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ORIGINAL RESEARCH

Long-lasting connectivity changes induced by intensive first-person shooter gaming

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Abstract
Action videogames have been shown to induce modifications in perceptual and cognitive systems, as well as in brain structure and function. Nevertheless, whether such changes are correlated with brain functional connectivity modifications outlasting the training period is not known. Functional magnetic resonance imaging (fMRI) was used in order to quantify acute and long-lasting connectivity changes following a sustained gaming experience on a first-person shooter (FPS) game. Thirty-five healthy participants were assigned to either a gaming or a control group prior to the acquisition of resting state fMRI data and a comprehensive cognitive assessment at baseline (T0), post-gaming (T1) and at a 3 months' follow-up (T2). Seed-based resting-state functional connectivity (rs-FC) analysis revealed a significant greater connectivity between left thalamus and left parahippocampal gyrus in the gamer group, both at T1 and at T2. Furthermore, a positive increase in the rs-FC between the cerebellum, Heschl's gyrus and the middle frontal gyrus paralleled improvements of in-gaming performance. In addition, baseline rs-FC of left supramarginal gyrus, left middle frontal gyrus and right cerebellum were associated with individual changes in videogame performance. Finally, enhancement of perceptual and attentional measures was observed at both T1 and T2, which correlated with a pattern of rs-FC changes in bilateral occipito-temporal regions belonging to the visual and attention fMRI networks. The present findings increase knowledge on functional connectivity changes induced by action videogames, pointing to a greater and long-lasting synchronization between brain regions associated with spatial orientation, visual discrimination and motor learning even after a relatively short multi-day gaming exposure.

Keywords Videogame · Functional connectivity · Cognitive training · Attention · Pulvinar

Introduction

Videogames are extremely diffused in our culture (Granic et al. 2014) and the number of investigations focusing on their impact on cognitive and brain function have significantly increased over the last few years. While the majority of research has been focused on the potentially negative impact of videogames, with evidences showing an inverse link with

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academic achievement, as well as an association with antisocial behaviour (Anderson and Dill 2000; Gentile et al. 2014), over the last 15 years multiple cross-sectional studies have reported cognitive-behavioral benefits following prolonged exposure to videogames (C.S. Green and Bavelier 2007; Latham et al. 2013; Li et al. 2010). For instance, videogame players (VGPs) have been shown to outperform non-videogamer counterparts (NVGPs) in a wide range of high and low cognitive skills, such as multitasking (C.S. Green and Bavelier 2012), mental rotation (Feng et al. 2007; Spence et al. 2009), decision making (C.S. Green et al. 2010) and attention (Feng et al. 2007; C.S. Green and Bavelier 2003, 2006a, 2006b; Spence et al. 2009). Interestingly, these benefits seem to be tightly linked to specific videogame genres (Dobrowolski et al. 2015), with a recent metanalysis showing that action videogame (AVG) enhances perceptual abilities, such as hand-eye coordination and contrast sensitivity (Bediou et al. 2018). AVG demands players to control an avatar in a 3D environment, requiring fast motion, constant monitoring of visual periphery and simultaneous tracking of multiple targets. Conversely, playing real-time strategy (RTS) games (e.g., "click and drag" games, involving tactics and planning in a simulated 2D battlefield) affect higher cognitive domains, such as cognitive flexibility, planning, and decision-making (Basak et al. 2011).

Although numerous studies have investigated the effects of videogaming at the behavioral level, the neural processes underlying these effects have received relatively little attention so far. However, since behavioral improvements in performance often offer little information without linking it to its underlying neural correlates, a recent systematic review has integrated brain and behavioural changes following a videogame experience (Palaus et al. 2017), linking performance/cognitive changes to their underlying neural correlates. As an example, this review highlighted the link between increase volume in the entorhinal cortex following a videogame experience, associated to visuospatial skills' improvement (Palaus et al. 2017).

Findings from electroencephalography (EEG) studies have suggested VGPs might be more efficient in suppressing distracting information compared to NVGPs, supporting that gaming can affect neural strategies with effects on the corresponding attentional networks (Krishnan et al. 2013; Mishra et al. 2011). In addition, recent evidences from magnetic resonance imaging (MRI) have shown how prolonged exposure to videogame might also induce changes in brain connectivity (Richlan et al. 2017) and brain structure (Momi et al. 2018). For instance, Kuhn and colleagues (Kühn et al. 2014) compared gray matter volume in a videogame group trained with the platform game "Super Mario", and a control group, with the former showing significant gray matter increase in the right hippocampal formation, right dorsolateral prefrontal cortex and bilateral cerebellum. A recent study using functional magnetic resonance imaging (fMRI) reported a less pronounced activation of the fronto-parietal and occipital networks during a visuo-attentional task in VGPs, compared to NVGPs (Bavelier et al. 2012). Less cortical activation in the absence of behavioral deficits implies that less neurons are necessary to produce the same response, suggesting more efficient processes to allocate a comparable level of attention in a less effortful manner in VGPs compared to NVGPs (Hubert-Wallander et al. 2011). Another event-related fMRI study, conducted during the execution of a complex visuomotor task, reported less activation of the fronto-parietal network in VGPs compared to NVGPs, especially during the preparation of non-standard visually guided movements (Granek et al. 2010). Expert VGPs were also found to have higher resting state functional connectivity (rs-FC) within insular regions compared to amateurs VGPs (Gong et al. 2015), such as that FC positively correlated with the average weekly amount of time spent playing. Additionally, a recent study revealed that VGPs outperformed NVGPs at the flanker task and further presented increased amplitude of low-frequency fluctuations (ALFF) in the left inferior occipital gyrus, left cerebellum and left lingual gyrus compared to NVGPs (Hou et al. 2019).

Nevertheless, most of the aforementioned studies have investigated the relationship between videogame and brain functional activity using cross-sectional approaches, which allow to define differences between VGPs and NVGPs, but fail to provide enough evidences to determine whether such effects are actually due to the videogame exposure or to other causes (Levin 2006). For instance, longitudinal gaming influences on reward processing (Lorenz et al. 2015) and reactivity to visual cues (Ahn et al. 2015) have been recently proposed. So far, rs-FC changes have been reported by only one study (Martínez et al. 2013), showing an effect after 16-h-training with RTS videogame (i.e., Professor Layton and the Pandora's box, Nintendo DS). Given the potential for game-specific brain changes, the present study aims at investigating behavioral and rs-FC changes after exposure to a competitive first person shooter (FPS) videogame, i.e., Counter-Strike: Global Offensive (CS:GO hereafter). Based on a 3D environment, FPS is a weapon-based combat genre of action videogame where the player experiences the action through the eyes of the protagonist, providing him or her a view of what an actual person would see and do in the game. Typically, the main goal of FPS is to maximize the individual score by eliminating enemies while avoiding getting killed. In particular, CS:GO is an extremely fast paced FPS where players are asked to continuously use both the keyboard and the mouse, requiring them a constant and intense eye-hand coordination, making thousands of goal-directed decisions per gaming session.

To monitor the link between cognition and functional brain changes, thirty-five subjects performed both a cognitive assessment and an fMRI scan, before (T0), immediately (T1) and 3 months (T2) after 4 weeks of intensive daily CS:GO exposure. We hypothesized that repetitive experience to FPS would modify pre-existing rs-FC patterns between brain regions subserving functions relevant for in-gaming success (e.g., orientation, visuo-motor coordination, attention, etc.), with such effects potentially persisting at T2. Moreover, we investigated whether FC changes could account for the improvements of both in-game and cognitive performances. In line with this, we examined whether individual FC profile at baseline could be useful in predicting individual in-gaming performance.

Materials and methods

Participants

Participants were healthy individuals contacted through flyers posted in several campus buildings of the University of Siena, Italy. Individuals responding to the flyers fulfilled an assessment questionnaire of their videogame habits (C. Shawn Green et al. 2017). We included only individuals who reported having less or none action videogame experience (< 3–5 h per week), neurologically and psychiatrically normal and did not consume drugs.

The final sample size consisted of 40 healthy individuals (15 females/25 males; 25.4 ± 2.8 years) which were randomly assigned either to the gamer group (9 females/16 males; 24.2 ± 2.6 years) or to the control group (6 females/9 males; 26.6 ± 3.2 years). Age, gender and education were balanced across the two groups, with no significant difference in terms of age (t-value = −1.09, $p = 0.067$). All participants had normal or corrected to normal vision acuity and normal colour vision. All gave a written informed consent to study participation. The study was approved by the Local Ethic Committee.

Study design

As shown in Fig. 1, the experimental design consisted of 30 h of gaming over a span of 5–7 weeks. All participants underwent both structural and functional MRI scan evaluations, as well as an ad-hoc cognitive assessment consisting of several cognitive tasks at three time points: before (T0), immediately (T1) and 3 months (T2) after videogame practice.

Training schedule consisted of 15 playing sessions lasting approximately 2 h each (minimum of 6 h per week, maximum of 10 h per week). The game was CS:GO, an FPS game currently used in the context of professional videogaming competitions of the Electronic Sport League (ESL) (www.eslgaming.com). This game allows the player to experience the action through the eyes of the protagonist and requires effective monitoring of the entire visual field. The game mode chosen was deathmatch, whose main goal is to kill as many opponents as possible, avoiding being killed back.

Each deathmatch game was played offline and the opponents were AI-guided enemies (so called "bot"), whose difficulty level was modulated based on subjects' previous performances in terms of kills/deaths ratio. Specifically, the level was increased every time a player scored at least twice as many kills as deaths in two consecutive games. In each game, the player joined one of the two teams (participants +4 AI-guided allies) with the aim of overpowering the opposite team (5 AI-guided enemies).

At T0, a 2-h introduction to the game mechanics and commands was provided for the participants to familiarize with the game commands. The remaining playing sessions consisted of a 10-min-warming-up block, followed by four 20 min rounds. Multiple investigators monitored the players during the training and saved their individual performances, i.e. the ratio between kills and deaths (K/D score). A break of 10 min was given between the second and the third round.

Software and hardware

Each session was carried out using dedicated desktop PCs running Windows 7 professional edition, equipped with a dedicated graphic card (ATI Radeon with 4GB), 8GB of RAM and 21″ LED displays, ensuring a constant graphic quality of >60 frames per second. Participants played the game using a mouse/keyboard/headset setup, with the possibility to adjust mouse sensitivity to their preferred level at any moment during the training.

Control group

The control group performed the cognitive and MRI evaluation with no training regime in-between T0 and T1 evaluations and no causal FPS gaming at home. Given that only few individuals from the control group (4 participants) performed the follow-up visit (T2) 3 months after the T1, the longitudinal evaluation with three time points (T0, T1 and T2) was possible only for the gamer group. Five participants in the gamer group dropped out either before the last training session or before the post-training MRI and were not included in the data analysis.

Cognitive assessment

Before and immediately after completing the training program, two tasks batteries were administered in two different visits, in order to get participants' cognitive and perceptual profiles. Each battery included several tasks that were completed in a fixed order, each task requiring approximately 5–25 min. Administered tasks covered many domains ranging from perceptual and attentional skills to high-level cognitive functions, such as fluid intelligence and working memory.

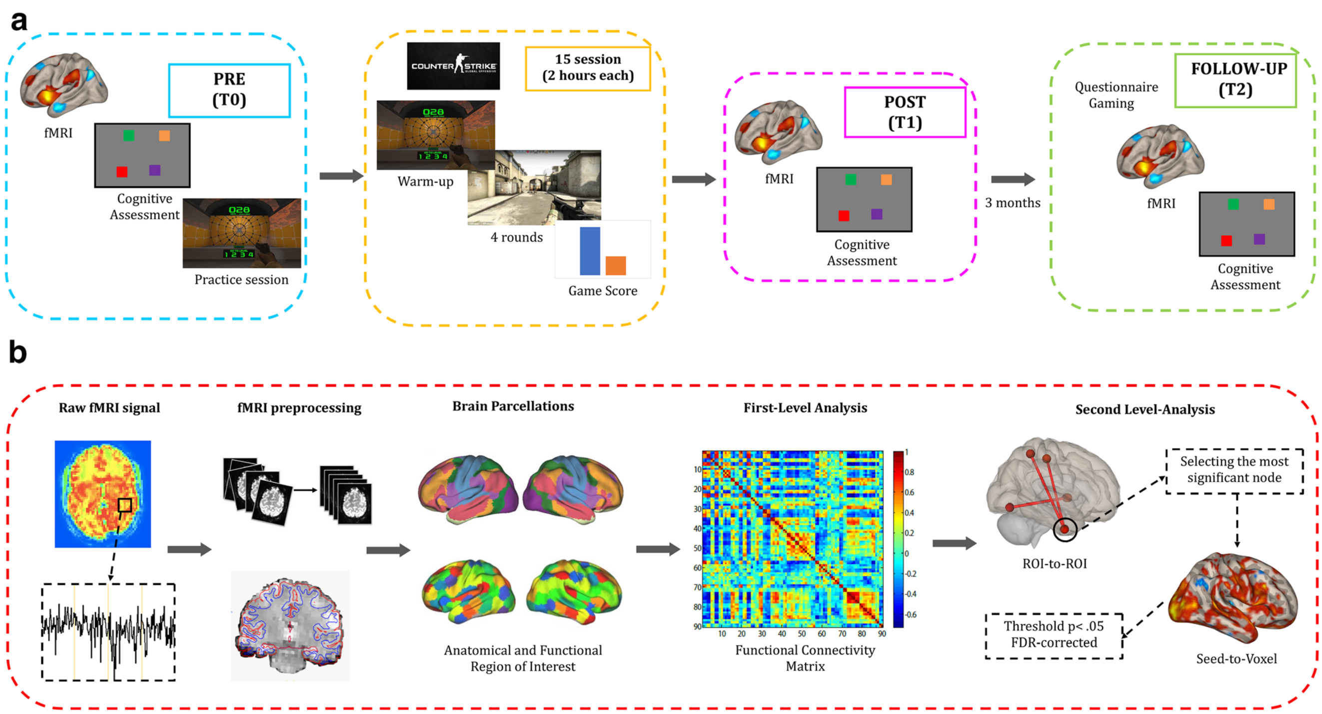

Fig. 1 **Schematic representation of the study and analysis pipeline.** **a** During the first visit (PRE T0) both a fMRI and a wide cognitive battery of tasks were performed, followed by a practice session with the FPS action videogame. Then, a training period lasting 15 sessions was carried out within approximately 1 month. At each visit, a warm-up match of 10 min was carried out, following by 4 deathmatch lasting 20 min. The game performance (calculated in term of K/D ratio) was registered after each match. Then, fMRI and cognitive assessment were performed once again both immediately (POST T1) and 3 months (FOLLOW-UP T2) after the end of the training program. A questionnaire was filled in the follow-up session where participants were asked to give a reasonable estimate on how many hours per week they had been playing videogames during the 3 months from the end of the training program. **b** The raw fMRI images were initially preprocessed. Then, two different atlas brain parcellation, either whole (Desikan et al. 2006) or network (Shirer et al. 2012) based, were employed for rs-FC analysis. The individual connectivity matrices were extracted in the first-level analysis. Finally, ROI-to-ROI comparisons were used to select the most significant node, which were employed for seed-to-voxel analysis in the second level-analysis.

Moreover, tasks where significant changes were detected after 15 sessions of the training program, were performed again at T2 (3 months after completion of training) to assess whether such changes were long lasting.

Each task was programmed and presented using E-Prime® 2.0 Professional (Psychology Software Tools Inc.; www.pstnet.com). The stimuli were presented on a 19-in. screen located 80 cm away from the participants. Based on the nature of the videogame used in our study, all tasks were concisely categorized as Near, Moderate and Far transfer tasks. We present below an overview of the cognitive assessment used, whereas a full description of each task is available in the supplementary materials and methods.

Near transfer The following tasks were used: Serial Reaction Time Task (SRTT) (Robertson 2007), Mental Rotation (MR) (Cooper 1973), Useful Field of View (UFOV) (Feng et al. 2007), Enumeration (ET) (C.S. Green and Bavelier 2006a), Visual Search (VS) (Treisman and Gelade 1980), Adaptive Flanker Compatibility Task (FT) (C.S. Green and Bavelier 2003), Attentional Blink (AB) (Raymond et al. 1992).

Moderate transfer The following tasks were used: Preparing to Overcome Prepotency (POP) (Rosano et al. 2005), Letter No-Go (LNG) (Thorell et al. 2009), Global-Local Features Task (GL) (Navon 1977).

Far transfer The following tasks were used: Raven's Advanced Progressive Matrices (RAPM) (Raven et al. 1998), Sandia Matrix Task (SM) (Matzen et al. 2010), Digit Span (DS) (Wechsler 1981), Change Localization Task (CL) (Luck and Vogel 1997).

MRI acquisition and data preprocessing

Imaging data were acquired on a Philips INTERA MRI scanner. A T1-weighted anatomical image and two resting state fMRI sessions (TR/TE 2500/40 ms, 200 scans, 23 slices, total scanning length 8 min) were acquired for each participant in rest condition. Subjects were asked to remain as still as possible and awake in the scanner, with their eyes open. SPM8 software (Statistical Parametric Mapping; http://www.fil.ion.ucl.ac.uk/spm/) was used for the preprocessing steps of the acquired images which included: slice-timing, physiological noise removal, motion-correction, normalization and smoothing. For further details on the preprocessing pipeline see supplementary materials and methods.

Behavioral statistical analysis

Cohen's d (Cohen 1988) was computed in order to provide a standardize mean difference of the effects. Then, changes of accuracy (ACC) and reaction times (RTs) were evaluated using the Statistical Package for the Social Sciences (SPSS) Version 20 (IBM Corp 2011), using a repeated measures ANOVA with a (between-subjects) factor "GROUP" (2 levels: Gamer; Controls), as well as a (within-subjects) factor "TIME" (2 levels: T0; T1). Post-hoc paired t-tests were used to detect performance changes for T1 > T0 contrast for the Controls group. Only for gamer group, another 1 × 3 repeated measures ANOVA with "Time" (3 levels: T0; T1; T2) as within-subjects factor was performed, in order to verify whether the significant effects found in the 2 × 2 ANOVA were long-lasting or not. The critical *p* value was then adjusted using Bonferroni correction to account for multiple comparisons (**.05; Bonferroni corrected; *.05 uncorrected). Even though multiple comparisons at T2 were fewer compared to T1, the same p value threshold was maintained to guarantee a more restrictive statistical inference. Mean, standard error, and *p*-values for each task are reported in Table S2.

Resting-state functional connectivity analysis

We aimed at investigating rs-FC changes at both the anatomical and network level. For this reason, both the Harvard-Oxford (cortical and subcortical) atlas (Desikan et al. (2006); www.fmrib.ox.ac.uk/fsl/) and the Shirer network-based atlas (Shirer et al. (2012); www.findlab.stanford.edu/functional_ROIs, Stanford University, Palo Alto, CA) were employed for rs-FC analysis providing a different parcellations of the same brain (Fig. 1b).

For all comparisons, a region of interest (ROI) analysis was initially conducted to identify potential differences between T0, T1 and T2. Specifically, rs-FC changes were calculated by computing the Pearson product-moment correlation coefficient between the average time series extracted from each individual ROIs. Multiple comparisons between ROIs were then performed using a two-sided contrast with a level of $p < .05$ false discovery rate (FDR) corrected (Chumbley et al. 2010).

In addition, the correlation coefficient was extracted from the most significant node and used as seed for voxel-wise analysis. A two-sided comparison with a threshold of $p < .005$ uncorrected and a cluster-level threshold of $p < .05$ FDR corrected was used. Rs-FC analyses were implemented in MATLAB using the CONN toolbox (Whitfield-Gabrieli and Nieto-Castanon (2012); www.nitrc.org/projects/conn) and different statistical testing were performed. In particular, we were interested in: (i) examine rs-FC differences between gamers and controls and evaluate their long-lasting effect, (ii) evaluate whether rs-FC changes between T1 and T0 could support in-gaming improvement, (iii) determine whether rs-FC at T0 could predict individual in-gaming performance, (iv) establish whether rs-FC changes between T1 and T0 could support the cognitive profile changes. We present below an overview of all rs-FC analyses that have been performed:

(i) **Longitudinal connectivity changes.** Two analyses were implemented contrasting both T1 > T0 (Gamer Group > Controls) and T2 > T0 (Gamer Group only). Group age and gender were entered as second-level nuisance covariates.
(ii) **Connectivity changes supporting in-gaming improvement.** Individual CS:GO raw scores at both T0 and T1 were initially corrected for the individual difficulty level during the first CS:GO session and then entered in the multiple regression model as second-level covariate of interest.
(iii) **Connectivity predicts in-gaming performance.** A multiple regression analysis was implemented to identify potential rs-FC "fingerprints" associated with more or less pronounced in-gaming performance gains after the fifteen gaming sessions. Individual changes were calculated as "T1 CS:GO score minus T0 CS:GO score" (i.e., positive value mean increase in gaming ability). In order to provide a net performance estimate, CS:GO raw scores were corrected for the individual difficulty level during the first CS:GO session.
(iv) **Connectivity changes supporting the cognitive improvement.** The cognitive tasks where a significant difference between gamer and controls was detected, were entered in the analysis as second-level covariates of interest.

Data and code availability statement

Data cannot be shared as participants were informed that their data would be stored confidentially, in accordance with the rules of the local ethics committee. Code is available upon request.

Results

Acute and long-lasting behavioral results

As shown in Fig. 2, a significant interaction Time*Group was found in the 2 × 2 ANOVA for: GL Global RTs ($F_{(1,34)}$ = 19.06, $p < 0.0001$, $d = 0.70$), AB 1st Target RTs ($F_{(1,34)}$ =

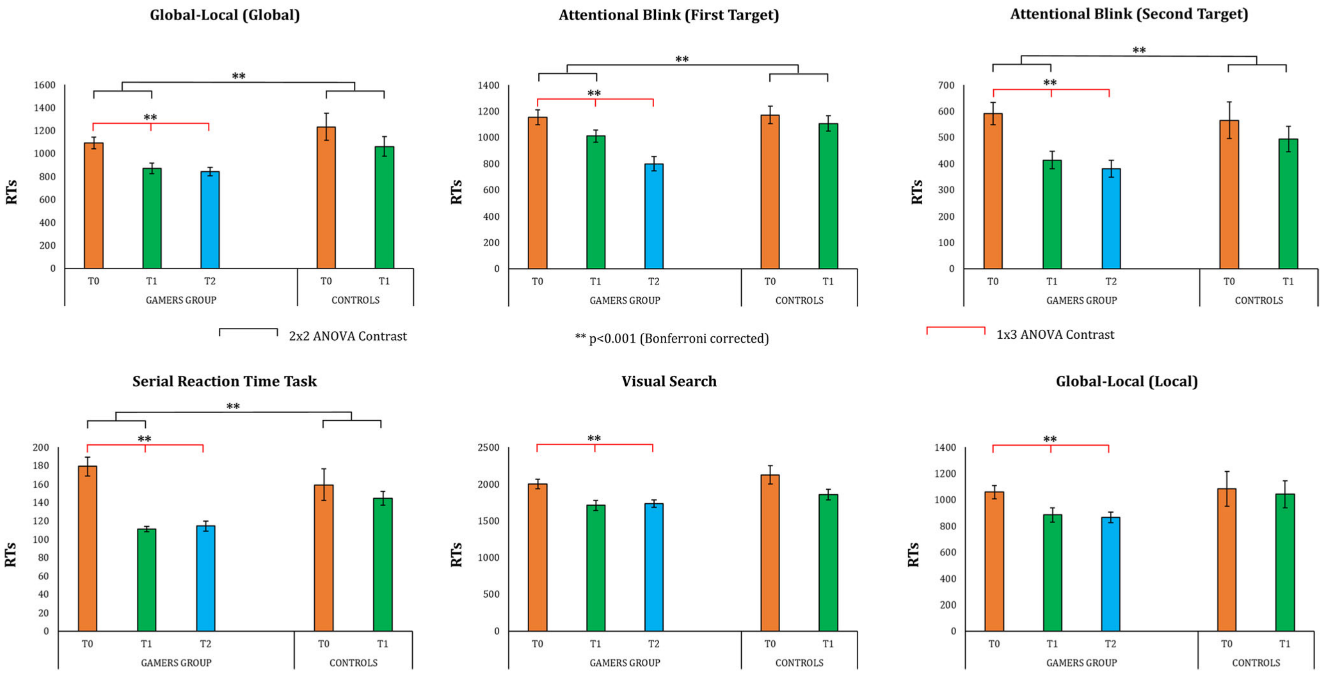

Fig. 2 Acute and long-lasting behavioural improvements after videogame practice. Means, standard error for T0 (orange), T1 (green) and T2 (blue) are reported. Significant differences between gamers and controls are shown for GL Global RTs, AB 1st Target RTs, AB 2nd Target RTs and SRTT RTs. The same improvements are present at T2 for the gamers group with addition significant improvement in VS RTs and GL Local RTs

11.41, $p < 0.0001$, $d = 0.16$), AB 2nd Target RTs ($F_{(1,34)} = 12.82$, $p < 0.0001$, $d = 0.49$), SRTT RTs ($F_{(1,34)} = 17.45$, $p < 0.0001$, $d = 0.99$).

As for the CS:GO group, the results of 1 × 3 ANOVA have shown significant differences corrected via Bonferroni (at the post-hoc level) for: VS RTs ($F_{(2,38)} = 12.38$, $p < 0.0001$, T1 > T0: speed decrease: 287.49, $p = 0.001$, $d = 0.88$; T2 > T0: speed decrease: 262.02, $p = 0.001$, $d = 0.91$), GL Global RTs ($F_{(2,38)} = 18.99$, $p < 0.0001$, T1 > T0: speed decrease: 220.87, $p < 0.0001$, $d = 0.94$; T2 > T0: speed decrease: 249.31, $p < 0.0001$, $d = 1.11$), GL Local RTs ($F_{(2,38)} = 8.18$, $p = 0.001$, T1 > T0: speed decrease: 144.17, $p = 0.01$, $d = 0.72$; T2 > T0: speed decrease: 192.93, $p = 0.001$, $d = 0.88$), AB 1st Target RTs ($F_{(2,38)} = 37.34$, $p < 0.0001$, T1 > T0: speed decrease: 141.99, $p < 0.0001$, $d = 0.60$; T2 > T0: speed decrease: 353.94, $p < 0.0001$, $d = 1.18$), AB 2nd Target RTs ($F_{(2,38)} = 30.76$, $p < 0.0001$, T1 > T0: speed decrease: 177.37, $p < 0.0001$, $d = 0.95$; T2 > T0: speed decrease: 211.18, $p < 0.0001$, $d = 1.09$), SRTT RTs ($F_{(2,38)} = 33.82$, $p < 0.0001$, T1 > T0: speed decrease: 67.99, $p < 0.0001$, $d = 1.46$; T2 > T0: speed decrease: 64.69, $p < 0.0001$, $d = 1.35$).

Moreover, an uncorrected significant change was also found for AB 2nd Target ACC ($F_{(2,38)} = 4.91$, $p = 0.01$, T1 > T0: accuracy increase:6.2%, $p = 0.01$, $d = 0.81$; T2 > T0:accuracy increase: 4.4%, $p = 0.02$, $d = 0.47$), FLA RTs ($F_{(2,38)} = 7.31$, $p = 0.002$, T1 > T0: speed decrease: 84.04, $p < 0.0001$, $d = 0.60$; T2 > T0: speed decrease: 53.21, $p = 0.07$, $d = 0.36$), MR ACC ($F_{(2,38)} = 4.54$, $p = 0.01$, T1 > T0: accuracy increase:4.8%, $p = 0.01$, $d = 0.49$; T2 > T0:accuracy increase: 3.7%, $p = 0.03$, $d = 0.37$). Notably, none of the participants reported significant changes in the amount of time spent playing videogame between T1 and T2.

Acute and long-lasting connectivity changes

As shown in Fig. 3, ROI-to-ROI analysis for rs-fMRI revealed significantly increased positive correlations for T1 > T0 comparison between the left thalamus and the left parahippocampal gyrus (F = 11.96, p-uncorrected = .0004, p-FDR = .031). The same positive connectivity change was present comparing T2 > T0 (t = 3.10, p-uncorrected = .0038, p-FDR = .34).

The left thalamus emerged as the most significant node and was therefore used for seed-to-voxel analysis. For the T1 > T0 comparison (see Fig. 3a middle left), a stronger connectivity is shown, with a large cluster of voxels in cortical and subcortical regions (k = 1292; −30, −34, −14) including the brain stem, left parahippocampal gyrus, left hippocampus and left temporal fusiform cortex. The same results were obtained considering the T2 > T0 comparison (see Fig. 3a middle right), where a significant positive connectivity increase with left parahippocampal and temporal regions (k = 541; −30, −34, −14) was found.

All regions showing more than 100 voxels of significant connectivity changes are listed in Table S3, both for T1 > T0 and T2 > T0 comparisons.

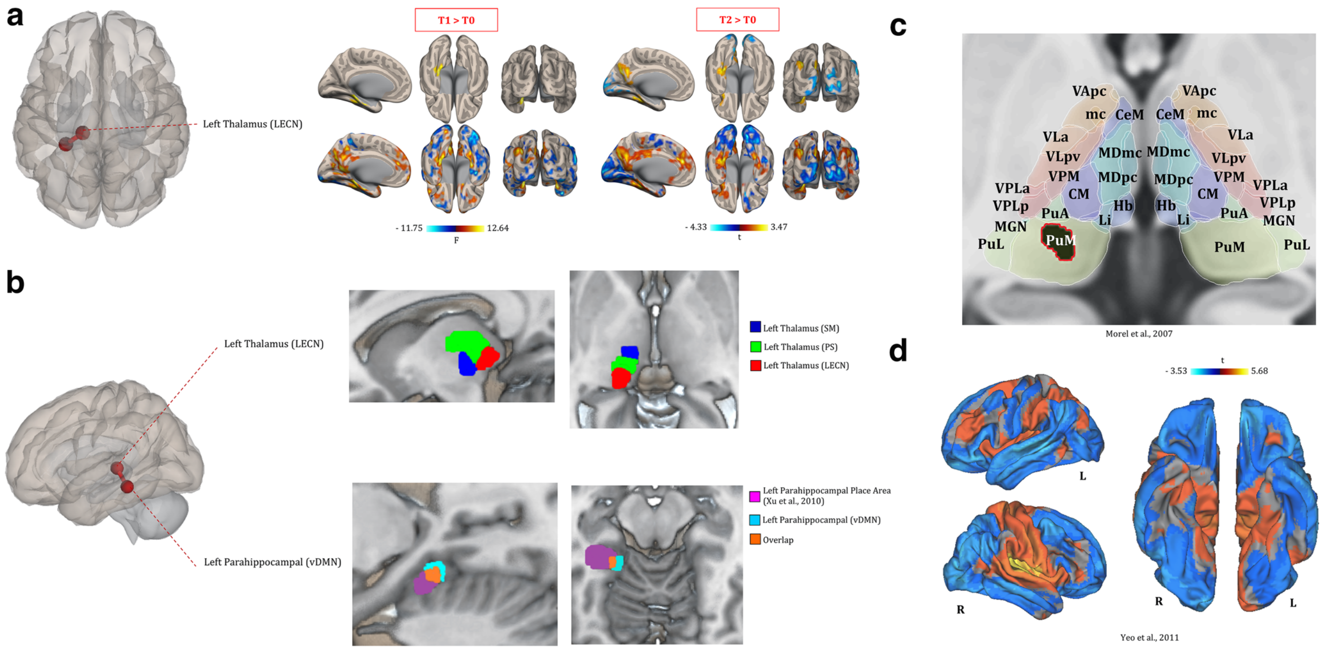

Fig. 3 **Acute and long-lasting functional connectivity changes after videogame practice**. **a** ROI-to-ROI analysis (top left) revealed a positive correlation between the Left Thalamus and Left Parahippocampal gyrus (two-sided $p < .05$, FDR-corrected). Resting State Functional connectivity (top middle) showed differences immediately (T1 > T0) and 3 months (T2 > T0) after the end of the training program. Increase (red) or decrease (blue) in Seed-to-voxel connectivity is shown for both thresholded (two-sided $p < .05$, FDR corrected) and unthresholded maps. **b** Lateral view (bottom left) of the positive correlation between the Left Thalamus and Left Parahippocampal gyrus is shown. Anatomical mapping of the ROIs (top middle) where a significant change in rs-FC was found for both Left Thalamus and Left Parahippocampal. Considering all the other Thalamic ROIs (blue and green) of the Shirer atlas (Shirer et al. 2012), the significant seed (red) was found to be the more posterior. Underneath, the structural overlap (orange) between the significant Left Parahippocampal gyrus (light blue) and the Left Parahippocampal Place Area (violet) (Xu et al. 2010) is shown. **c** Anatomical mapping of the left Thalamus showed an overlap with the left Medial Pulvinar (Niemann et al. 2000). **d** Spontaneous functional connectivity profile run on a database of 1000 healthy subjects (Yeo et al. 2011) when the significant Left Thalamus was taken as seed. A positive correlation with the Left Parahippocampal gyrus was confirmed. Note: LECN: left executive control network (Shirer et al. 2012); vDMN: ventral default mode network (Shirer et al. 2012); VApc: ventral anterior nucleus (parvocellular part); VLa: ventral lateral nucleus (anterior); VLpv: ventral lateral posterior nucleus (dorsal part); mc: ventral anterior nucleus (magnocellular part); CeM: central medial nucleus; MDmc: mediodorsal nucleus (magnocellular part); MDpc: mediodorsal nucleus (parvocellular part); CM: centre médian nucleus; Hb: habenular nucleus; Li: limitans nucleus; VPM: Ventral posterior medial nucleus; VPLa: ventral posterior lateral nucleus (anterior); VPLp: Ventral posterior lateral nucleus (posterior); MGN: medial geniculate nucleus; PuA: anterior pulvinar; PuM: medial pulvinar; PuL: lateral pulvinar

Anatomical mapping

Given the heterogeneity of both the thalamic nuclei and the parahippocampal cortex, two previously validated parcellation atlases were used to characterize the rs-FC results related to T1 > T0, T2 > T0. For instance, the significant thalamic ROI was found to be more posterior (Fig. 3b top) in respect to the other thalamic seeds of the Shirer atlas (Shirer et al. 2012). On the other hand, the significant left parahippocampal gyrus overlapped (Fig. 3b bottom) with the left parahippocampal place area (Xu et al. 2010).

As for the left thalamus, the ROI which was reported as significant in rs-FC analysis was further mapped on the anatomo-functional thalamus parcellation by Niemann et al. (Fig. 3c) (Niemann et al. 2000). The significant change seems to be exclusively related to left medial pulvinar (PuM) both for T1 > T0 and T2 > T0. Moreover, a seed-to-voxel rs-FC analysis was conducted using a large dataset ($N = 1000$)(Yeo et al. 2011) to uncover the connectivity pattern of that specific ROI (Fig. 3d). Overall, results showed a positive correlation with the lingual gyrus and the parahippocampal gyrus, as well as negative correlation with medial prefrontal cortex.

Connectivity changes supporting in-gaming improvement

As shown in Fig. 4a, ROI-to-ROI analysis revealed a hyperconnectivity between left cerebellum (lobule VII VIIb) and fronto-temporal brain regions, such as left ($t = 4.07$, p-uncorrected = .0003, p-FDR = .021) and right ($t = 3.87$, p-uncorrected = .0005, p-FDR = .021) Heschl's gyrus and the superior/middle frontal gyrus ($t = 3.46$, p-uncorrected = .0015, p-FDR = .045), both of which are related to visuo-spatial processing.

When the left cerebellum (lobule VII VIIb) was taken as node for the seed-to-voxel analysis, a significant positive

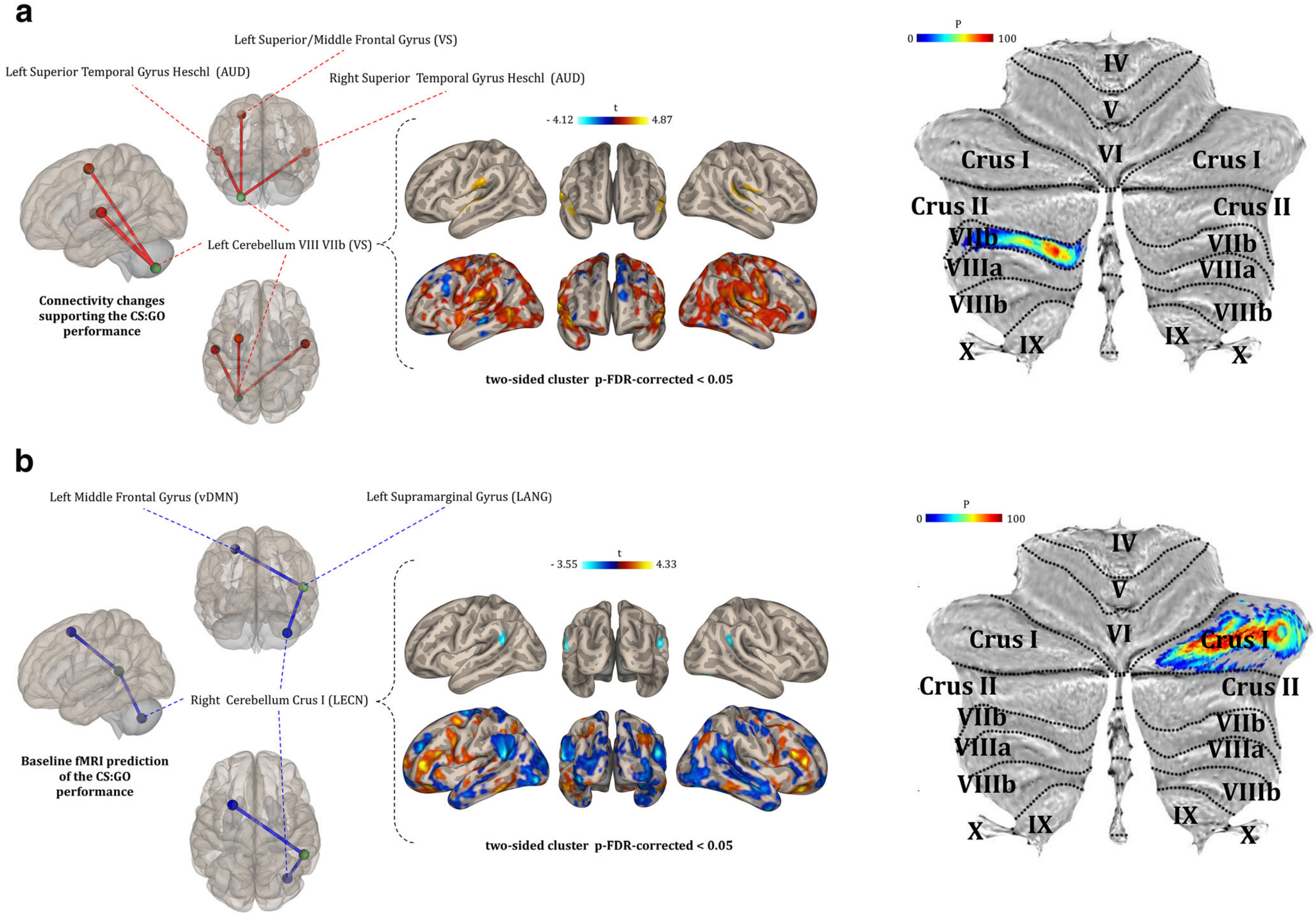

Fig. 4 Functional connectivity accounts for in-gaming performance. **a** ROI-to-ROI analysis revealed that in-gaming better performance following the training program is supported by a rs-FC increase between the left cerebellum (lobule VII VIIb), the bilateral Heschl's gyrus and the superior/middle frontal gyrus. **b** ROI-to-ROI analysis showed how participants having less rs-FC between the left supramarginal gyrus, the left middle frontal gyrus and the right cerebellum scored better in-gaming performance. Increase (red) or decrease (blue) in Seed-to-voxel connectivity threshold (two-sided $p < .05$, FDR corrected) and unthreshold maps are shown (right). Note: LECN: left executive control network (Shirer et al. 2012); VS: visuo-spatial network (Shirer et al. 2012); AUD: auditory network (Shirer et al. 2012); LANG: language network (Shirer et al. 2012); vDMN: ventral default mode network (Shirer et al. 2012)

correlation with a large cluster of voxels in the right (k = 597; 58, −20, −10) (k = 255; 50, −14, −4) and left (k = 566; −50, −22, 20) temporal brain regions was found.

Connectivity predictors of response to FPS practice

As shown in Fig. 4b, a negative correlation between the left supramarginal gyrus and both the left middle frontal gyrus (t = −4.20, p-uncorrected = .0006, p-FDR = .038) and the right cerebellum (lobule crus I) (t = −4.03, p-uncorrected = .0009, p-FDR = .038) was found following ROI-to-ROI analysis. The right cerebellum (lobule crus I) was then taken as seed for seed-to-voxel analysis, where a strong negative connectivity with the left (k = 293; −56, −62, 26) and right angular gyrus (k = 249; 54, −44, 18) and the fusiform gyrus (k = 208; −28, −76, −32) was reported.

All regions with more than 100 voxels are listed in Table S4 for both CS:GO performance indexes.

Connectivity changes supporting the cognitive gains

As for the cognitive performance, RTs were transformed as shown in Baayen (Harald Baayen 2010), so that higher rs-FC values are indicative of a better performance. When the GL RTs for Global stimuli (Fig. 5a) were taken into account, ROI-to-ROI analysis for T1 > T0 contrast revealed a negative correlation between the right brain stem and the bilateral areas of the occipital cortex, including the bilateral lingual gyrus (left F = −3.81, p-uncorrected = .0006, p-FDR = .023; right F = −13.45, p-uncorrected = .0016, p-FDR = .028), the bilateral intracalcarine cortex (left t = −13.51, p-uncorrected = .0013, p-FDR = .028; right F = −12.72, p-uncorrected = .0007, p-FDR = .023), the bilateral supracalcarine cortex (left F =

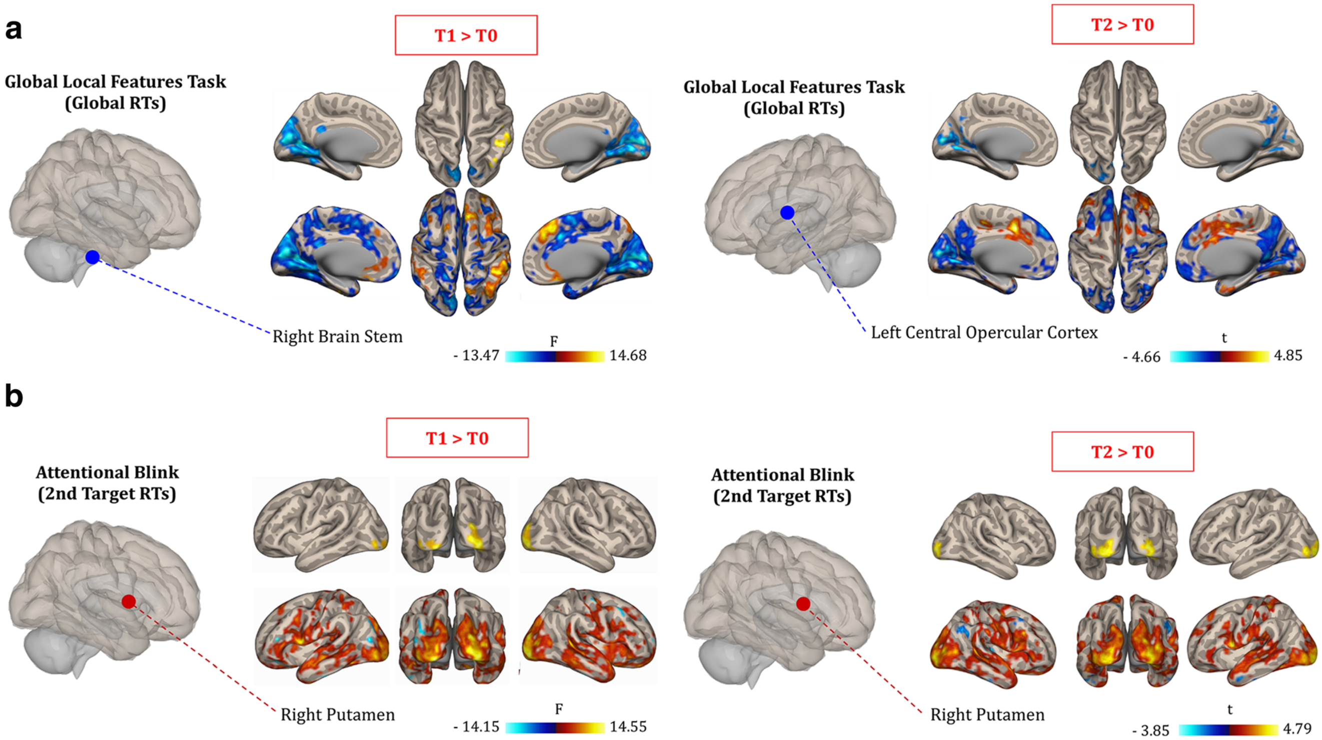

Fig. 5 Functional connectivity biomarker of cognitive improvements. **a** ROI-to-ROI analysis for Global Local Feature Task RTs revealed a connectivity decrease in occipital regions. Seed-to-voxel threshold (*p* < .005, FDR corrected) and unthreshold are showed for both T1 > T0 (left) and T2 > T0 comparisons (right). **b** ROI-to-ROI analysis for Attentional Blink 2nd target RTs showed an increased in rs-FC between right putamen and occipital brain areas. Seed-to-voxel threshold (*P* < .005, FDR corrected) and unthreshold are showed for both T1 > T0 (left) and T2 > T0 comparison (right)

−13.27, p-uncorrected = .0025, p-FDR = .039; right F = −12.67, p-uncorrected = .0008, p-FDR = .023) and the left cuneal cortex (F = −13.92, p-uncorrected = .0004, p-FDR = .023) (see Fig. 4a left).

The same connectivity changes in occipital regions were present comparing T2 > T0. Specifically, ROI-to-ROI analysis revealed a strong negative correlation between the left central operacular and the right supracalcarine cortex (t = −4.01, p-uncorrected = .0003, p-FDR = .025), the bilateral lingual gyrus (left t = −3.22, p-uncorrected = .0029, p-FDR = .046; right t = −3.57, p-uncorrected = .0011, p-FDR = .041), the bilateral intracalcarine cortex (left t = −3.38, p-uncorrected = .0019, p-FDR = .041; right t = −3.31, p-uncorrected = .0023, p-FDR = .042), the bilateral cuneal cortex (left t = −3.89, p-uncorrected = .0005, p-FDR = .025; right t = −3.16, p-uncorrected = .0034, p-FDR = .047) and the right occipital pole (t = −3.48, p-uncorrected = .0014, p-FDR = .040) (see Fig. 5a right).

As for the T1 > T0 contrast, the significant brain stem node was taken as seed for the seed-to-voxel analysis, revealing a hypo-connectivity in several bilateral occipital regions (k = 1950; 2, −94, 6), including the right occipital pole, the bilateral lingual gyrus and the bilateral intracalcarine cortex.

The same pattern was found when the left central opercular node was considered for the seed-to-voxel analysis in the T2 > T0 comparison. Again, a negative correlation was detected with the occipital pole and the bilateral cuneal cortex (k = 1339; −4, −82, 12), the right (k = 129; 26, −62, −10) and left (k = 123; −12, −74, 6) lingual gyrus.

As for the AB RTs for 2nd Target (Fig. 5b), an increase in rs-FC was found between the bilateral putamen and brain regions belonging to the occipital and temporal cortices for T1 > T0 contrast (see Fig. 4b left). Specifically, a strong positive correlation was reported between the right putamen and the right fusiform gyrus (F = 13.04, p-uncorrected = .0003, p-FDR = .016), the left putamen and the bilateral fusiform gyrus (right F = 13.59, p-uncorrected = .0001, p-FDR = .006; left F = 13.59, p-uncorrected = .0008, p-FDR = .045).

Analogous results were obtained looking at T2 > T0 comparison (see Fig. 4b right). Specifically, an increase in rs-FC was found between the right putamen and occipito-temporal brain regions, including the right occipital fusiform gyrus (t = 4.59, p-uncorrected = .0001, p-FDR = .008) and the left occipital pole (t = 3.99, p-uncorrected = .0003, p-FDR = .019). Moreover, a significant positive correlation was obtained between the left putamen and the right fusiform cortex (t = 3.86, p-uncorrected = .0005, p-FDR = .027).

When the right putamen was chosen as seed for the seed-to-voxel analysis, T1 > T0 comparison revealed a hyper-connectivity with a large cluster of voxels in the right (k = 532; −26, −94, −26) and left (k = 1235; 26, −104, −4) occipito-temporal brain regions. These findings were confirmed in the T2 > T0 comparison, whereby significant positive changes in the fusiform and occipital cortices were detected for both right (k = 746; 20, −88, −24) and left (k = 2977; −28, −80, 24) hemispheres.

All regions with more than 100 voxels are listed in Table S5 for both GL and AB. Significant performance at all the other tasks showed less consistent rs-FC patterns (see supplementary results, Fig. S1 and Table S6).

Discussion

The present study shows how even a relatively brief, albeit intense, gaming practice is able to induce connectivity changes in brain regions related to spatial orientation and perception, with effects lasting up to 3 months after gaming exposure. Individual differences in rs-FC of the left supramarginal gyrus, left middle frontal gyrus and right cerebellum were further identified as predictors of in-gaming performance changes. Below we comment on the relevance of the observed changes in connectivity, their potential link to behavior and future directions.

Acute and long-lasting connectivity changes

The most prominent functional change was evident between the left thalamus and the left parahippocampal gyrus in terms of greater connectivity. According to anatomo-functional criteria, the thalamus can be divided into five major clusters: lateral, medial, posterior, anterior nuclei and the reticular nucleus (Niemann et al. 2000). Through the use of both diffusion tensor imaging (Behrens et al. 2003; Horn and Blankenburg 2016) and fMRI data (D. Zhang et al. 2008), recent studies have identified specific connections between thalamic nuclei and cortical regions, showing highly organized patterns of coherent activity. Specifically, the anterior part of the thalamus has been shown to connect with the prefrontal cortex, forming a network playing a pivotal role in attention, learning and episodic memory. Lateral and medial parts project instead to the sensorimotor cortex, while posterior nuclei, such as the one involved in the present study, exchange connections with occipital, parietal, and temporal cortices, forming networks that are thought to play a pivotal role in attentional, as well as orientation, processing (D. Zhang et al. 2010). More specifically, changes induced by CS:GO practice exclusively involved the left medial pulvinar (PuM), which has been shown to send projection fibers to the posterior cingulate gyrus (area 23), the retrosplenial area and the posterior parahippocampal gyrus (areas TH and TF)(Baleydier and Mauguiere 1985). Remarkably, after the videogame exposure, the PuM showed an increase of rs-FC with the left parahippocampal gyrus, more specifically with PPA, which is linked to topographical learning (Aguirre et al. 1996), navigation skills and the creation of a cognitive map coding both the relationships between paths and landmarks in episodic memory (Ekstrom and Bookheimer 2007; Rauchs et al. 2008).

Interestingly, egocentric to allocentric navigation strategy was already reported to show a correlation with significant grey matter increase in the right hippocampal formation (HC) following a 2 months exposure to a 3D game (i.e. Super Mario)(Kuhn and Gallinat 2014). However, the navigation experience in a competitive FPS game is different and might explain the specificity of the results related to PPA observed in our study. Indeed, navigation abilities are put under a huge demand by FPS games, which require players to learn every detail of each map, to identify and remember useful landmarks in order to take advantage of enemies. Such detailed environment mapping is unique to this type of game and translates in competitive players being able to keep playing for up to 30 s even when blinded (i.e. hit by smoke or flashbang grenades), just relying on memory. In this context, PPA might play a fundamental role in storing and retrieving information about landmarks and navigation paths. Remarkably, the rs-FC increase between PuM and parahippocampal gyrus was still significant 3 months after gaming, even with no further exposure to CS:GO. The same was true for the increased volume of the PuM (Momi et al. 2019). So far, rs-FC changes outlasting the duration of the videogame exposure have been reported only in one study (Martínez et al. 2013) using a real-time strategy game (i.e., Professor Layton and the Pandora's box, Nintendo DS). To our knowledge, the current study provides the first longitudinal evidence of long-lasting functional changes following exposure to an FPS action videogame.

Connectivity changes supporting in-game improvement

In regard of videogame performance, we found a positive correlation between CS:GO scores and networks' dynamic, in terms of greater connection between the left cerebellum (lobule VIII and VIIb), the bilateral Heschl's gyrus and the left superior and medial frontal gyri. Theories on cerebellum's functioning have been dominated by the idea that this structure is exclusively responsible for motor control aspects, such as timing (Braitenberg et al. 1997), learning (Thach 1998), or execution (Welsh et al. 1995). However, recent studies have emphasized a role for the cerebellum in a wide variety of processes involving cognitive (Ackermann 2008; Stoodley 2012) and sensory functioning (Rondi-Reig et al. 2014; Petacchi et al. 2005). Specifically, there is strong evidence for a subcortical short loop between the cerebellum and the auditory system involving the olivocochlear system, which is held responsible for the fine control of sensory transduction properties of the hearing organ (Warr 1992). By means of both positron emission tomography (PET) (Petacchi et al. 2011) and fMRI (Baumann and Mattingley 2010), recent studies have indeed reported an increased cerebellar activity in lobules VII and VIIIB during pitch discrimination, as compared to passive listening. Further neuroimaging observations have identified a network involved in auditory processing in which the cerebellum (mostly lobule VII and VIIIB) was activated together with some other neural structures, such as the posterior temporal cortex (e.g. Heschl's gyrus), the prefrontal cortex and the supplementary motor area (SMA)(Andreasen et al. 1995; Burton et al. 2001; Chee et al. 1999; Sens and de Almeida 2007). Such network might be strongly engaged by FPS games, where the success depends on the ability to localize enemies exploiting sensory information regardless of visual inputs, such as auditory sounds (e.g. footsteps, gunshots). Rs-FC increase in these structures might reflect enhanced ability to extrapolate and elaborate acoustic information, providing tangible in-gaming advantages, like the ability to estimate opponents' number and position based on their footsteps or the echo of their gunshots.

Baseline connectivity predictors of changes in gaming performance

Apart from the estimation of the impact of a given intervention, the identification of the specific features that might help predicting the likelihood of higher or lower responsiveness to a given treatment or therapy, is becoming crucial in clinical and non-clinical settings (Drysdale et al. 2017). We highlighted a very interesting, yet preliminary, predictor of responsiveness to FPS gaming in the left supramarginal gyrus, the left middle frontal gyrus and the right cerebellum (Crus I), where participants with less rs-FC between these regions scored better at the CS:GO performance. Numerous studies have shown the involvement of the supramarginal gyrus in a wide range of processes responsible for the executive control of behavior (Kübler et al. 2006), response to aversive stimuli (Lloyd et al. 2006), visuomotor integration (Meister et al. 2004), response to visual motion (Dupont et al. 1994) and motor planning (Fincham et al. 2002). Moreover, a recent study has reported the existence of a negative connectivity at rest between the supramarginal gyrus, the cerebellar crus I and the middle frontal gyrus (S. Zhang and Li 2014). Apart from its predictive value, prospective gaming studies including a predefined assignment to a low and high rs-FC group are needed to causally validate this hypothesis.

Connectivity changes supporting cognitive enhancement

As for the cognitive performance, FPS gaming induced changes in visual and attention tasks. Cognitive improvements were limited to low level functions, accounting for near and moderate transfer. Most of the findings fit previous evidence, with selective enhancements reported at the attentional blink (Murphy and Spencer 2009), filtering (C.S. Green and Bavelier 2006b), mental rotation (Feng et al. 2007), serial reaction time (Morin-Moncet et al. 2016) and useful field of view (Murphy and Spencer 2009) tasks. However, our data further show enhancement of performance at the global-local features task, measuring inhibition/flexibility skills (Navon 1977). As for rs-FC patterns, we found a negative (Global Local Feature Task) and positive (Attentional Blink) correlation between RTs and a bilateral network including mostly visual regions, such as the intracalcarine cortex, the occipital pole and the lingual gyrus. Interestingly, a crucial role of occipital regions has been reported in previous studies using fMRI, both for Global-Local Feature (Fink et al. 1997) and Attentional Blink (Marcantoni et al. 2003) tasks. Occipital brain areas have been related to the detection of light intensity (Mentis et al. 1997), visuospatial information processing (Waberski et al. 2008), tracking visual motion patterns (Deutschländer et al. 2002), sustained attention to color and shape (Le et al. 1998), orientation-selective attention (Larsson et al. 2006), horizontal saccadic eye movements (Darby et al. 1996), visual mental imagery (Platel et al. 1997) and in predicting trajectories of moving objects (Cheong et al. 2012). Success in a FPS videogame depends on how skillful is the ability to finely discriminate and localize relevant stimuli. For this reason, changes in rs-FC across these regions might reflect a brain that is more prompt to gain better performance in attentional and visual functioning tasks.

Limitations of the study and future directions

Our results must be interpreted carefully, as the neurophysiological nature of functional connectivity changes is highly debated in the literature (Gorges et al. 2017). Despite the technical advancement in denoising the fMRI signal (Glasser et al. 2013), a perfect separation between truthful neural brain activity and noise is practically impossible (Power et al. 2014). For this reason, observed changes in FC must be interpreted with caution and additional studies are needed to investigate the information flow, accounting for more sophisticated models of effective connectivity, such as the Granger Causality (Granger 1969) and Dynamic Causal Modelling (Friston et al. 2003). In addition, current diffusion tensor imaging studies aim at investigating whether these functional changes are supported by structural white matter modifications, moving toward the integration of structural connectomes and fMRI FC. Finally, future studies should be conducted in order to evaluate the specificity of the observed rs-FC changes, including an active control group playing with an FPS videogame deprived of any economic, strategy and competitive component. Moreover, given that the FPS games, and CS:GO in particular, have originally been released as online games, future efforts should be put in monitoring rs-FC changes of a team of five players playing together on a competitive online server.

Conclusion

Our findings extend over the notion that videogaming might impact cognitive and brain functioning in a beneficial way, showing long-lasting brain functional changes after intensive gaming exposure. Interestingly, observed behavioral changes might rely on functional changes affecting posterior thalamic structures and their connections with PPA, further confirming the pivotal role – and capacity for fast adaptation in response to training – played by these regions in spatial navigation, orientation and environment recognition processes.

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