



Research report

Acute and long-lasting cortical thickness changes following intensive first-person action videogame practice



Davide Momi^{a,1}, Carmelo Smeralda^{a,1}, Giulia Sprugnoli^a, Salvatore Ferrone^a, Simone Rossi^{a,b,c,d}, Alessandro Rossi^{a,d}, Giorgio Di Lorenzo^e, Emiliano Santarnecchi^{a,f,*}

^a Brain Investigation & Neuromodulation Lab, Department of Medicine, Surgery and Neuroscience, Neurology and Clinical Neurophysiology Section, University of Siena, Italy

^b Siena Robotics and Systems Lab (SIRS-Lab), Engineering and Mathematics Department, University of Siena, Italy

^c Human Physiology Section, Department of Medicine, Surgery and Neuroscience, University of Siena, Siena, Italy

^d Department of Medicine, Surgery and Neuroscience, University of Siena, Siena, Italy

^e Laboratory of Psychophysiology, Chair of Psychiatry, Department of Systems Medicine, University of Rome "Tor Vergata", Rome, Italy

^f Berenson-Allen Center for Non-Invasive Brain Stimulation, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

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ABSTRACT

Recent evidence shows how an extensive gaming experience might positively impact cognitive and perceptual functioning, leading to brain structural changes observed in cross-sectional studies. Importantly, changes seem to be game-specific, reflecting gameplay styles and therefore opening to the possibility of tailoring videogames according to rehabilitation and enhancement purposes. However, whether if such brain effects can be induced even with limited gaming experience, and whether if they can outlast the gaming period, is still unknown. Here we quantified both cognitive and grey matter thickness changes following 15 daily gaming sessions based on a modified version of a 3D first-person shooter (FPS) played in laboratory settings. Twenty-nine healthy participants were randomly assigned to a control or a gaming group and underwent a cognitive assessment, an in-game performance evaluation and structural magnetic resonance imaging before (T0), immediately after (T1) and three months after the end of the experiment (T2). At T1, a significant increase in thickness of the bilateral parahippocampal cortex (PHC), somatosensory cortex (S1), superior parietal lobule (SPL) and right insula were observed. Changes in S1 matched the hand representation bilaterally, while PHC changes corresponded to the parahippocampal place area (PPA). Surprisingly, changes in thickness were still present at T2 for S1, PHC, SPL and right insula as compared to T0. Finally, surface-based regression identified the lingual gyrus as the best predictor of changes in game performance at T1. Results stress the specific impact of core game elements, such as spatial navigation and visuospatial coordination on structural brain properties, with effects outlasting even a short intensive gaming period.

1. Introduction

Videogames are pervasive throughout our society [1]. Given their recreational nature, videogames have been under severe scrutiny for their potentially detrimental effects on players, with evidence showing an inverse link between videogaming and academic achievement, with some studies suggesting an association with anti-social behaviour [2,3]. On the other hand, in the last two decades a large amount of studies have argued that, in reasonable doses, videogames might have quite powerful and positive effects on many aspects of human cognition, ranging all the way from low-level visual abilities up to high-level

executive functions [4]. Following a sufficient exposure to videogames, a selective enhancement of perceptual and cognitive skills has been found for a variety of tasks, including those measuring visual sensitivity [5,6], perceptual decision making [7], processing speed [8,9], perceptual simultaneity and temporal order judgments [10], selective attention [5,9,11–17], cognitive control [18], mental rotation [15,19,20], visual short-term memory [21–23] and divided attention [18,24,25]. Interestingly, Li and colleagues [26] have shown that such cognitive effects might last up to 4 months after the end of the training.

Even though these results provide a compelling evidence of videogames' impact on cognition, neuroanatomical and neurophysiological

* Corresponding author at: Berenson-Allen Center for Non-Invasive Brain Stimulation, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA.

E-mail address: esantarn@bidmc.harvard.edu (E. Santarnecchi).

¹ These authors contributed equally.

studies investigating the neural substrates of such behavioral improvements are quite scarce [27–30]. Furthermore, most of the behavioral and neuroimaging studies addressing the issue of videogame-related cognitive enhancement have so far employed cross-sectional designs, which allow to define differences between videogame players (VGPs) and non-videogame players (NVGPs), but with obvious limitations in defining causality between gaming and individual changes at the cognitive profile level.

The magnitude and localization of brain structural changes following videogame practice remains an open question, as much as the long-lasting nature of such effects on the brain. **One recent evidence has suggested significant changes in hippocampal volume following exposure to a videogame mostly involving spatial navigation in a 3D environment [31], making the case for game-specific brain changes reflecting the intrinsic properties of the game being played. If this holds true, different games could be used to elicit different structural brain changes, potentially constituting a restorative approach in neurological and psychiatric disorders [32].** In this framework, the present study evaluated the acute and long-lasting effects of a specific videogame type called **First-Person Shooter (FPS)**. The game requires the player to navigate a 3D environment using a first-person view, while fighting against other players or Artificial Intelligent (AI) - controlled opponents during fast paced, intense rounds. The high load on visuomotor coordination required in FPS players has recently being demonstrated to result in better performances in laparoscopic surgery simulations, compared to surgeons with multiple years of training experience [33]. Indeed, the continuous use of a computer keyboard and a mouse while playing, requires constant, intense eye-hand coordination, with players making thousands of goal-directed movements per gaming sessions (estimated around 80,000 keystrokes in the 15 sessions performed in the present study). To monitor the link between cognition and neurostructural changes, both cognitive and neuroimaging data were collected before (T0) and immediately after (T1) intensive practice (four weeks), on a modified FPS game, in a controlled laboratory environment, with a follow-up assessment (T2) three months after the gaming experience. Cognitive tasks assessing both near and far transfer were administered, as well as an ad-hoc in-game performance assessment built using the same 3D game-engine. Given the combination of navigation and visuomotor coordination, changes involving grey matter properties of regions within the somatomotor and hippocampal-parahippocampal systems were predicted, as well as changes in structures of the visual and auditory systems.

2. Material and methods

2.1. Participants and design

The study was approved by the Local Ethic Committee of the University of Siena School of Medicine (Siena, Italy). Thirty-six participants were recruited through flyers posted across campus buildings of the University of Siena. Twenty-four (9 females/15 males; 23.2 ± 2.5 years) were randomly assigned to a gaming group and twelve (6 females/ 6 males; 25.6 ± 3.1 years) to a control group, balanced for age, gender and schooling. No significant difference was found between the ages of the gaming and control group (t -value = -1.09 , $p = 0.067$). All participants reported normal or corrected to normal vision acuity and normal colour vision. All participants signed an informed consent form.

As shown in Fig. 1, each participant filled out a questionnaire investigating the amount of time spent playing different videogame genres during the past year [34]. All individuals were labelled as action videogame players (AVGPs) following recent study criteria (i.e. play more than 5 h per week), but none of them have had previous direct experience with the type of action videogame used in the present study (i.e. competitive First-Person Shooter, see the dedicated paragraph). All participants performed a structural MRI scan and 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. Participants in the FPS group carried out 30 h of gaming over a period of 4 weeks. The game practice consisted of 15 sessions lasting approximately 2 h each (minimum of 6 h per week, maximum of 10 h per week) with the prohibition of gaming at home with any videogames. Participants practiced with a videogame called “Counter-strike: Global Offensive” (CS:GO), a widely diffuse FPS game currently used in the context of professional video-gaming competitions of the Electronic Sport League (ESL) (www.eslgaming.com). The game requires high visuomotor coordination, fast reaction times and appropriate perceptual skills, on top of executive functions such as planning, flexibility and inhibition when played cooperatively in competitive matches. The game differs from any other FPS game due to its competitive nature, requiring mastering and refining tactic and strategy skills related to specific game arena played over multiple short-paced rounds. While in typical FPS games players have multiple scenarios to play and often switch scenario every few minutes of gameplay, CS:GO is played on a limited number of maps (usually 2), thus requiring a deep knowledge of team-play strategies and fine 3D navigation. The game also has an economic system, implying that performance at each round translates in specific amounts of (virtual) money earned as a result of different actions (e.g. enemies killed, support enemies killed, hostages saved), which are used to buy weapons and equipment for the team at the beginning of the following round. This requires an additional layer of executive functioning (flexibility, updating, inhibition) and long-term planning, making CS:GO an unique FPS gaming experience with a significant strategy component.

To control for practice effects due to test-retest measurement of cognitive skills, as well as to control for longitudinal fluctuations of MRI-based morphometric estimates that might be associated with practice effects, the control group completed the cognitive and MRI assessment with no training regime in-between pre (T0) and post (T1) evaluations and no causal FPS gaming at home. Only few of controls (4 participants) performed the follow-up visit (T2) 3 months after the T1, thus the longitudinal evaluation with three time points (T0, T1 and T2) was possible only for gaming group. Even though a debate about the validity of a no-contact control condition for videogame training is open [35], several evidences have shown how any game induces game type-specific cognitive and brain changes (e.g. a platform game like Super Mario [36]; an arcade game like Tetris [37]), making the comparison with any other videogame even more difficult. For this reason, we opted for a no-contact control and a rigid control of gaming practice in the active group (see the next paragraph). Five participants in the CS:GO group dropped out either before the last training session or before the post-training MRI and were not included in the data analysis and 2 others were excluded from the analyses because their CS:GO score exceeded group mean by 2 standard deviations. Final analyses were conducted on a total sample of 29 participants (i.e. training group = 17; control group = 12).

2.2. Videogame training software and hardware

CS:GO is a FPS videogame developed by the Hidden Path Entertainment and Valve Corporation (www.counter-strike.net). The game mode chosen for the 15 gaming sessions was Team-Deathmatch, consisting of 5-minutes rounds where players belonging to two opposing teams must gain the highest possible scores, increasing their rate of survival while maximizing the number of opponents being defeated at each round. The game was played offline, with participants battling against AI-guided enemies (so called “bot”), whose number was fixed to 5vs5. Each participant joins in a game independently from the other subjects which took part in our study. This was performed to gain full control over game parameters, such as the number of opponents, their difficulty level, available weapons and game scenarios. Introduction to the game was given throughout the first 2-hours session, allowing

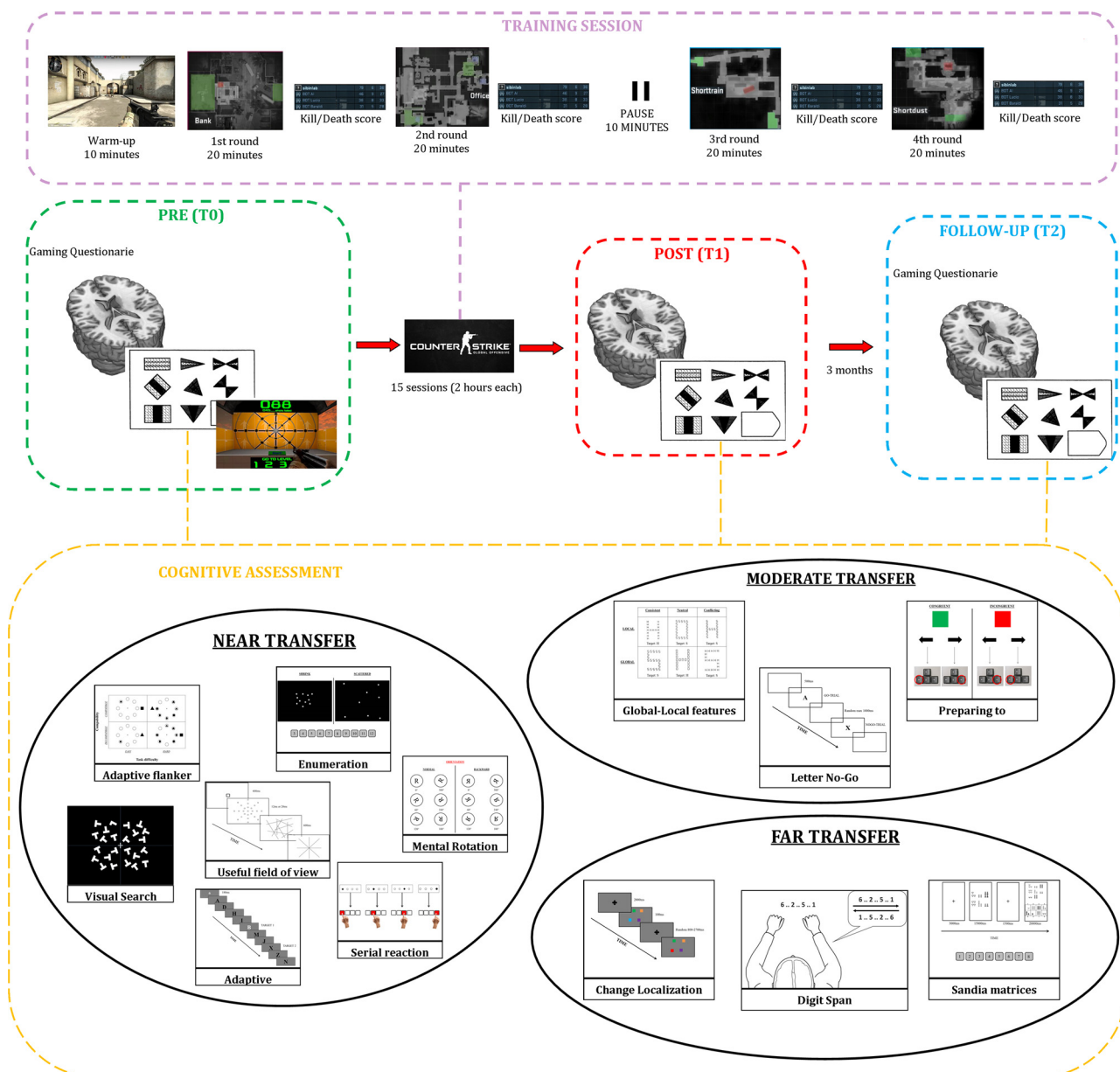


Fig. 1. Study Design. During the first visit (PRE T0) both a magnetic resonance image (MRI) and a cognitive battery of task were performed, followed by a practice session with the FPS action videogame. Then a training period lasted 15 sessions were carried out within approximately 1 month. In each visit a warm map match of 10 min were carried out following by 4 Team-Deathmatch lasted 20 min. The kill/death ratio was registered after each match and a pause of 10 min were permitted between the 2nd and the 3rd round. Then, MRI and cognitive assessment were administrated once again both immediately (POST T1) and 3 months (FOLLOW-UP T2) after the end of the training program. A questionnaire was filled both at the T0 and T2, when participants were asked to give a reasonable estimate on how many hours per week they had been playing videogames during the past year (T0) and during the 3 months from the end of the training program (T2). At the bottom, an overview of the tasks used for cognitive assessment is provided. Additional details are reported in the supplementary material.

players to become familiar with the game commands. Game mechanics included the player joining one of the two teams (i.e. participants + 4 bots) with the aim of increasing the CS:GO score of his/her team. Each session lasted two hours, with players playing non-stop for 40' (approximately 8 to 10 rounds of 5' each), then resting for 10', playing additional 40', resting for 10' and playing a final 20' round to complete the two-hours daily session. In each two-hours daily session, each participant joint one of the two teams (participants + 4 AI-guided allies) with the aim of overpowering the opposite team (5 AI-guided enemies). Each session also included a 10' warm-up where players were allowed to play freely with no performance monitoring.

Multiple investigators monitored players during training and saved their individual performances after each round in terms of the ratio between kills and death (K/D score). The initial practice session was

carried out using dedicated desktop PC 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.

2.3. MRI data acquisition

Structural magnetic resonance images (MRI) were acquired using a Philips INTERA 1.5 T MRI scanner. Whole brain structural images (T1-weighted Fast Field Echo) with 1 mm³ resolution were acquired along the AC-PC line (slices = 150; matrix size = 256 × 256; TR/TE = 30/4.6 ms; field of view = 250 mm; flip angle = 30°). To verify the absence

of grey and white matter lesions or hyperintensities, neuroradiological exams also included (i) 1-mm coronal FFE and (ii) 3-mm T2-weighted Turbo Fluid Attenuated Inversion Recovery (FLAIR) images.

2.4. Behavioral assessment

Cognitive testing at T0 was carried out over two different visits (120 min each) via E-prime 2.0 software (Psychology Software Tools Inc.; www.pstnet.com/eprime) on a Windows laptop PC at T0. The battery consisted of fifteen tasks covering multiple cognitive functions such as attention, abstract reasoning, inhibition, verbal and visuospatial working-memory, and switching (Fig. 1). Moreover, seven ad-hoc visuo-spatial tasks – tailored to assess the impact of videogames as previously shown by other groups [11–13,38]— were administered in order to control for near, moderate and far transfer. In fact, as presented in the Introduction, FPS AVG can have a direct impact on basic skills, such as attention and filtering (in the light of the continuous requirement to discriminate distractors among salience target [12]), hand-eye coordination and contrast sensitivity (greater in AVGP than respect to NVGPs [39]), and even on executive functions (i.e. cognitive flexibility, planning and decision making [40]) for the continuous real-time strategy. Therefore, tasks were categorized as “Far”, “Moderate” and “Near” transfer based on the nature of the videogame implicated in our study as considering precedent findings [11,12,38]. The entire battery was performed also at T1 (immediately after the end of the training for AVGP, that correspond in both groups to 4 weeks after T0), while at T2 (3 months later) a reduced battery composed by tasks showing a significant effect at T1 was administered. Each participant carried out the cognitive tasks after the MRI and were not allow to smock cigarette for the 2h before MRI scan, given that nicotine could affect resting-state brain network dynamics [41]. We present here an overview of the cognitive assessment used, in-length description and graphic representation of each tasks are available in the Supplementary Material and Fig. 1.

Near transfer. The following tasks were used: Serial Reaction Time Task (SRTT) [42], Mental Rotation (MR) [43], Useful Field of View (UFOV) [15], Enumeration (ET) [38], Visual Search (VS) [44], Adaptive Flanker Compatibility Task (FT) [11], Attentional Blink (AB) [45].

Moderate transfer. The following tasks were used: Preparing to Overcome Prepotency (POP) [46], Letter No-Go (LNG) [47], Global-Local Features Task (GL) [48].

Far transfer. The following tasks were used: Raven's Advanced Progressive Matrices (RAPM) [49], Sandia Matrix Task (SM) [50], Digit Span (DS) [51], Change Localization Task (CL) [52].

2.5. Cortical thickness estimation

Cortical thickness analysis was performed using the Computational Anatomy Toolbox (CAT12) (www.neuro.uni-jena.de/cat) for SPM (Statistical Parametrical Mapping, v. 12; Wellcome Trust Centre for Neuroimaging, London, UK— www.fil.ion.ucl.ac.uk/spm) and Matlab R2014a (Mathworks, inc.). Pre-processing included (i) brain tissue segmentation into cerebrospinal fluid (CSF), grey matter (GM) and white matter (WM), (ii) separation of the cortex into two hemispheres, (iii) removal of the cerebellum and brainstem, (iv) filling of subcortical regions and interpolation for the creation of a uniform surface, (v) creation of surface maps based on the cortical thickness information obtained via projection-based thickness (PBT). Specifically, tissue segmentation allows to estimate the white matter and cerebrospinal fluid distance maps [53], based on an optimized Rician non-local mean [54] and a Gaussian Hidden Markov Random Field [55] filter to increase the signal/noise ratio. Then, a probability image (“SEG”) was computed from the combination of the CSF, GM and WM probability maps [56] and subsequently masked to exclude regions with no GM layer, such as the cerebellum, the brainstem and the ventriculi. The masked SEG map was linearly interpolated to $0.5 \times 0.5 \times 0.5 \text{ mm}^3$, thereby taking into

account the small sulci with thickness of around 1 mm [57,58].

Cortical thickness was then calculated as the sum of the inner white matter distance (WMD) and outer cerebral spinal fluid distance (CSFD). Specifically, grey matter thickness (GMT) map is represented by the highest local WMD within the GM, projecting back to the GM inner boundary. The resulting surface map was then reduced to around 300,000 vertices, where each vertex of the mesh is assigned a thickness value via linear interpolation of the closest GM thickness map value. Cortical thickness estimation of certain brain regions can be difficult due to e.g. sulcal blurring and sulcal asymmetries, which might lead to partial volume error. Here we applied the aforementioned PBT method based on the reconstruction of cortical thickness using flipped boundaries [59]. Specifically, a surface reconstruction topology correction based on spherical harmonics was used to repair topological defects of the surface generated with the PBT [60]. Spherical inflation [61] and spherical registration [62] were also included in the surface reconstruction to simulate different curvature, thickness, noise, and resolution levels. The former was performed to reparametrize the surface mesh into a common coordinate system to allow inter-subject analysis using a fast algorithm to reduce spherical maps distortion. The latter was developed adapting the volume-based diffeomorphic Darte algorithm to the surface [63] in order to work with spherical maps [62]. The resulting “adjusted” images were resampled and smoothed with a 15-mm full-width-half-maximum filter (FWHM) isotropic Gaussian kernel to facilitate inferences about regionally specific group differences and to minimize smoothing across sulci. Given the longitudinal nature of the present study, customized processing steps were adopted to control for both within and between-subjects variability across time points [64]. Full images segmentation and surface reconstructions were constructed for all subjects at each time point. For each subject, a template was created based on all time points to estimate average subject anatomy. Each time points were processed taking into account intra-subject longitudinal trajectories which were then summarized at the group level providing the reliable inputs for post-processing or subsequent statistical analysis.

2.6. Analysis of longitudinal changes

The smoothed normalized tissue surfaces were analyzed using a 2×2 Flexible Factorial design with the factors “Time” (2 levels: T0, T1) and “Group” (2 levels: Gaming, Control) at the vertex-level, independently for each hemisphere, resulting in two distinct ANOVA models. Once a significant effect in the 2×2 design had been identified, a 1×3 Flexible Factorial design with the (within subjects) factor “Time” (3 levels: T0, T1 and T2) was performed. Both statistical models were based on an alpha level equal to 0.05, and results were corrected for multiple comparisons using False Discovery Rate (FDR) correction. Ages, gender, years of education and previous experiences with videogames (questionnaire responses) were entered as nuisance covariates.

2.7. Prediction of individual response to gaming practice

We aimed to determine whether if local thickness values at T0 could explain individual changes in gaming performance measured at T1. Two surface-based multiple regression analyses were implemented, independently for each hemisphere, to identify potential brain regions associated with more or less pronounced gain ingame performance after the 15 gaming sessions. Individual changes were calculated based on the difference between CS:GO scores – computed in term of Kill/Death ration (K/D) - at T1 and T0. CS:GO scores were corrected for the difficulty level of each round, providing a weighted measure of individual performance accounting for differences in game difficulty across participants. Participants with a CS:GO score exceeding group mean by 2 standard deviations were excluded from the analyses ($n = 2$).

2.8. Behavioral data analysis

Accuracy (ACC) and Reaction Times (RTs) were evaluated using the Statistical Package for the Social Sciences (SPSS) software version 20 [65]. RTs from trials on which the participant made an error were excluded from the analysis with the exception of tasks where error trials are of particular interest, such as in the LNG, GL and POP. A repeated measure ANOVA with “Time” (2 levels: T0, T1) as a within-subjects factor and “Group” (2 levels: Gaming, Control) as between-subjects factor, was used to detect between-groups changes in performance over time, T0–T1.

Then, a 1×3 repeated measures ANOVA with “Time” (3 levels: T0, T1 and T2) as within-subjects factor was performed only for the gaming group, in order to verify whether the significant effects found in the 2×2 ANOVA were replicated 3 months after training. In both ANOVA models, the critical p-value was adjusted using Bonferroni correction for multiple comparisons ($p = 0.001$ for 30 comparisons). Even though fewer tasks were administered at T2 compared to T1, the same critical p-value was maintained to guarantee a more conservative statistic. Mean, standard deviation and p-values for each contrast are summarized in Table S1 for $T1 > T0$ and in Table S2 for $T2 > T0$ comparisons.

2.9. Associations of cortical thickness and behavioral performance

Correlation between behavioral changes and significant cortical thickness changes in the participants was performed using partial correlation after correcting for age, gender, years of education and previous experience with videogames (questionnaire responses). We computed behavioral changes (T1 minus T0), as well as cortical thickness changes in the significant regions (T1 minus T0). Moreover, the same analysis was conducted correlating gaming performance changes with cognitive and morpho-volumetric changes (Fig. 7).

3. Results

3.1. Behavioral effects

As shown in Fig. 2, significant interaction Time*Group was found ($F_{(1,31)} = 4.57$, $p < 0.003$), with the CS:GO group showing significant changes in behavioral scores both at T1 and T2. Post-hoc comparisons showed significant differences in RTs for: VS ($T1 > T0$: t -value = 3.56, $p = 0.002$; $T2 > T0$: t -value = 4.19, $p < 0.001$), GL Global ($T1 > T0$: t -value = 4.28, $p < 0.001$; $T2 > T0$: t -value = 5.03, $p < 0.001$), SRTT ($T1 > T0$: t -value = 6.68, $p < 0.001$; $T2 > T0$: t -value = 5.97, $p < 0.001$), AB First Target ($T1 > T0$: t -value = 4.78, $p < 0.001$; $T2 > T0$: t -value = 7.64, $p < 0.001$), AB Second Target ($T1 > T0$: t -value = 4.89, $p < 0.001$; $T2 > T0$: t -value = 7.97, $p < 0.001$). Changes in ACC were found for: GL Global ($T1 > T0$: t -value = -123.01, $p < 0.001$; $T2 > T0$: t -value = 3.01, $p = 0.007$). Additionally, significant differences in RTs were found in the Control group for AB First Target ($T1 > T0$: t -value = 5.59, $p < 0.001$) and AB Second Target ($T1 > T0$: t -value = 5.33, $p < 0.001$).

3.2. Acute changes in cortical thickness

As shown in Fig. 3, significant regional differences in cortical thickness were observed at T1 for the CS:GO group, specifically in the bilateral parahippocampal cortex (PHC) (left: $p = 0.001$, $k = 575$; right: $p < 0.0001$, $k = 2793$), bilateral somatosensory cortex (S1) (left: $p < 0.0001$, $k = 847$; right: $p = 0.003$, $k = 912$), bilateral superior parietal lobule (SPL) (left: $p = 0.0002$, $k = 1848$; right: $p < 0.0001$, $k = 4557$) and right insula ($p = 0.003$, $k = 37$) (Fig. 3). No changes were detected in the control group.

3.3. Long-lasting thickness changes

As shown in Fig. 4, a similar pattern was present at T2, where significant increase in cortical thickness was found in the bilateral S1 (left: $p = 0.0001$, $k = 829$; right: $p < 0.0004$, $k = 1371$), left PHC ($p = 0.0001$, $k = 1468$), left SPL ($p = 0.0003$, $k = 1344$) and right insula ($p = 0.0004$, $k = 309$) (Fig. 4B).

3.4. Prediction of response to FPS gaming

A significant positive correlation between improvement in game performance (i.e. increase in CS:GO score) and cortical thickness of the left lingual gyrus was found ($R^2 = .34$, $p < 0.005$; Fig. 5), suggesting that higher thickness at baseline was predictive of a greater improvement in game accuracy throughout the training sessions.

3.5. Anatomical mapping of PHC and S1 clusters

Given that both PHC and S1 are characterized by a functional heterogeneity, two previous published parcellations were employed to functionally characterize the thickness changes observed at T1. Specifically, significant clusters were mapped using a somatotopic hand representation mask for S1 results [66], and the parahippocampal place area (PPA) mask for PHC [67]. As shown in Fig. 6, a significant overlap was found for both clusters.

3.6. Associations of cortical thickness and behavioral performance

As shown in Fig. 7, significant correlations ($p < 0.001$) between cortical thickness changes and specific cognitive functions changes in scores were found. Specifically, a significant positive correlation was observed between: left SPL-VS RTs ($R^2 = .55$, $p < 0.001$), right PHC-AB Second Target ACC ($R^2 = .37$, $p < 0.001$), right SPL-AB Second Target ACC ($R^2 = .43$, $p < 0.001$). A significant negative correlation was reported for left PHC and SRTT RTs ($R^2 = .35$, $p < 0.001$). No significant association between cortical thickness changes and in gaming performance changes was observed. However, a significant negative correlation between GL Global ACC changes and CS:GO scores was found ($R^2 = .40$, $p < 0.001$).

4. Discussion

We investigated structural neural changes resulting from a high density exposure to an FPS action gaming (~30 h). Structural brain changes in multiple cortical regions associated with attention and perceptual processes were found after training, with some long-lasting modifications persisting up to three months after the gaming experience. Moreover, the lingual gyrus, a brain structure extensively associated with visuospatial information processing, was identified as a significant predictor of changes in game performance during the training.

4.1. Acute cortical thickness changes

The most interesting result following FPS practice was a significant increase in thickness of the bilateral inferior temporo-occipital cortex, corresponding to the parahippocampal place area (PPA) (Fig. 6B). Multiple studies in the literature have claimed that PPA plays a pivotal role in navigation processing responsible for landmark retrieval [68,69] as well as in spatial route knowledge [70,71]. From a theoretical perspective, the precise role of PPA is still debated, with two different schools of thought [72]. The *spatial layout hypothesis* [73] posits that PPA processes the geometrical spatial layout of a scene (such as walls and ceiling), regardless of other elements in the scene (e.g., furniture) or of experience, memory, or semantics. On the other hand, the *spatial defining hypothesis* [74] suggests PPA might be sensitive to the

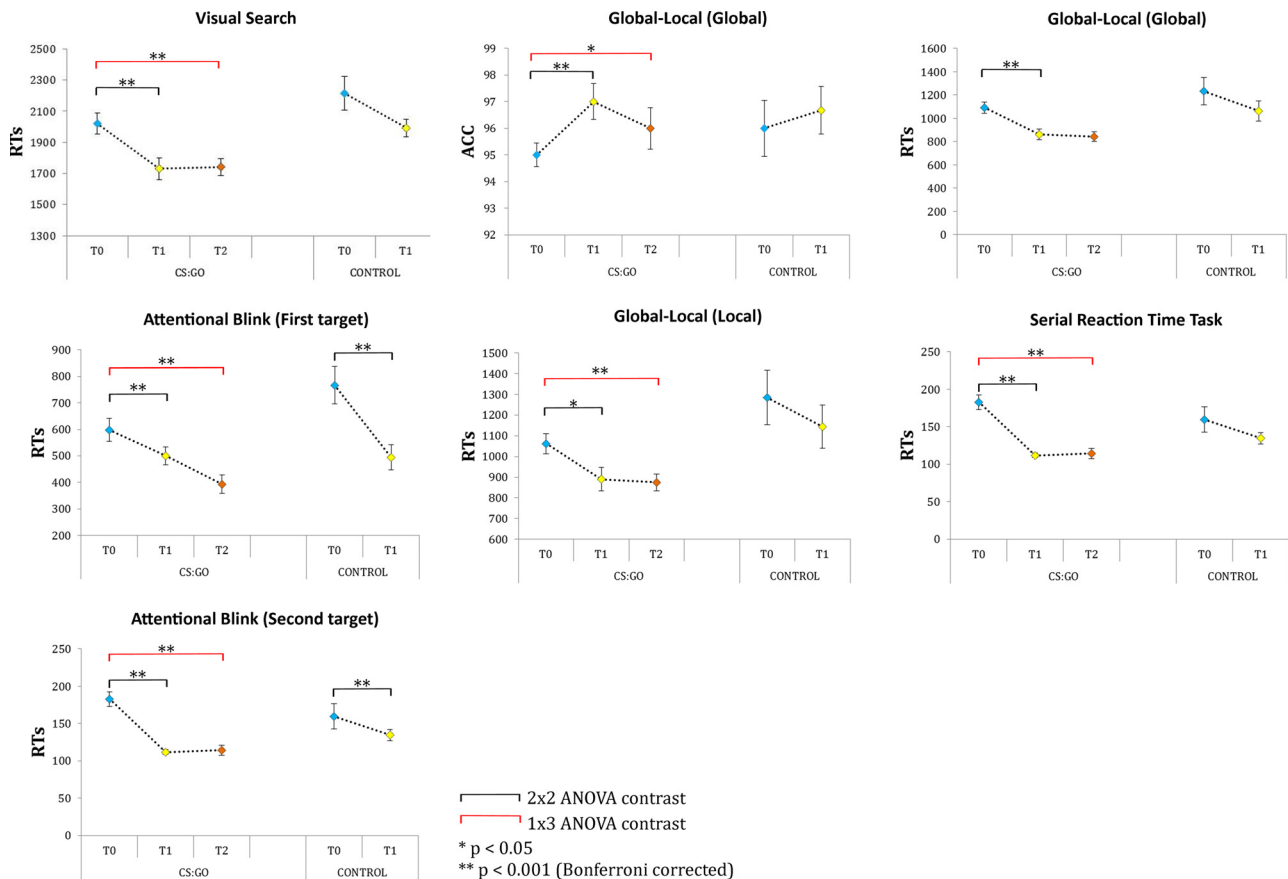


Fig. 2. Immediate and long-lasting behavioral improvement after videogame practice. Means, standard error for T0 (blue), T1 (yellow) and T2 (orange) are reported.

experience of “basic 3D space”, where even a single-object can generate a sense of 3D space regardless of spatial layouts or other contextual elements. In the context of videogames, a significant grey matter increase in the right hippocampal formation (HC) has been reported following 2 months exposure to a third-person view, 3D platform game (i.e. Super Mario), which has also been found to correlate with changes from egocentric to allocentric navigation strategies [75]. 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, differently from arcade platform games like Super Mario, where the game scenario constantly changes with progression through game levels, competitive FPS is played in few selected virtual arenas (4 in the present study). This requires players to learn even the small details of each map, in order to identify and remember useful locations spots necessary to subsequently take advantage of enemies. Such detailed environmental mapping is unique to this type of games and translates in competitive players being able to keep playing (i.e. to navigate the map while shooting enemies) up to 20 s even when virtually blind (i.e. when hit by smoke or flashbang grenades which temporarily turn the screen completely grey or white), just relying on spatial memory representations of the map. In this context, PPA might play a fundamental role in storing and retrieving information about landmarks and navigation paths.

In addition to the PPA, acute changes in thickness were found in the bilateral SPL. Numerous studies have shown the involvement of SPL in visuospatial and attentional skills, with specific contribution to mental rotation [76], stereopsis [77], visuomotor attention [78], motor imagery [79], motor execution [80], bimanual manipulation [81] and saccadic eye movement [82]. Moreover, SPL is known to play a crucial role in the early integration of visuospatial information carried by somatosensory, proprioceptive and auditory stimuli [83,84,87], providing guidance for motor operations via reciprocal connections with

the premotor cortex [83–86]. All these functions come into play during FPS gaming, which requires to continuously process and integrate auditory (e.g. footsteps, gunshots) as well as visual stimuli (e.g. teammates and enemies position).

Changes in the right insula were also observed. This might reflect its role in controlling goal-directed behaviour [88] and salience processing for inhibitory control [89]. A FPS videogame can be conceptualized as a continuous goal-directed task which requires high levels of attention and good visuospatial skills. Studies have pinpointed the insula as a critical hub for high-level cognitive control and attentional processes [90], which are put under a huge demand by FPS, where players have to maintain a high level of sustained attention and vigilance to task relevant stimuli (e.g. footsteps, visual opponent). Moreover, a recent study suggested the right insula as the neural core underlying the switch between task-relevant activation and deactivation of the default-mode network (DMN) [91], suggesting that changes in thickness might reflect player’s increased ability to engage the attentional network while disengaging other systems that are not task-relevant for the task at hand.

Finally, changes in thickness were found in bilateral S1, corresponding to the hand somatotopic representation (Fig. 6A). So far, numerous studies have shown the involvement of S1 in the somatosensory processing responsible for finger proprioception [92–94], voluntary hand movement [95], coordination of bimanual finger movements [96–98], as well as motor learning [99]. Increase in S1 thickness has been documented in professional musicians (i.e. keyboard players), suggesting its role in the planning, preparation, execution, and control of finger movements [100]. Previous studies have described a significant degree of plasticity within S1 following brief repetitive stimulation [101–103]. In FPS videogames like CS:GO, the representation of keyboard buttons to enable moving of the avatar in the 3D environment is subject to intensive remodeling, with players performing an

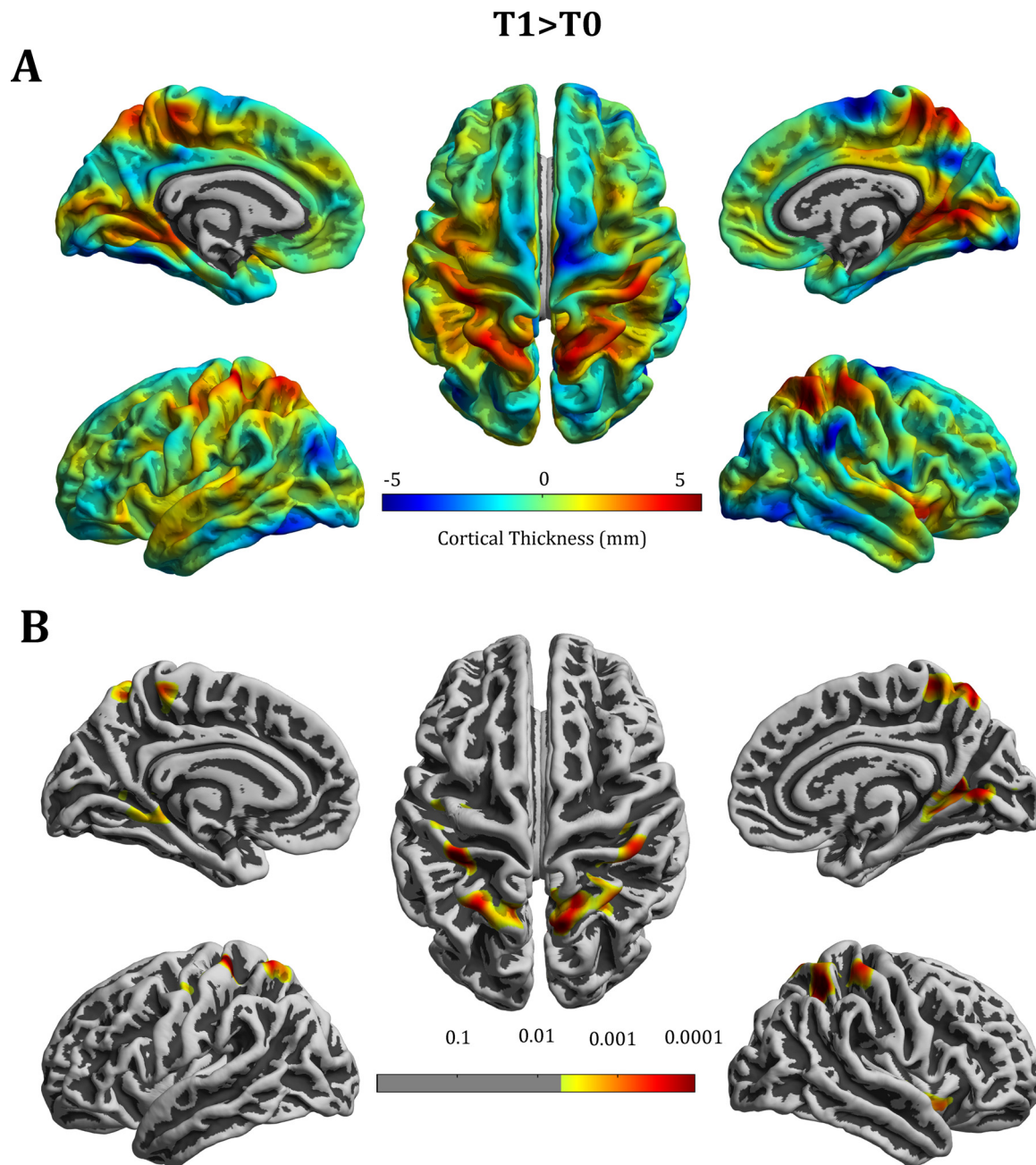


Fig. 3. Results of the 2×2 cortical thickness analysis for $T1 > T0$ comparison. The unthreshold maps (A) display increase (red) or decrease (blue) in cortical thickness (mm) while the threshold surface (B) shows only the significant cluster ($p < .001$).

estimated ~80,000 button presses during the four weeks of training. Such effect might also be amplified by the nature of each keystroke, reflecting a goal-directed selection of movements based on planned actions as well as on numerous visual feedbacks, which also engage the reward system [104]. Moreover, participants are asked to maintain a high attentional and arousal level throughout the duration of the four 20-minutes death-match rounds, constantly trying to detect relevant targets (e.g. opponents) among distractors (e.g. teammates), while planning the next 60–120 seconds of gameplay. In this regard, evidence is present on the role of attentional levels in modulating fingers' cortical somatosensory representation, which appear to depend not only on the afferent inputs, but to vary accordingly to spatial attention demands as well [105].

4.2. Long-lasting cortical thickness changes

Interestingly, our data showed the same thickness changes observed in bilateral S1, SPL (more left-lateralized) and left PPA even 3 months after the gaming experience and in the absence of any further gaming practice (according to a self-report questionnaire). Long-term changes in cortical thickness following a systematic exposure to stimulation of any kind (e.g. visual, motor) have not been documented so far. Thus, nevertheless our results provide a first evidence, such long-lasting effects also pose a more general question on the controversial nature of experience-dependent thickness changes, which are poorly understood. In fact, they do not necessarily constitute the neural basis of learning but they might rather be related to changes in the metabolic demands driven by new levels of neural activity [106]. Recent researches have reported activity-specific regional brain changes, ruling out the claim

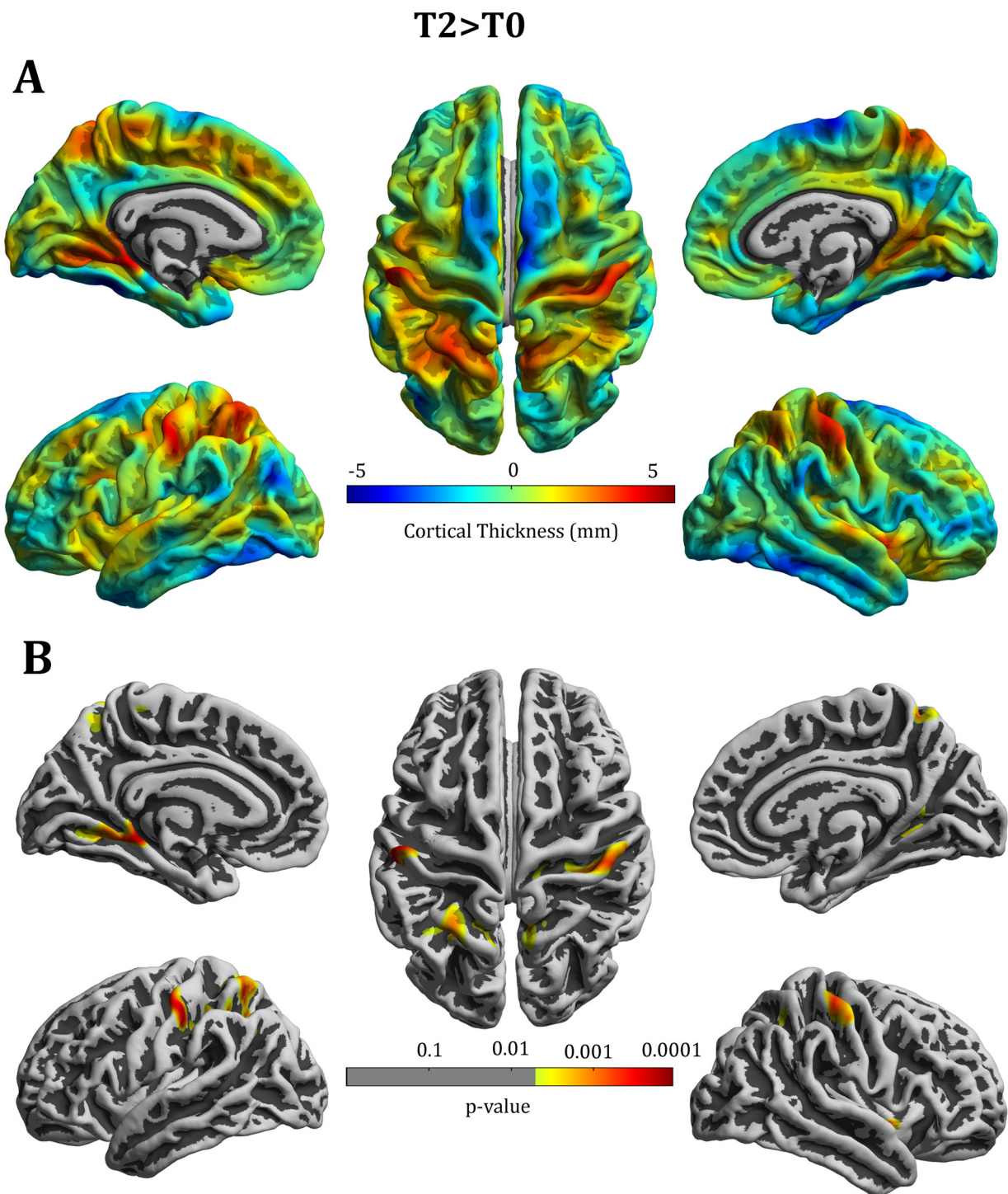


Fig. 4. Results of the 1×3 cortical thickness analysis for T2 > T0 comparison. The unthreshold maps (A) display increase (red) or decrease (blue) in cortical thickness (mm) while the threshold surface (B) shows only the significant cluster ($p < .001$).

that structural alterations might result from other confounding factors, such as changes in body size, stress or novelty of the MRI scanning environment that might have caused increased alertness and changes in perfusion [107–109]. Moreover, several human studies have demonstrated that changes in cortical thickness occur over the specific brain regions that are functionally relevant for the activity being performed [110,111]. In the present study, this might translate in the observed structural changes being modelled by the long-lasting impact of visuo-motor coordination and spatial navigation efforts that characterize the intensive gaming experience.

4.3. Structural predictors of performance enhancement

We also identified a link between baseline thickness of the left lingual gyrus and improvement in game performance. Interestingly, the lingual gyrus has been related to many visuospatial functions and skills relevant in a FPS game, such as detection of light intensity [112], visuospatial information processing [113], tracking visual motion patterns [114], sustained attention to colour and shape [115], orientation-selective attention [116], horizontal saccadic eye movements [117], visual mental imagery [118]. Even more relevant, a recent study

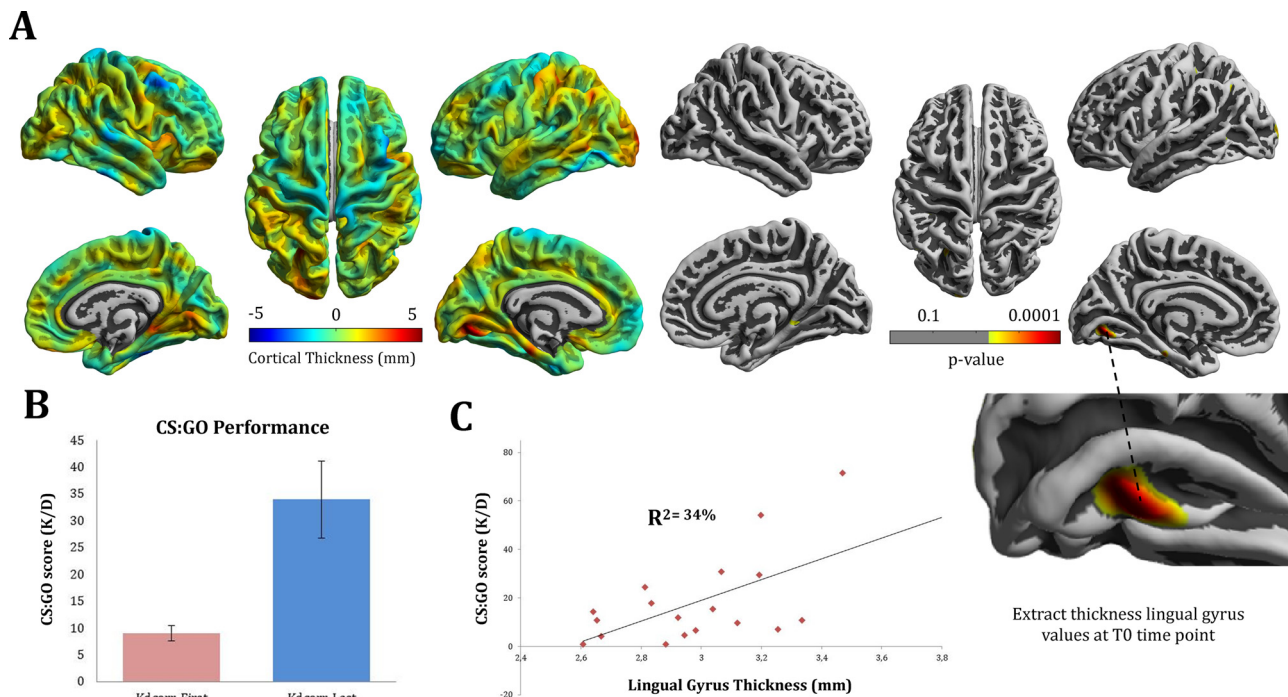


Fig. 5. Prediction of CS:GO performance based on cortical thickness at T0. A) Results of multiple regression analysis showing significant cortical thickness values at T0 for unthreshold maps (left) displaying increase (red) or decrease (blue) in cortical thickness (mm) and a threshold surface (right) with an uncorrected $p < .005$. B) Bar graph showing the in-gaming performance improvement computed in term of Kill/Death ratio (K/D) C) The positive correlation ($R^2 = .34$) between POST > PRE CS:GO scores and thickness values in lingual gyrus at T0. Two statistical outliers with CS:GO performance exceeding the sample mean ± 2 SDs were excluded from the analysis.

identified the lingual gyrus as involved in predicting the trajectories of moving objects [119], which probably constitutes the second biggest component of playing a FPS game after the ability to navigate in a 3D environment. Given that the repetitive practice in AVG has been found effective in improving cognitive functions like attention and vision [4], a better understanding of the underlying brain structural properties that could enable us to predict changes in game performance could be helpful to maximize the efficacy of FPS-based interventions for both enhancement [120] and clinical purposes [75,121].

4.4. Limits of the study and future directions

A comparison with other FPS games would be informative about the specificity of the observed structural changes, including a control group

playing a modified version of CS:GO deprived of any economic, strategy and competitive component. Moreover, for the present study we opted for a more controlled single-player experience, where the dynamics of artificial intelligence were systematically modulated to provide a challenging experience for any player. However, FPS games and CS:GO in particular, have originally been conceived as online games, such as that future efforts should be put in monitoring brain structural and functional changes of a team of five players playing together on a competitive online server. Finally, an investigation based on novel techniques for the quantification of neurite morphology (e.g. NODDI) [122] and perfusion MRI (e.g. ASL) should be considered in order to disentangle the contribution of neurite and cerebrovascular changes induced by FPS.

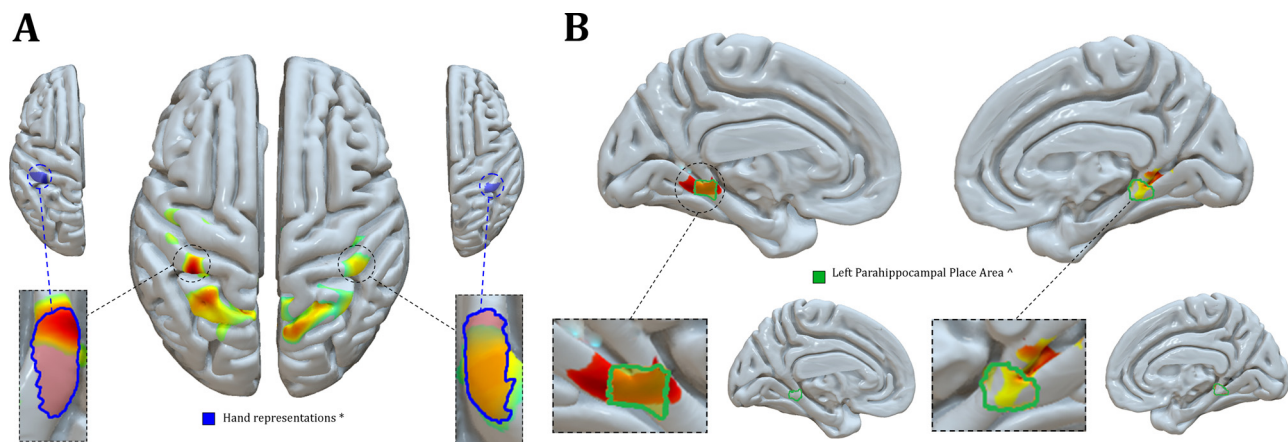


Fig. 6. Anatomical mapping of cortical thickness activation. A) Overlap between cortical thickness in the S1 results and hand somatotopic representation * [66]. B) Overlap between cortical thickness in the PHC and PPA activation * [67]. Note: S1: somatosensory cortex (S1); PHC: Parahippocampal Cortex; PPA: parahippocampal place area.

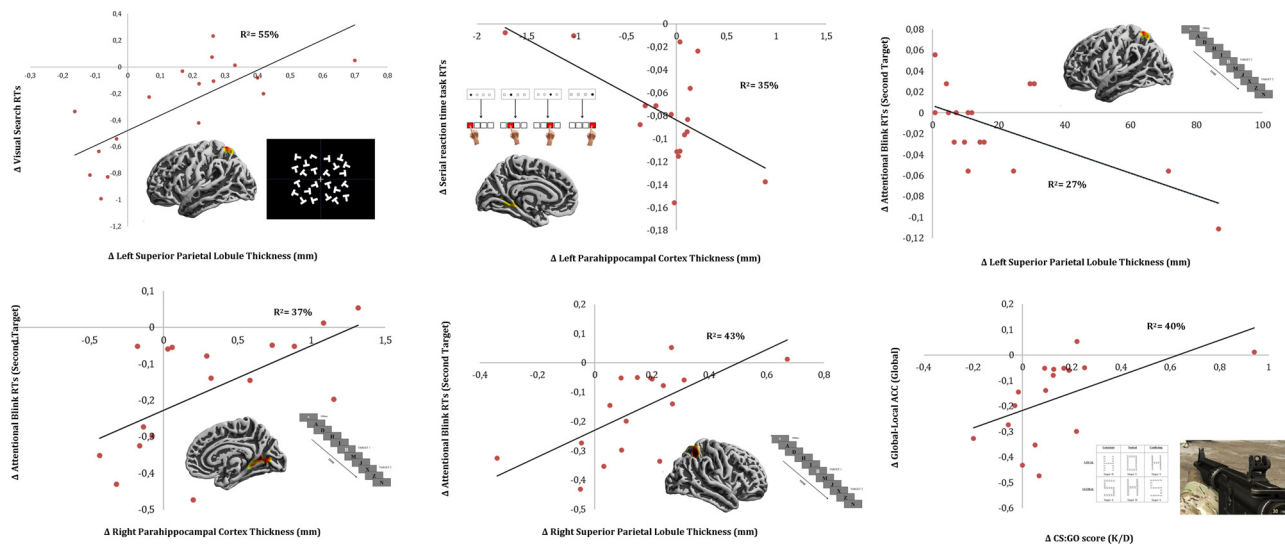


Fig. 7. Significant correlation between morpho-volumetric changes (Δ cortical thickness) and behavioral performance changes (Δ cognitive and gaming scores). Significant positive correlation ($p < 0.001$) was observed between: left SPL-VS RTs ($R^2 = .55$, $p < 0.001$), right PHC- AB Second Target ACC ($R^2 = .37$, $p < 0.001$), right SPL- AB Second Target ACC ($R^2 = .43$, $p < 0.001$). Significant negative correlation ($p < 0.001$) was found between left PHC and SRTT RTs ($R^2 = .35$, $p < 0.001$), as for GL Global ACC changes and CS:GO scores ($R^2 = .40$, $p < 0.001$). For details about the tasks, please see Supplementary Materials and Fig. 1. Note: SPL: Superior Parietal Lobe; VS: Visual Search; PHC: Parahippocampal Cortex; AB: Attentional Blink; SRTT: Serial Reaction Time Task; GL: Global-Local Features Task.

5. Conclusions

Our results extend previous cross-sectional evidence by demonstrating how videogames might affect the brain in a beneficial way, inducing changes in cognitive skills with high promises for cognitive transfer, as well as structural modifications of potential usefulness in clinical scenarios, including neurorehabilitation and neurodegenerative disorders.

Financial disclosures

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.bbr.2018.06.013>.

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