Action video game players display increased resting state functional connectivity in the striatum and the decreased functional connectivity in the hippocampus

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Abstract

Habitual action video game playing is associated with both increased grey matter and activity in the striatum and decreased grey matter in the hippocampus. To further investigate this relationship, we tested differences in resting state functional connectivity (rsFC) between action video games players (actionVGPs) compared to non-video game players (NVGPs) using the hippocampus, the caudate nucleus and the nucleus accumbens as regions of interest. Seventeen actionVGPs and 16 NVGPs were scanned using fMRI to measure rsFC. Results show that when compared to NVGPs, actionVGPs have increased rsFC between the nucleus accumbens and the subgenual anterior cingulate cortex and between the caudate nucleus and the precentral gyrus. ActionVGPs also displayed decreased rsFC between the hippocampus and the superior temporal gyrus and between the nucleus accumbens and the ventral tegmental area. Together, these results support the previously observed relationship between frequent action video game playing and higher grey matter and activity in the reward circuit and lower grey matter within the hippocampus.

Introduction

Video game consumption is rising across the globe. It is estimated that there are 2.2 billion video game players worldwide as of 2017, with the video game market value reaching 101.1 billion in 2016 (1). Moreover, 50% of the copies of the best-selling games sold in the United Stated in 2016 are considered to be first person shooting or action video games (actionVGs) (2). The consequences of actionVG on cognition and neural structures are mixed. For example, action video game players (actionVGPs) have been shown to have enhanced visual attention, motor control and short term memory performance (3–5). On the other hand, video game playing has been associated with an increased risk of depression, addiction and lower social functioning (6,7).

Action video game playing also has a significant impact on brain function, as actionVG were observed to be associated with lower grey matter in the hippocampus (HPC) (West et al., 2017) and higher grey matter and activity in the caudate nucleus (CN) and in the nucleus accumbens (NAcc) (Kuhn & Gallinat, 2013; Kuhn et al., 2011). In parallel, the HPC and CN also play an important role in navigational strategies (Bohbot, Lerch, Thorndycraft, Iaria, & Zijdenbos, 2007; Etchamendy, Konishi, Pike, Marighetto, & Bohbot, 2012; Iaria, Petrides, Dagher, Pike, & Bohbot, 2003; Lerch et al., 2011). Specifically, the spatial strategy, linked to increased grey matter and activity in the HPC, consists in using multiple landmarks in an environment in order to create a mental representation of it, while the response strategy, linked to increased grey matter and activity in the CN, consists in the memorization of directions associated with landmarks that indicate one's position (8,9). Further supporting the relationship between action video game playing and increased activity in the CN, actionVGPs were found to use non-HPC dependent response strategies at a significantly higher rate compared to non-video

game players (NVGPs) (10,11).

The aim of the current study was to investigate differences in resting state functional connectivity (rsFC) between actionVGPs and NVGPs. Resting state functional connectivity assesses activity between brain regions at a resting state, that is, when the subject is not performing an explicit task. It is done by using temporal correlations of blood-oxygen level (BOLD) signal when lying inside an fMRI scanner with the eyes closed (12). Changes in rsFC are thought to reflect the history of network activation from the consolidation of previous experiences (13). Further, changes in rsFC have previously been observed after a puzzle/adventure video game training (14), providing evidence that functional changes from video game playing can be detected using this method. Based on the previous evidence examining the impact of habitual action video game playing on neural structures involved in learning and memory we examined the following neural structures:

1) Nucleus accumbens

The nucleus accumbens (NAcc) holds an important role in the reward circuit and addiction. For example, it was observed that both placebo and amphetamine consumption caused a similar increase in dopamine (DA) liberation in the region, suggesting its role in reward anticipation (15). An increase in DA transmission in the NAcc is putatively present in addiction (16) and its DA response following cocaine consumption was increased in participants who had previously used the substance (17). Moreover, the bottom-up processes linked to addictions and reward-seeking behaviours have been associated with subcortical circuits including most notably the NAcc (18,19). Similar observations have been made in frequent VGPs, who have shown an increased activity in the ventral striatum, which is mostly composed of the NAcc, during a monetary incentive task. The increased ventral striatum grey matter volume and functional

activity have also been linked to increased risk-taking behavior (20). An increase in DA response has also been observed when exposing frequent VGPs to game-related stimuli (21). Further, Koepp and colleagues (22) observed an increase in dopamine update within the striatum, particularly in the CN and the NAcc, during video game play. This particular increase was also correlated with video game performance.

Specific rsFC differences involving the NAcc are expected based on previous evidence examining non-video game related media. For example, Porges and Decety (23) found that there was a correlation between the rsFC and ventral anterior cingulate cortex (vACC) and the pleasure felt by watching violent sports. ActionVGs, which are often based on violence and combat, could potentially trigger a similar mechanism in its players (24). On the other hand, a decreased in rsFC linking ventral tegmental area (VTA) and the NAcc can be found in both cocaine users and problematic video game use (25,26). Since actionVGPs are regular users, we expect similar findings to studies involving problematic video game players. It is therefore expected that actionVGPs will display increased functional connectivity linking the vACC while having reduced functional connectivity between NAcc and VTA.

2) Caudate nucleus

The CN holds an important role in the use of response strategies during navigation, which consists in the memorization of directions and the use of fewer landmarks in an egocentric procedural-based learning (8,9). Moreover, it is centrally involved in the brain's reward circuit and is therefore involved in addiction, cravings and motivation to seek rewarding stimuli (27,28). Importantly, it has been found that actionVGPs spontaneously use response strategies more often

than NVGPs (10,11). The implication of the CN in video gaming is further supported by findings that the dorsal striatum volume, from which the CN is a major component, allows to predict the learning curve for video game, which gets steeper with higher volumes (29). Consequently, we predict to observe increased functional connectivity involving the CN amongst actionVGPs.

3) Hippocampus

The hippocampus and the medial temporal lobe plays a central role in episodic memory (30,31) and in spatial memory and navigation (32–34). Concretely, its grey matter volume and functional activity has been linked to the spontaneous use of spatial strategies, which relies heavily on exterior stimuli in order to create a cognitive map when navigating in an environment (8,9). It was found that habitual action video game players relied more on response strategies while displaying lower amounts of grey matter in the HPC (11). Action video game playing is also associated with lower grey matter in the functionally and structurally connected entorhinal cortex (35). In addition, 90-hours actionVG training has been shown to significantly affect HPC grey matter, increasing in people who use spatial navigational strategies while reducing in response strategy users. Because actionVGPs were found to display lower grey matter in the hippocampus (11) we predicted that habitual actionVGPs will show reduced functional activity in the HPC, resulting in reduced functional connectivity. To test this, we used a seed analysis using the peak coordinate of the voxel based morphometry analysis from West et al. (11) showing reduced grey matter in the hippocampus amongst actionVGPs.

In summary, we tested four hypotheses: We predicted that actionVGPs will display increased rsFC linking the NAcc with the vACC when compared to NVGPs. ActionVGPs will also display decreased rsFC linking the NAcc with VTA when compared to NVGPs.

ActionVGPs are expected to show increased rsFC in the CN when compared to NVGPs. Finally, we hypothesize that actionVGPs will display decreased rsFC in HPC when compared to NVGPs.

Methods

Participants

A total of thirty-three participants (Twenty-nine males), who were on average 23.99 ± 3.43 years old were recruited through word of mouth and advertisements for the study. Seventeen participants were classified as actionVGPs and sixteen were classified as NVGPs in respect to the same criteria used in past studies examining differences between these equal-sized groups (10,11), participants reporting a minimum of 6 hours a week of action video game usage during the previous 6 months have been classified as players, while NVGPs have reported no action game playing during the previous 6 months. The groups did not significantly differ in terms of age (t (31) = 0.37, p = .71) and education (t (31) = 1.32, p = .18). Participants were also screened for neurological or psychiatric disorders and heavy substance use. Alcohol consumption was under 14 drinks per week and cigarette use was under 10 cigarettes per day. Informed consent was obtained in conformity with the local ethics committee requirements. Testing occurred at the Douglas Hospital Research Centre. The participants who came on site to complete the study were offered a monetary compensation equal to $9 CAD per hour.

Resting state functional connectivity analysis

The resting state fMRI data was pre-processed using the same script as described in the 1000 functional connectome project (www.nitrc.org/projects/fcon_1000) (36). This includes signal equilibration discarding the first 3 volumes, slice timing, field map and motion correction, removal of linear and quadratic trends, followed by temporal filtering (0.0005-0.1 Hz) and spatial smoothing using a 6-mm full width at half-maximum Gaussian kernel, nuisance signal

regression and resampling into Montreal Neurological Institute space with the concatenated transformations, including rigid transformation from the mean functional volume to the individual anatomical volume via FLIRT (37). This was followed by spatial normalization of the individual anatomical volume to the MNI152 brain template (3 mm isotropic resolution) using FNIRT (38). Finally, a four-dimensional time-series dataset in standard MNI space with 3mm isotropic resolution was obtained for each subject after preprocessing.

Seed-based analysis was performed as described in Zhang et al. (39) using a priori defined ROIs. Bilateral connectivity from the Nucleus accumbens, Caudate Nucleus and Hippocampus was examined. Further, an additional seed analysis was performed using the peak coordinate from the VBM analysis in West et. al. (11) – Study 1 showing reduced grey matter in the HPC amongst actionVGPs (bilateral area around the peak coordinate x = -27, y = -7.05, z = -27.97). All result were corrected for the whole volume of the brain using the false discovery rate (FDR) method.

The mean time-course of the ROI was extracted individually to calculate the whole-brain functional connectivity using Pearson's correlation along with normalization by Fisher's z-transform. This generated a z-score connectivity map for each ROI on each individual subject. Additional group analysis of these connectivity maps was performed using paired *t*-tests in SPM8, with correction for multiple comparisons (false discovery rate (FDR) corrected $p > 0.05$ and a *t*-statistic threshold of 3.16). Finally, a functional connectivity statistical map was generated for each ROI.

Results

Nucleus accumbens Seed

Higher rsFC was found between the left NAcc and right subgenual anterior cingulate cortex (sgACC), the most ventral sub-region of the vACC, in actionVGPs versus NVGPs (peak voxel: (x=3, y=15, z= -12), $t = 4.57$, $p < 0.05$ with whole brain FDR correction; Figure 1). In addition, the rsFC was significantly lower between the left NAcc and ventral tegmental area (VTA) in actionVGPs versus NVGPs (peak voxel: x=-6, y=-27, z= -6, $t = -4.98$, $p < 0.05$ with whole brain FDR correction—see Figure 2).

Caudate nucleus Seed

Resting state functional connectivity was significantly higher between the right CN and right precentral gyrus in actionVGPs compared to NVGPs (peak voxel: x=-45,y=-30, z=33; $t = 4.62$, $p < 0.05$ with whole brain FDR correction; Figure 3).

Hippocampus Seed

No significant results passed whole brain correction when examining the hippocampus-based seed. The seed based on the peak coordinate in the VBM analysis in West et al., (11)-Study 1 that showed decreased grey matter in the HPC amongst actionVGPs did, however, produce a significant result. Resting state functional connectivity was significantly lower between the right HPC and right superior temporal gyrus (STG) in actionVGPs versus NVGPs (peak voxel: x= 63, y= -54, z=18; $t = -5.25$, $p = 0.05$ with whole brain FDR correction; Figure 4)

Discussion

The present study aimed to characterize changes in resting state functional connectivity in actionVGPs when compared to NVGPs. The data supported our hypotheses involving the rsFC between the NAcc and the vACC and the NAcc and the VTA. Functional connectivity between the NAcc and the vACC was higher amongst actionVGPs compared to NVGPs, while connectivity between the NAcc and the VTA was lower amongst actionVGPs. Our results also

support previous observations that actionVGPs display higher activity and grey matter within the CN and lower grey matter within the HPC. ActionVGPs where shown to have more rsFC between the CN and precentral gyrus and lower connectivity between the HPC and STG.

With respect to the significant increase in rsFC between the left NAcc and right sgACC that we observed in actionVGPs, we hypothesize that this finding can be linked to altered function in the reward circuit. An altered NAcc is believed to be linked to addiction through reward expectations (15) while the is associated with emotional regulation (40). Further the sgACC is abnormally small in depressive people, who are hypothesized to have impaired emotional management abilities and a reduced ability to feel pleasure (41). Specifically, the rsFC linking the sgACC to the NAcc has been found to be lowered in depressive participants (42). In the same line of thinking, pleasure felt while watching combat sports was positively correlated with the rsFC, suggesting that it is particularly linked to experiencing pleasurable emotions (23). Together this suggests that pleasurable experiences in actionVG could be linked to the increase of this particular functional connectivity.

The significant decreased in rsFC between the left NAcc and the left VTA found in actionVGPs compared to NVGPs suggests a link between video game playing and addiction. These two structures are linked through the mesocorticolimbic circuit, which is implicated in addiction by shifting the hedonic set point, making rewards less satisfying in its stimulation of the reward circuit. This shift would originate from a recurrent stimulation of the reward circuit, thus blunting the reward pathways with a down-regulation of the DA in the NAcc (43,44). Further supporting its link to addiction, the functional connectivity between the VTA and the NAcc has been found to be significantly reduced and inversely correlated with video games cravings in participants with internet gaming disorder (26). This stands in line with the

previously interpreted results linking the NAcc to the sgACC by supporting the role of actionVG as a hedonic activity that would, on the long run, affect dopaminergic circuits. Also, it is worth mentioning that the link between VTA and NAcc plays an important role in long-term memory formation and emotional learning (45), suggesting that the reward circuit and emotional learning may be affected in actionVGPs. Further research is needed to confirm this hypothesis.

A significant increase in rsFC linking the right CN to the right precentral gyrus was found in actionVGPs when compared to NVGPs. The precentral gyrus is associated with motor tasks (46). Since actionVG constitutes a motor task and that general video game playing has been linked to enhanced motor skills, the increased rsFC in the region for actionVGPs was expected (5). Further suggesting its role in motor control, a similar increase in rsFC was found following administration of methylphenidate, a drug that increases DA transmission, improving gait and fine motor skills in Parkinson's disease patients (47–50). The motor-skill training explanation is further supported by a study comprised of an unsupervised 10-days actionVG training that caused an increase in functional activity in the precentral gyrus , suggesting that video games would have an impact on motor skills (51). Therefore, the increased rsFC in the regions could be associated with motor training with actionVGs.

Lastly, a significant decrease of rsFC between the right HPC and the right STG in actionVGPs when compared to NVGPs was found. While the HPC plays a role in spatial and long-term memory (8,9,30), it is worth mentioning that both functions are linked, as spatial learners tend to have better episodic memory (32). Previous researches suggest the rsFC between the STG and the HPC to be associated with long-term memory in particular, as signal strength was positively correlated with declarative memory loss in epilepsy patients after a hippocampal surgery (52). Notably, it has been found that Alzheimer's disease, which has an increased onset

risk in elderly with lower grey matter in the hippocampus and primarily affects declarative memory, negatively affected the functional connectivity (53,54). It is also correlated with episodic memory function in diabetes patients (55,56). The decreased rsFC has also been observed in schizophrenic patients, who often experience memory impairment (57). Therefore, our results suggest that declarative memory could be affected in actionVGPs through the reduced rsFC linking the HPC to the STG. This hypothesis requires further study.

Although there are several limitations to this study, the most important one would be its correlational nature. This means that no causality can be establish from the results. Therefore, future training studies will be required to establish causality. Also, no neuropsychological assessments were included in the study. We suggest that, based on the current data, future researches include measures such as episodic and general long-term memory tasks, pleasure felt when playing games and motor tasks in order to better understand the behavioural consequences of such rsFC differences. These would be particularly informative if included in a training study.

The current study demonstrates that actionVGPs' functional connectivity differences at a resting state when compared to NVGPs are, at least in come points, similar to what would be expected in addicted participants through the reduces connectivity between the NAcc and the VTA and increased connectivity between the NAcc and the sgACC. Notably, the similarities are specifically related to the hedonic aspects of the activity, meaning that actionVG are strongly pleasurable activities that significantly affect the reward system. It also suggests potential differences in motor abilities and declarative memory, the former through the increased rsFC between the CN and the precentral gyrus and the latter through the decreased rsFC between the HPC and the STG. This study also lays ground for further experimental studies involving training in a controlled environment to investigate the possible causal link of actionVG playing

on the brain. Considering the prevalence of action video gaming, it is of great importance to better understand its effects and the reasons for these effects, as this would allow suggesting improvements to the video game industry in order to negate the undesirable effects while maximizing the more desirable consequences.

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Figures

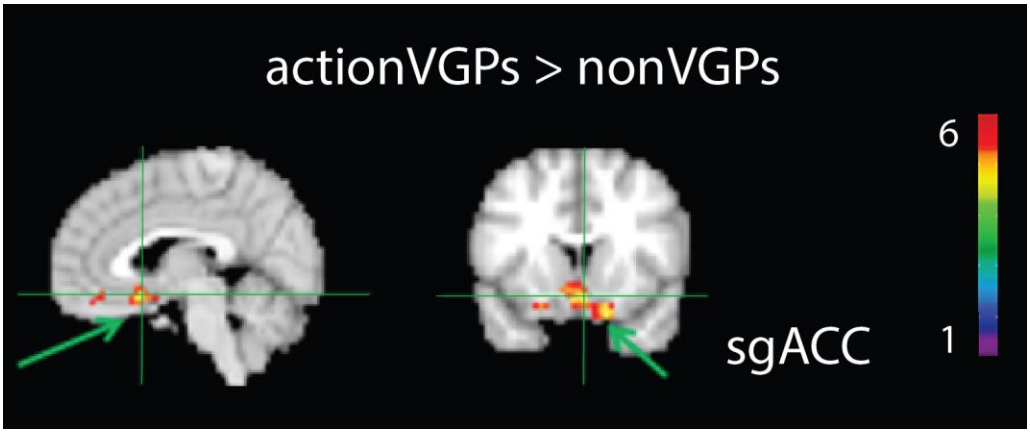

Figure 1. A significantly higher amount of rsFC was found between the left nucleus accumbens and right subgenual anterior cingulate cortex (sgACC) in actionVGPs versus nonVGPs (peak voxel: x=3, y=15, z= -12; $t = 4.57$, $p < 0.05$ whole brain FDR corrected). The color code in the bar represents the *t* statistics of regions showing the greatest difference.

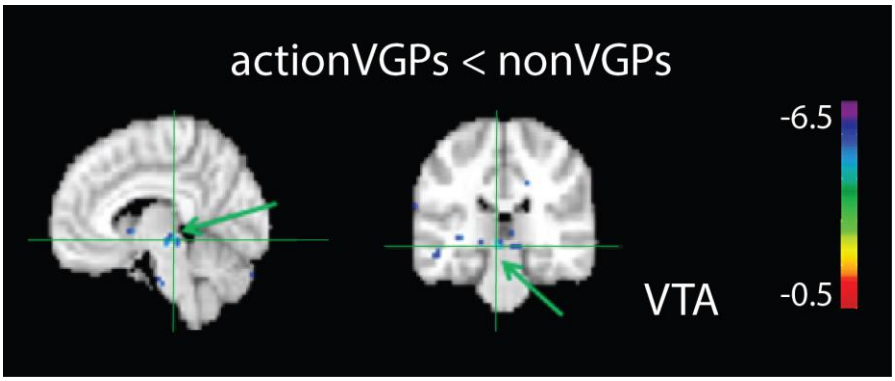

Figure 2. Lower rsFC in actionVGPs was found between the left nucleus accumbens and left ventral tegmental area (VTA) compared to nonVGPs (peak voxel: x=-6, y=-27, z= -6; t = -4.98, $p < 0.05$ with whole brain FDR correction).

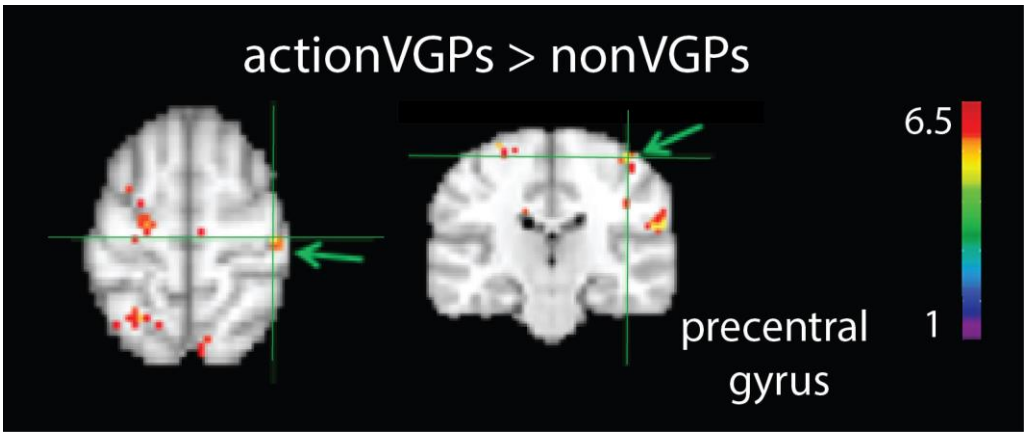

Figure 3. Higher rsFC in actionVGPs was observed between the right caudate nucleus and right precentral gyrus compared to nonVGPs (peak voxel: x=-45, y=-30, z=33; $t = 4.62$, $p < 0.05$ with whole brain FDR correction).

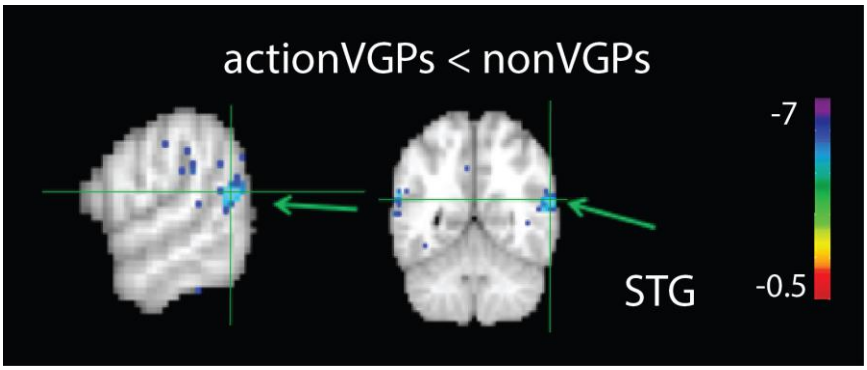

Figure 4. Significantly lower rsFC in actionVGPs was observed between the right hippocampus and the right superior temporal gyrus (STG) compared nonVGPs (peak voxel: x= 63, y= -54, z=18; t = -5.25, p = 0.05 with whole brain FDR correction).