaming training with the three-dimensional platformer/action adventure game *Super Mario 64* in an adult population. The game also allows the user to navigate by means of a first-person or a bird's eye view perspective to explore the environment. The first-person view may potentially enhance egocentric navigation strategies that have been related to caudate processing, whereas the bird's eye view may potentially facilitate allocentric strategies that have been shown to rely more strongly on hippocampal activation.[13,14]

MATERIALS AND METHODS

Participants

The local ethics committee of the Charité University Clinic, Berlin, Germany, approved of the study. Forty-eight healthy participants (mean age = 24.1, s.d. = 3.8) were recruited by means of newspaper and internet advertisements. After complete description of the study, the participants' informed written consent was obtained. According to personal interviews (Mini-International Neuropsychiatric Interview) participants were free of mental disorders. In addition, exclusion criteria for all participants were abnormalities in magnetic resonance imaging, general medical disorders and neurological diseases. Participants reported little, preferably no video game usage in the past 6 months (none of the participants played the game *Super Mario 64* before). The participants received a financial compensation for the testing sessions, but not for the video gaming itself.

Training procedure

The participants were randomly assigned to the video game training group or to a passive control group. The training group ($n = 23$, mean age = 23.7, s.d. = 3.0, 17 females and 6 males) was instructed to play the video game *Super Mario 64* on a portable Nintendo Dual Screen (DS) XXL console for at least 30 min per day over a period of 2 months. *Super Mario 64* is a three-dimensional platformer game in which a princess has to be saved. The gamer can freely move through the environment and needs to collect stars by exploring the levels precisely, solving puzzles or defeating enemies to be able to proceed to higher levels. On the top half of the screen, the environment is seen from a third-person perspective (behind the character), on the bottom half of the screen a map is shown from a bird's eye view, enabling orientation and in particular the localization of stars (see Figure 1). Participants were instructed how to use the keys on the gaming console and learned about the rules of Super Mario by means of a standardized presentation before the training phase. During the training period, we offered support in case participants were frustrated or unable to solve game-related problems. The participants were not paid for the hours they played. However, we introduced the reward of a 20 Euro Internet voucher when they fulfilled the requirement of playing 30 min per day over the course of the 2 months. Furthermore, the participants were informed that the three best players would be rewarded by means of an additional 20 Euro voucher.

The passive control group ($n = 25$, mean age = 24.5, s.d. = 4.4, 17 females, 8 males) had no task in particular but underwent the same testing procedure as the training group 2 months apart.

Scanning procedure

Structural images were collected on a Siemens Tim Trio 3T scanner (Erlangen, Germany) and a standard 12-channel head coil was used. The structural images were obtained using a three-dimensional T1-weighted magnetization prepared gradient-echo sequence (MPRAGE) based on the ADNI protocol (www.adni-info.org; repetition time = 2500 ms; echo time = 4.77 ms; TI = 1100 ms, acquisition matrix = $256 \times 256 \times 176$, flip angle = 7°; $1 \times 1 \times 1$ mm voxel size).

Figure 1. Screenshot from the platformer video game trained (Super Mario 64).

Questionnaires and tests

During the training period, participants were asked to note down their daily hours of gaming and the amount or game-related reward (stars) they obtained on each day in weekly questionnaires. Furthermore, they rated on a seven-point scale how much fun, frustration, desire to play and thoughts about video games they had. The stars collected were additionally assessed in means of the video gaming console so that the stars reported by the participants were objectively verified.

Before and after the training procedure, the training as well as the control group underwent several cognitive performance tests, one of them being a tunnel task to assess orientation preferences.[15] Participants saw a sparse visual flow, at the end of the visual flow they had to indicate the direction where the starting position was. To determine whether participants are so called 'turners' (egocentric frame, participants react as if they had taken on the new orientation during turns of the path by mentally rotating their sagittal axis) or 'nonturners' (allocentric frame, participants tracked the new orientation without adopting it) or rather to which degree they adopt which strategy. At the end of each path, participants had to choose between two homing vectors indicating their end position relative to the origin, one being the correct answer from an egocentric, one from an allocentric perspective. To determine the frame participants use regularly, 10 trials were administered and the egocentricity ratio was computed as the fraction of egocentric choices (ego/ego + allocentric-ratio).

Data analysis

Voxel-based morphometry. The structural images were processed by means of the longitudinal processing stream provided by the VBM8 toolbox (http://dbm.neuro.uni-jena.de/vbm.html) and the SPM8 software package (http://www.fil.ion.ucl.ac.uk/spm) using default parameters. The VBM8 toolbox involves bias correction, tissue classification and affine registration. The affine registered GM and white matter segmentations were used to build a customized DARTEL template (diffeomorphic anatomical registration through exponentiated lie algebra).[16] Then warped GM and white matter segments were created. Modulation was applied in order to preserve the volume of a particular tissue within a voxel by multiplying voxel values in the segmented images by the Jacobian determinants derived from the spatial normalization step. In effect, the analysis of modulated data tests for regional differences in the absolute amount (volume) of GM. Finally, images were smoothed with a FWHM kernel of 8 mm. Statistical analysis was carried out by means of a whole-brain flexible factorial design with a focus on the interaction of time (pre vs post) $\times$ group (training vs control group). The resulting maps were thresholded using family wise error correction $P<0.001$ together with a non-stationary smoothness correction.[3,4,17]

Pearson correlations were computed between extracted GM volumes from significant clusters of the VBM analysis with the mean reported desire to play the video game and the egocentricity ratio of the tunnel task. Comparisons between correlation coefficients were computed by means of Fisher's *r* to *Z* transform for between group comparisons and Meng's *z*-test when comparing correlated correlation coefficients.[5,18]

RESULTS

On average, participants played 50.2 h (s.d. = 14.6) per day and obtained 74.7 (s.d. = 37.4) stars.

When computing a whole-brain analysis on GM volume in search of clusters that show an interaction of time $\times$ group, we found a significant interaction in right HC (26, −21, −21), right dorsolateral prefrontal cortex (DLPFC, Montreal Neurological Institute coordinates: 52, 39, 25) and in the cerebellum spanning lobules IV, V and VI bilaterally (−6, −49, −23; $P<0.001$, family wise error corrected; Figure 2, Table 1). *Post-hoc t*-tests revealed that the GM volume in DLPFC shows a clear increase in the training group, $t(46)=2.31$, $P<0.05$, and a significant difference between both groups at post-test, $t(46)=2.28$, $P<0.05$. Also, the HC, $t(46)=2.95$, $P<0.01$, and the cerebellum, $t(46)=2.11$, $P<0.05$, differed significantly at post-test. With a more lenient threshold of $P<0.01$ (family wise error corrected) no additional brain regions reach significance.

On the basis of evidence that the HC is involved in allocentric spatial navigation while egocentric orientation is more strongly related to caudate processing, the participants' navigation strategy in the so-called tunnel task was submitted to further analysis.[6,13,14] In the training group, we found a negative correlation between orientation strategy (ego/ego + allocentric-ratio) change and HC change, $r(22)=-0.46$, $P<0.05$, Figure 3, indicating that a shift toward an allocentric strategy was associated with more HC growth. In the control group on the other hand, no significant association was observed, $r(24)=0.16$, $P=0.45$. The two correlation coefficients were significantly different from one another, Fisher's *r* to $Z=-2.07$, $P<0.05$.

The GM change in DLPFC and HC of the training group showed a positive association with the average self-reported desire to play the video game, DLPFC: $r(20)=0.66$, $P<0.01$; HC: $r(20)=0.46$, $P<0.05$; Figure 4. The cerebellum, however, did not, $r(20)=0.37$, $P=0.11$. To explore the putative directionality of this effect, we computed the self-reported desire to play separately for the first and second month. During the first month, the association between desire and GM in DLPFC was stronger than during the second month, first month: $r(20)=0.72$, $P<0.001$; second month: $r(20)=0.43$, $P=.057$. The two correlation coefficients were significantly different from one another, Meng-$z=2.31$, $P<0.05$. This pattern of results suggests that DLPFC growth does most likely not lead to the increase in reported desire. The separate analysis for the first and the second month in the HC did not reveal any significant correlation, nor a significant difference of the correlation coefficients.

DISCUSSION

We investigated structural neural changes resulting from a video game training intervention. Video game naive participants played the three-dimensional platformer game *Super Mario 64* over a

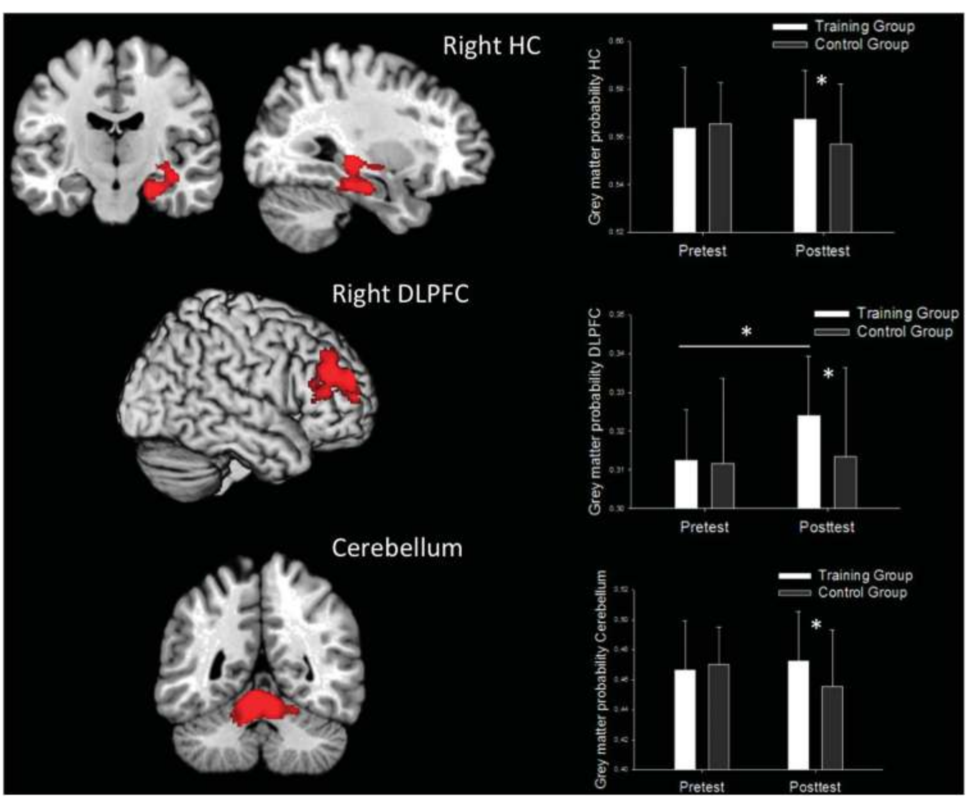

Figure 2. Brain regions showing a significant group (training vs control) $\times$ time (pre vs post-test) interaction in gray matter volume. Bar graphs depict the interaction effects for the clusters displayed, error bars illustrate s.d., *t-test, $P<0.05$. DLPFC, dorsolateral prefrontal cortex; HC, hippocampal formation.

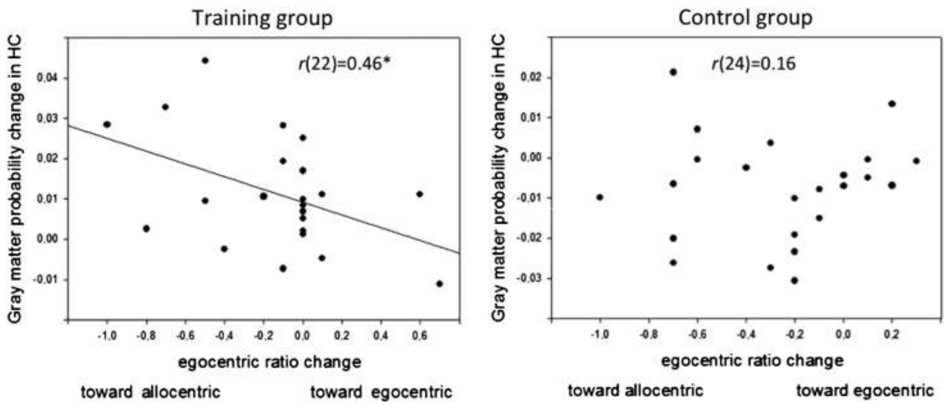

Figure 3. Scatter plot of gray matter volume change in hippocampal formation (HC) and change of egocentric orientation ratio when comparing pre- and post-test. Values below zero on the egocentricity ratio imply a change toward an allocentric strategy, values higher than zero a change toward an egocentric strategy.

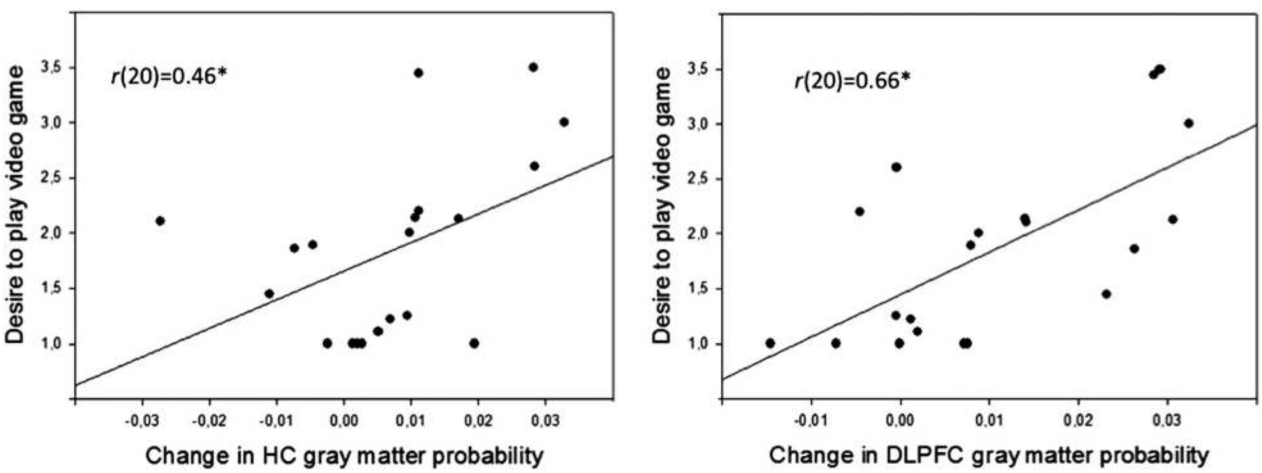

Figure 4. Scatter plot of gray matter volume changes in the hippocampal formation (HC, on the left side of the figure) and dorsolateral prefrontal cortex (DLPFC, on the right side of the figure) cluster and the average self-report of the desire to play the video game (average of all weekly reports).

period of 2 months for at least 30 min per day. In this, video game participants had to navigate through a virtual world and collect items. On the top screen of the console, participants saw their character from the back; on the bottom screen they saw the surrounding that they were placed in as a map from a bird's eye perspective.

When comparing GM volume changes between pre- and post-test and between experimental and control group, significant interaction effects were observed in right HC, right DLPFC and bilateral cerebellum. The observed interactions were mostly driven by an increase of GM in the experimental group and a tendency toward shrinkage in the control group. This tendency for volume decrements is within the range of previously reported estimates of age-related decline from longitudinal studies[19–22] and has previously been observed in training studies.[23]

The volume increase in the right HC of the experimental group was associated with a change from an egocentric orientation strategy to an allocentric one. This was not the case for the control group. Participants weekly ratings of the desire to play the video game correlated positively with GM increase in HC and DLFPC. In DLPFC, this association was stronger during the first month compared with the second month, suggesting that the reported desire to play the game leads to DLPFC growth, rather than vice versa.

Structural plasticity in HC and its association with spatial orientation and desire to play

In the literature, right posterior HC has been associated with spatial processing and navigation. In humans[3–5,24] as well as in primates,[7,25] an anterior–posterior distinction (also referred to as rostral–caudal distinction and equivalent to a ventral–dorsal distinction in rodents) within the hippocampus has been proposed; the posterior part being more strongly involved in spatial navigation. Another frequently suggested division of labor across species is the lateralization of hippocampal involvement, with navigation dominating in the right and memory in the left hemisphere.[8,26,27] Similar patterns of rightward lateralization in navigation have also been reported in rodents[28] and avians.[29] In a recent coordinate-based meta-analysis, we have illustrated this distinction between the involvement of subregions of the HC in episodic memory and spatial navigation.[11,30] The consistent activation during retrieval of spatial information across several studies was located in close proximity to the region where structural change in HC was detected in this study: in right hippocampal body and tail and the adjacent parahippocampal gyrus.

Building on this knowledge, we explored the association between hippocampal GM changes with changes in navigation strategy. For this purpose, we used a task in which participants

Table 1. Brain regions showing a significant interaction effect of group (experimental vs control) and time (pre-test vs post-test) in gray matter volume ($P < 0.001$, family wise error and nonstationary smoothness corrected)

Area	*BA*	*Peak coordinates (MNI)*	*T-score*	*Extent*
Right hippocampal formation		26, −21, −21	17.08	4652
Right dorsolateral prefrontal cortex	46, 9	52, 39, 25	12.33	1823
Bilateral cerebellum, lobules IV, V and VI		−6, −49, −23	13.55	2003

Abbreviations: BA, Brodmann area; MNI, Montreal Neurological Institute.

saw a sparse visual flow depicting a tunnel and at the end position had to indicate where the starting position was. This enabled us to determine whether participants navigated within an egocentric frame, where participants act as if they had taken on a new orientation at each turn, or an allocentric frame, were participants track their new orientation without actually adopting it.

Allocentric strategies have been demonstrated to depend on the hippocampus.[12,31,32] In a functional neuroimaging study, participants using an allocentric strategy showed stronger activation in parahippocampal regions, the hippocampus, thalamus and the cerebellum.[13,14,33] It has been assumed that initially egocentric imagery decays rapidly as more stable allocentric representations are encoded.[34] Older adults overwhelmingly prefer an egocentric strategy, while younger adults are equally distributed between egocentric and allocentric preferences. Furthermore, a preference for allocentric strategy was found to benefit performance on an independent assessment of navigation in younger adults.[35]

In addition to the association between HC change and navigation strategy, we also observed a positive association between hippocampal growth and reported desire to play the video game. This kind of desire or liking has been associated with the brain's reward system, and in particular dopaminergic processes, with the ventral tegmental area as the origin of dopaminergic cells and the ventral striatum.[36] Ventral tegmental area neurons have been shown to project to both dorsal and ventral parts of the hippocampus in rats.[37] Dopamine has been suggested to determine the duration of plasticity in HC since application of D1 and D2 receptor agonists produces long-lasting activation and inhibition of CA1 pyramidal neuron firing rate, respectively.[38] This neurophysiological link between reward-related dopaminergic neurons and hippocampal plasticity effects may explain the association between the reported desire to play and hippocampal GM increase.[39] In a training study in which participants played a video game for 10 days, a positive relationship between the desire for the game was correlated with blood oxygenation level dependent activity during game-related film fragments in right parahippocampal gyrus and right medial frontal lobe in individuals who played more.[40] This functional over-activation may have triggered the desire-associated structural plasticity effects observed in this study.

Structural plasticity in DLFPC and its association with desire

The prefrontal cortex, which showed a video gaming-related increase, supports an assortment of cognitive functions including working memory, behavioral flexibility, attention and future planning. The DLPFC, in particular, is well interconnected with other parts of the prefrontal cortex and is able to represent many types of information, reaching from object and spatial information to response and reward outcomes as well as action strategies.[41] Therefore, the DLPFC is considered a key area for the integration of sensory information with behavioral intentions, rules and rewards. This information integration is thought to result in the facilitation of the currently most relevant action by exerting cognitive control over motor behavior.[42] In video gaming, controlled action is an important ability that is crucial for success. The observed significant increases of GM volume in the DLPFC of the training group are potentially a reflection of plasticity processes elicited by exercise of cognitive processes housed in the DLPFC. In the domain of navigation, the right lateral prefrontal cortex has been shown to be recruited during the receipt of ambiguous navigational information,[43] which might arise from the situation in which participants need to integrate the information for the first-person perspective on the top screen and the bird's eye view information provided on the bottom of the screen.

A study attempting to predict behavioral improvements in a real-time strategy video game from magnetic resonance imaging measures acquired before training found a positive relationship between GM volume in left DLPFC and improvement in game time.[44] The authors discuss the role of DLPFC in video gaming according to its role in motor skill acquisition[45] as well as in executive control and working memory. The structural plasticity in DLPFC that we observed in this study may therefore be the neural basis of training effects in the domain of motor skill acquisition, executive function or both.

Concerning potential mechanisms of structural change in prefrontal cortex, first evidence has shown that long-term potentiation and long-term depression can be induced in the local circuitry within the prefrontal cortex of rats.[46] A notable characteristic of cellular mechanisms of synaptic plasticity induction in prefrontal cortex is its dopamine dependency.[47] This is consistent with the current knowledge about the rats' anatomy, namely, that prefrontal cortex receives mesocortical dopamine innervations from neurons originating from ventral tegmental area.[48] This could be the neurophysiological link to the observed positive correlation between GM volume increase in DLPFC and reported desire to play the video game. This is in line with a reported increase of striatal dopamine release during video game playing as assessed with raclopride positron emission tomography.[49]

There is evidence that dopamine levels influence the direction of plasticity. The long-term potentiation -facilitating action of higher levels of background dopamine follows an inverted-U shape curve, where both too-low and too-high levels of background dopamine fail to facilitate long-term potentiation but tend to facilitate long-term depression instead.[50] This connection between dopamine and plasticity in prefrontal cortex could relate to our finding of an association between the desire for video games and DLPFC increase. The desire-related dopamine level might foster plasticity in DLPFC. This directionality of the relationship is in line with our observation that the correlation between desire and DLPFC volume is stronger during the first compared with the second month of training. Having potential mechanism of video gaming addiction in mind one may have predicted the exact opposite, namely that the DLPFC structural change may facilitates the desire to play video games. Quite on the contrary, we interpret the directionality of effects as evidence for the notion that the initial subjective desire to play facilitates DLPFC increase.

Structural plasticity in the cerebellum

Recent functional imaging studies have substantiated the role of the cerebellum in motor control, automation and learning, in particular in the domain of motor skill acquisition.[51] In this study, we observed bilateral structural changes in lobules IV, V and VI. Anatomically, the cerebellar motor cortex spans the hemispheres of the lobules V, VI and VIII. Lobules V and VI correspond to the representation of the hand.[52] In line with this, ipsilateral cerebellar activation in lobules IV, V and VI has been shown during finger tapping in a functional magnetic resonance imaging study.[53] In a structural neuroimaging study, we have shown a cross-sectional association between GM volume in the right lobule VI in association with manual dexterity assessed by means of the Purdue Pegboard Dexterity test.[54] Next to the motoric involvement of the cerebellum, a recent meta-analysis on cerebellar function in neuroimaging studies came to the conclusion that spatial processing is similarly associated with left lobule VI and less prominently with right lobule VI.[55]

However, the more likely explanation seems to be that the structural plasticity observed as a result of video gaming is a reflection of the training effects of using the buttons on the gaming console to navigate the avatar. Previous studies investigating motor skills in frequent gamers have shown superior precision of arm-hand movements.[56] In therapeutic settings, video games have been successfully used to enhance motor control,[57] and in medical students to increase motor skills needed for laparoscopic surgery.[58]

Potential clinical applications

The observed neuroplastic effects of the presented video gaming intervention could be well suited as an intervention counteracting known risk factors for mental disease. Post-traumatic stress disorder[59,60] as well as neurodegenerative diseases such as dementia of the Alzheimer type[61,62] have consistently been associated with reduced hippocampal volume. Similarly, prominent biological markers of schizophrenia are volume reductions in hippocampus and prefrontal cortex.[63,64] It is highly likely that the acceptance and motivation of patients to engage in the presented video game training is superior to compliance to other types of interventions. Future studies are needed to test the effectiveness of video game training in patients, and to evaluate whether the related plasticity effects in hippocampus and DLPFC lead to symptom reduction.

Limitations

Future video game training studies should consider adding an active control group that gets a new technical device to explore, similar to the training group. This could preclude the possibility that the observed training effects are due to the examination of the novel equipment, not to the game play itself.

The prior study that assessed structural effects of video game training investigated the game Tetris.[65] The authors focused on cortical thickness measures but found no increase in DLPFC or HC, but in frontal eye fields and the temporal pole. This suggests that the structural growth of HC and DLPFC may be unique for the game genre used in this study. Future studies should test different game genres to demonstrate the specificity of structural plasticity in HC for navigation-related video games.

Furthermore, a more precise documentation of gaming success might be helpful to associate observed structural changes with performance parameters.

Another limitation of this study is the scarcity of transfer measures. Future studies should administer test batteries that cover more of the abilities that are presumably being trained by the game, including executive control and working memory.

CONCLUSION

We have been able to show structural plasticity effects in right HC, right DLPFC and bilateral cerebellum elicited by a platform video gaming intervention of 2 months. The volumetric increase in the right HC of the trained participants was associated with a change from egocentric to allocentric navigation. Participants' weekly ratings of the desire to play video games correlated positively with GM increase in HC and DLPFC. In DLPFC, this association was stronger during the first month, compared with the second month, suggesting that the reported desire causes the DLPFC growth, not the DLPFC growth an increase in desire. Future research should apply video game training in the clinical context to counteract known risk factors for mental disease such as smaller hippocampus and prefrontal cortex volume in, for example, post-traumatic stress disorder, schizophrenia and neurodegenerative disease.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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