




# Thalamic morphometric changes induced by first-person action videogame training

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## Abstract

Cross-sectional data suggest videogaming as promoting modifications in perceptual and cognitive skills of players, as well as inducing structural brain changes. However, whether such changes are both possible after a systematic gaming exposure, and last beyond the training period, is not known. Here, we originally quantified immediate and long-lasting cognitive and morphometric impact of a systematic gaming experience on a first-person shooter (FPS) game. Thirty-five healthy participants, assigned to a videogaming and a control group, underwent a cognitive assessment and structural magnetic resonance imaging at baseline (T0), immediately post-gaming (T1) and after 3 months (T2). Enhancements of cognitive performance were found on perceptual and attentional measures at both T1 and T2. Morphometric analysis revealed immediate structural changes involving bilateral medial and posterior thalamic nuclei, as well as bilateral superior temporal gyrus, right precentral gyrus, and

**Abbreviations:** AB, attentional blink; ACC, accuracy; AVGPs, action video game players; CAT12, computational anatomy toolbox; CeM, central medial nucleus; CL, change localization; CM, centre median nucleus; CS:GO, counter-strike: global offensive; DLPFC, dorsolateral prefrontal cortex; DS, digit span; ESL, electronic sport league; ET, enumeration; FEF, frontal eye fields; FPS, first-person shooter; FT, flanker; GL, Global-Local features task abilities; GMV, gray matter volume; Hb, habenular nucleus; HC, hippocampal formation; IES, inverse efficiency scores; IFG, inferior frontal gyrus (IFG); L, Left; Li, limitans nucleus; LNG, Letter No-Go; MC, motor cortex; mc, ventral anterior nucleus (magnocellular part); MDmc, mediodorsal nucleus (magnocellular part); MDpc, mediodorsal nucleus (parvocellular part); MGN, medial geniculate nucleus; MOG, middle occipital gyrus; MR, mental rotation; MRI, magnetic resonance imaging; NVGPs, non-videogamer peers; POP, preparing to overcome prepotency; PuA, anterior pulvinar; PuL, lateral pulvinar; PuM, medial pulvinar; R, right; RTs, reaction times; RTS, real-time strategy; SM, Sandia matrices; SPM12, statistical parametrical mapping; SPSS, statistical package for the social sciences; SRTT, serial reaction time; STG, superior temporal gyrus; T0, pre-training; T1, post-training; T2, follow-up; TIB, test di intelligenza breve; TIV, total intracranial volume; UFOV, useful field of view; VApc, ventral anterior nucleus (parvocellular part); VBM, voxel-based morphometry; VLa, ventral lateral nucleus (anterior); VLpv, ventral lateral posterior nucleus (dorsal part); VPLa, ventral posterior lateral nucleus (anterior); VPLp, ventral posterior lateral nucleus (posterior); VPM, ventral posterior medial nucleus; VS, visual search.

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left middle occipital gyrus. Notably, significant changes in pulvinar volume were still present at T2, while a voxel-wise regression analysis also linked baseline pulvinar volume and individual changes in gaming performance. Present findings extend over the notion that videogame playing might impact cognitive and brain functioning in a beneficial way, originally showing long-term brain structural changes even months after gaming practice. The involvement of posterior thalamic structures highlights a potential link between FPS games and thalamo-cortical networks related to attention mechanisms and multisensory integration processing.

#### KEYWORDS

attention and learning, Pulvinar, thalamus, videogame, Voxel based morphometry

## 1 | INTRODUCTION

Videogames are considered the most popular pastime activity of the last two decades (Granic, Lobel, & Engels, 2014), with an emerging trend to their exploitation for neurorehabilitation purposes, both in cognitive and sensorimotor domains (Horne-Moyer, Moyer, Messer, & Messer, 2014), as well as for neuropsychiatric disorders (Kühn, Berna, Lüdtkke, Gallinat, & Moritz, 2018). According to cross-sectional evidence in healthy individuals, videogaming induces several cognitive-behavioral effects, enhancing skills such as selective attention (Green & Bavelier, 2003), short-term memory (Boot, Kramer, Simons, Fabiani, & Gratton, 2008), spatial cognition (Greenfield, 2009), multitasking (Green & Bavelier, 2006a), task-switching (Green & Bavelier, 2012), decision-making (Green, Pouget, & Bavelier, 2010), and cognitive control (Anguera et al., 2013). Interestingly, these benefits seem to be tightly linked to specific videogame genre (Dobrowolski, Hanusz, Sobczyk, Skorko, & Wiatrow, 2015) with a recent meta-analysis showing that action videogame players (AVGPs)—i.e., games where players control an avatar in a 3D environment while fighting enemies or solving puzzles—outperform their non-videogamer peers (NVGPs) on perceptual abilities such as hand-eye coordination and contrast sensitivity (Bediou et al., 2018). On the other hand, playing real-time strategy (RTS) games (i.e., “click and drag” games, involving tactics and planning in a simulated 2D battlefield) influences executive functions such as cognitive flexibility, planning, and decision-making (Basak, Voss, Erickson, Boot, & Kramer, 2011).

Even though game-specific cognitive effects might be relevant for cognitive rehabilitation, studies exploring the neural substrates of behavioral improvements are quite scarce, and those available are either based on cross-sectional evidence or cover only immediate effects (Kuhn, Gleich, Lorenz, Lindenberger, & Gallinat, 2014). For instance, Kim and colleagues (Kim et al., 2015) compared white matter connectivity in players of a RTS games (i.e., *StarCraft* and *WarCraft*)

and NVGPs, with the former showing significantly higher connectivity in the visual cortex as well as in high-order cognitive regions such as inferior frontal gyrus (IFG) and anterior cingulate cortex, while a recent study has suggested gaming-related differences in event-related potentials (Föcker, Mortazavi, Khoe, Hillyard, & Bavelier, 2018).

Evidences also suggest that the neurobiological effects of gaming are much more pronounced in people who play professionally, or for a very long time daily. For instance, the comparison of frequently vs. infrequently gaming adolescents shows a correlation between the amount of videogaming and thickness of left dorsolateral prefrontal cortex (DLPFC) and frontal eye fields (FEF) (Kuhn et al., 2014).

However, a few studies have evaluated longitudinal cognitive and brain changes in response to intensive videogame exposure. Gaming influence on reward processing (Lorenz, Gleich, Gallinat, & Kühn, 2015) and reactivity to visual cues (Ahn, Chung, & Kim, 2015) have been recently proposed, while only one study has demonstrated gray matter changes after a 2-months videogame training based on a third-person view platform game (i.e., *Super Mario 64*, Nintendo Inc.) (Kuhn et al., 2014). Given the potential for game-specific brain changes, the present study was aimed at originally investigating behavioral and morphometric 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 are typically extremely fast-paced combat games in which the main goal is to defeat enemies and maximize own chances of survival. The game can take place in present, past or futuristic scenarios, and might come in the form of either an adventure unfolding over multiple scenarios (e.g., *Super Mario 64*) or as a pure “shooter” game (i.e., *CS:GO*) where the game experience is limited to a given arena played repeatedly, stressing the focus on individual's shooting skills. In general, FPS requires intense visuomotor coordination abilities, with FPS players even performing better at laparoscopic surgery simulations than surgeons with multiple years of training (Schlickum, Hedman, Enochsson,

Kjellin, & Felländer-Tsai, 2009). CS:GO is currently the #1 FPS game in the context of professional videogaming competitions of the Electronic Sport League (ESL), with a total prize amount as its release equal to 32M\$ (www.eslgaming.com). The game requires extreme visuomotor coordination, reaction times and perceptual skills as a typical action videogame, 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 to master and refine tactic and strategy abilities related to specific game arena played over multiple short-paced rounds. While in classical FPS games (e.g., Halo, Call of Duty) players have multiple scenarios to play and often switch scenario every few minutes of gameplay, during tournaments CS:GO is played on a limited number of maps, thus requiring a deep knowledge of team-play strategies and fine 3D navigation of specific environments. The game also has an economic system, implying that performance at each round translate in specific amounts of (virtual) money earned by means of different specific actions (e.g., enemy kill, support enemy kill, hostage save), 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 (i.e., flexibility, update, inhibition) and long-term planning, making CS:GO a unique FPS gaming experience with a significant strategy component.

Here, we implemented a longitudinal design including structural MRI, an ad-hoc gaming performance test based on custom-made CS:GO scenarios, as well as an extensive cognitive evaluation performed before (T0), immediately after (T1), and 3 months after (T2) exposure to CS:GO. We hypothesized CS:GO will impact brain structures related to visuo-motor coordination, attention, perception, control of eye-movements, and multisensory integration, with such effects potentially persisting at T2.

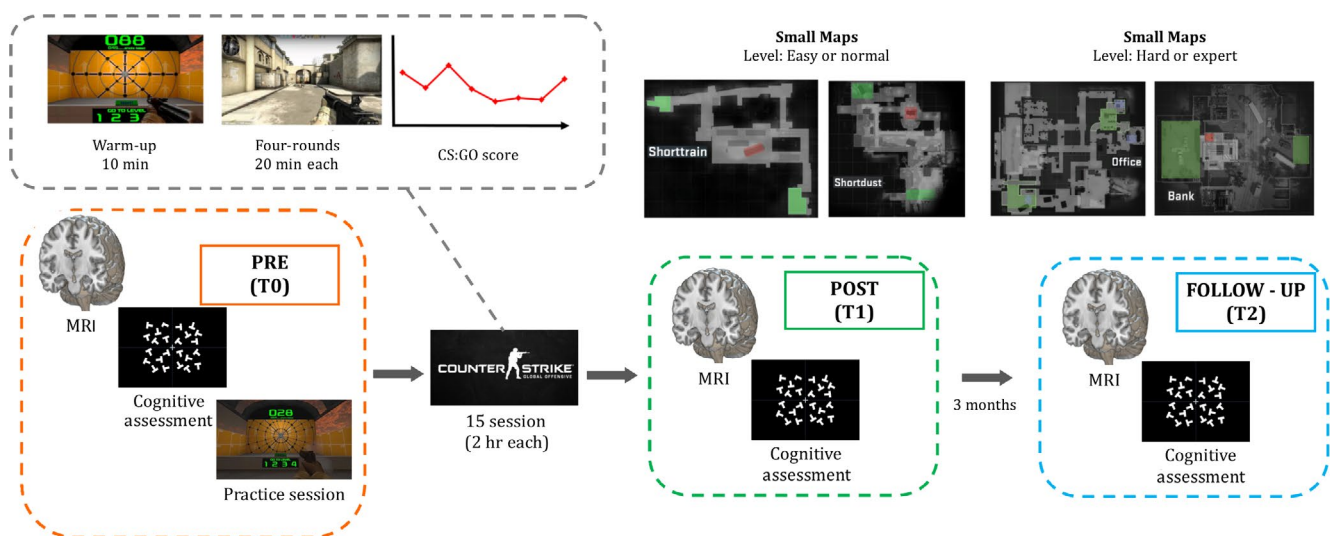
## 2 | MATERIALS AND METHODS

### 2.1 | Overall design and participants

The study was approved by the Local Ethics Committee at the Le Scotte Hospital and University of Siena School of Medicine. Each participant provided written informed consent and was compensated 70€ for the entire study. Twenty-five healthy individuals (16 males,  $24.2 \pm 2.6$  years), right-handed (Oldfield, 1971) with normal neurological and psychiatric evaluation and no history of drugs acting on the central nervous system were recruited through flyers and on-line advertisement. The same participants were used for additional morphometric and functional connectivity analyses not included as part of the present publication.

Participants carried out a pre-training cognitive assessment battery over two different days, followed by one gaming session where an introduction to CS:GO was given (Figure 1). They also underwent an in-game assessment of their gaming skill (e.g., reaction time, shooting accuracy) and a structural MRI exam (T0). Cognitive, in-game performance and MRI assessment were then repeated immediately after CS:GO practice (T1) as well as 3 months later on (T2).

After cognitive assessment and practice session, fifteen 2 hr-long daily CS:GO sessions (Monday–Friday) were carried out at the Brain Investigation and Neuromodulation Laboratory of the University of Siena School of Medicine. To control for practice effects due to test-retest measurement of cognitive skills, as well as to control for longitudinal fluctuations in MRI-based morphometric estimates that might be associated to practice-effects, a separate group of healthy young participants ( $N = 15$ ; 6 females/9 males,  $26.6 \pm 3.2$  years) completed the cognitive and MRI assessment with no training regimen in-between pre- and post-evaluations, and no FPS gaming activity at home (total sample  $25 + 15 = 40$ ). Even though a living debate



**FIGURE 1** Study overview. Schematic representations of the experimental timeline (bottom) and training session (top). [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

about the validity of a no-contact control condition for videogame training exists, several evidences have shown how any game induces game type-specific cognitive and potentially brain changes (e.g., platform games like Super Mario (Kuhn et al., 2014); arcade games like Tetris (Haier, Karama, Leyba, & Jung, 2009), making the interpretation of the comparison with other videogame potentially even more challenging, if not confounding. For this reason, we opted for a no-contact control and a rigid control of gaming practice (at home and at the lab) in both groups. In order to monitor previous videogames experience, both the CS:GO and the control group filled out a questionnaire investigating the amount of time spent playing several videogame genres during the past year (Green et al., 2017). All the participants qualified as AVGPs (>5 hr week), but did not report any previous experience with the videogame used in the present study (CS:GO, see below). Moreover, an adapted version of the gaming questionnaire was also administered at T2, to establish how many hours participants kept playing videogames during the 3 months interval from T0. 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 (final sample  $40 - 5 = 35$ ).

For further details on the pre-training in-game assessment as well as on how the in-game individual difficulty level was established, see Supporting Information Data S1.

## 2.2 | Videogame software and hardware

CS:GO is an FPS videogame developed by Hidden Path Entertainment and Valve Corporation ([www.counter-strike.net](http://www.counter-strike.net)). The game mode chosen for the study was Team-Deathmatch, consisting of 5-minute rounds where players in two opposing teams must gain the highest possible score, i.e., increase their rate of survival while maximizing the number of opponents defeated at each round. The game was played offline, with participants battling against artificial intelligence-guided enemies (i.e., “bot”) whose number was fixed to 5 vs. 5 (5 opponent bots vs. 1 participant + 4 allies). The decision about using offline modality allowed to fully control game dynamics (e.g., number of enemies and allies, map size) and provide a constant balancing of difficulty level within and between gaming sessions. An introduction to the game was provided throughout the first 2 hr session, allowing players to become acquainted with the game commands. Game mechanics included the player joining one of the two teams (i.e., participant + 4 bots) with the aim of increasing the score of his/her team. Each session lasted for two hours, with subjects playing non-stop for 40 min (approximately eight 5-minutes rounds), then resting for 10 min, playing an additional 40 min, resting for 10 min and playing a final

20 min round. Each session also included a 10 min warm-up round, where players were able to play freely under no performance monitoring.

Multiple investigators monitored players performing the training and saved individual scores after each round. The CS:GO score was used as primary performance metric, as usually done within the online multiplayer professional gaming community (Green & Bavelier, 2006b). The training was carried out using dedicated desktop PC running Windows 7 (professional edition) equipped with a dedicated graphic card (ATI Radeon with 4GB of dedicated RAM), 8GB or RAM and a 21” LED display, allowing to play at high graphic quality (1600\*1200 pixels resolution, >100 frames/second). Participants played the game using a mouse/keyboard/headset setup, with the possibility to adjust mouse sensitivity at any time.

## 2.3 | Cognitive assessment

Two sets of cognitive tasks were used over two different visits (Figure 1), spanning from perceptual to high order cognition skills.

Tasks were categorized as “Near,” “Moderate,” and “Far” transfer based on the nature of the videogame implicated in our study, in accordance with precedent findings (Green & Bavelier, 2003, 2006a, 2006b).

The entire battery was performed also at T1 (immediately after the end of the training for AVGPs, that corresponded 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. For each task, participants were asked to respond as soon and accurate as possible.

Cognitive assessment was performed on Windows laptop PC (Microsoft) equipped with E-prime 2.0 software (Psychology Software Tools Inc.; [www.psnet.com](http://www.psnet.com)).

## 2.4 | Near transfer

### 2.4.1 | Attention

The ability to allocate the attention on two consecutive stimuli was evaluated by means of adaptive Attentional Blink (AB) (Green & Bavelier, 2003) task. A rapid stream of black letters was flashed at the center of the screen where a white letter (B, G, or S) was randomly showed (first target). After the first target, a X-letter (second target) could appear or not (50% of the trials). Participants were asked to detect the identity of the first target, pressing the corresponding letter on the pc keyboard, as well as specify whether an X-letter was presented or not. The X-detection judgment was the primary metric, which represents the cost of attentional switching between the first and the second target.

The Enumeration task (ET) (Green & Bavelier, 2006a) was administered to measure the attentional buffer; stimuli were presented on a screen and each participant was asked to report as quickly and accurately as possible (by pressing the corresponding key button) the number of randomly placed white squares (between 3 and 12) briefly presented on the screen for few milliseconds. The task included trials with stimuli of different sizes, to estimate field-of-view dependent attention capacity. Both accuracy and reaction times were recorded.

A Visual Search (VS) (Treisman & Gelade, 1980) task required to locate a target letter (“L”) among distractors (“T”), providing an index of selective attention and perceptual skills. Participants were asked to press the corresponding key on the pc keyboard, indicating the quadrant (top/bottom, left/right) where the target letter appeared.

The ability to suppress inappropriate responses was measured using an Adaptive Flanker (FT) (Green & Bavelier, 2006b) task. A structure composed by six rings was briefly shown (16 ms duration) in the center of the screen where different kinds of shapes were presented inside and outside the rings. Participants were asked whether a square or a triangle was presented within one of the six rings (target). The distractors could be either other shapes present within the six rings (incompatible distractors), or squares and triangles presented outside the six rings (compatible distractors).

The Useful Field of View (UFOV) is commonly used to describe the size of visual field over which visual stimuli can be caught without eye or head movements (Ball, Beard, Roenker, Miller, & Griggs, 1988). In the present study, we used a modified UFOV to measure the ability of the attentional system to locate a target among distractors, according to (Feng, Spence, & Pratt, 2007; Green & Bavelier, 2003, 2006b). A structure composed by 24 squares (distractors) and 1 circle (target) was flashed at the center of the computer screen. Participants were asked to determine as quickly and accurately as possible in which of the eight possible directions the circle appeared. Target stimulus was presented at different eccentricities to evaluate the spatial distribution of visual attention. When the target eccentricity was 2.3 cm, the stimulus lasted 12 ms, and duration was increased up to 20 ms when the circle was at 5.3 or 8.3 cm. The task was presented for a total of 120 trials. No feedback or time limit were given.

## 2.4.2 | Mental rotation

The ability to rotate mental representations of two-dimensional objects was evaluated through a Mental Rotation (MR) (Shepard & Metzler, 1971) task. Either a letter (“R”) or a number (“2”) were showed, then an arrow pointing in one specific direction appeared. Finally, the same stimuli appeared mirror-reversed or in upright position. Participants were asked to

indicate whether the stimulus was facing the correct direction indicated by the arrow or was mirror-reversed.

## 2.4.3 | Motor learning

The Serial Reaction Time Task (SRTT) (Robertson, 2007) was administered to index visuo-motor learning. A visual cue was presented at one of four possible positions at the center of the computer screen. Participants were asked to press the keyboard button corresponding to the position of the visual cue. The sequence of visual cues was either fixed or random. A questionnaire was collected at the end of the task, asking whether participants recognized a recurring sequence of stimuli or not. Subjects were unaware of the questionnaire while performing the task.

## 2.5 | Moderate transfer

### 2.5.1 | Flexibility

The Global-Local features task abilities (GL) (Navon, 1977) task was administered in order to evaluate selective attention, inhibition, and switching skills. Compound stimuli representing letters were showed and required participants to pay attention alternatively to either local or global stimulus characteristics.

Switching ability was evaluated by means of Preparing to Overcome Prepotency (POP) task (Rosano et al., 2005) where participants were asked to select context-appropriate responses. They were administered either a green or red square followed by either a right- or left-pointing arrow. If the arrow follows the green square, subjects had to respond by pressing the corresponding key (e.g., left-pointing arrow, left arrow key). Conversely, when the arrow follows the red square, the subjects were required to press the opposite arrow key (e.g., left-pointing arrow, right arrow key), inducing a stronger engagement of cognitive control abilities.

### 2.5.2 | Inhibition

A Letter No-Go (LNG) (Thorell, Lindqvist, Bergman Nutley, Bohlin, & Klingberg, 2009) task was used, where participants were asked to press a button when a specific item appears (“Go” trials) and withhold the overbearing response when different stimuli appear (“No-Go” trials).

## 2.6 | Far transfer

### 2.6.1 | Working memory

An index of verbal working memory was provided by the Digit Span (DS) task, a subtest of the Wechsler Memory

scale (Wechsler, 1981). A series of digits were presented and participants were asked to immediately repeat the sequence in the same exact order (DS forward) as well as in reverse order (DS backward). Individual span was calculated by considering the longer list of digits where participants fail none or only one sequence out of two.

Visuospatial working memory resources were tested through the Change Localization (CL) task, where subjects are asked to detect which one of four squares changed color between two consecutive presentations. The delay between the first and second presentation increased with trials progression, thus increasing working memory load.

### 2.6.2 | Fluid intelligence (gf)

Each participants carried out a recently developed PC-based version of Raven's Matrices (Raven, Raven, & Court, 1998), i.e., the Sandia matrices (SM) (Matzen et al., 2010). With respect to the original Raven stimuli, the SM includes multiple sets of stimuli which allow for longitudinal assessment of gf (Santarnecchi et al., 2013). Each matrix is composed of a 3 × 3 grid, with each cell in the grid containing a set of shapes. A blank cell in position 3–3 of the grid (bottom right) is present. Participants were required to complete the matrix choosing between eight alternative solutions. Participants answered by pressing the corresponding key on the PC keyboard (1–8). A maximum of 60 seconds was given for each matrix.

### 2.6.3 | Premorbid intelligence quotient

At the end of the battery, a premorbid intellectual abilities estimation was done by means of a verbal task: Test di Intelligenza Breve (TIB) (Nelson, 1982; Sartori, Colombo, Vallar, Rusconi, & Pinarello, 1997). Participants were requested to read aloud a total of 54 words, focusing on pronunciation. An estimated premorbid IQ scores was calculated based on number and type of mistakes.

### 2.6.4 | Cognitive judgment

Finally, an estimation of frontal lobe functioning was provided by Cognitive Judgement (Della Sala, MacPherson, Phillips, Sacco, & Spinnler, 2003) task, a paper-and-pencil tests assessing executive functioning and deductive reasoning. A set of 21 questions related to estimating e.g., length, weight, area, speed, and quantity of different objects was administered.

## 2.7 | Structural MRI data analysis

Structural magnetic resonance images (MRI) were acquired using a Philips INTERA MRI scanner. Whole brain structural images (T1-weighted Fast Field Echo) with 1 mm<sup>3</sup> resolution were acquired along the AC-PC line (slices = 150;

matrix size = 256 × 256 × 150; voxel size = 1 mm × 1 × 1; repetition time = 25 ms, flip angle = 30). To verify the absence of gray and white matter lesions or hyper-intensities, neuroradiological exams also included (a) 1-mm coronal Fast Field Echo (FFE) and (b) 3-mm T2-weighted Turbo Fluid Attenuated Inversion Recovery (FLAIR) images.

Unlike cross-sectional studies, where images are processed independently and results are based on group-level comparisons, longitudinal data offer the opportunity to look at changes in brain morphology at the individual level. This requires specific analytic procedures to overcome potential biases due to the reference normalization template applied during preprocessing of data at different time points (Ashburner & Ridgway, 2012). Therefore, morphometric changes induced by gaming experience were computed using a study-specific normalization template based on individual MRIs of study participants at T0, created using the DARTEL module (Ashburner, 2007) for Statistical Parametrical Mapping software (SPM12, Wellcome Trust Centre for Neuroimaging, London, UK—www.fil.ion.ucl.ac.uk/spm). Moreover, a specific toolbox for longitudinal statistical analysis of voxel-based morphometry (VBM) data (Computational Anatomy Toolbox - CAT12, www.neuro.unijena.de/cat) was used, taking into account intra-subject longitudinal trajectories which were then summarized at the group level.

Further details regarding the preprocessing and data analysis of neuroimaging images are provided in the Supporting Information Data S1.

## 2.8 | Statistical analysis

### 2.8.1 | Behavioral data analysis

Changes in accuracy (ACC) and reaction times (RTs) were combined in the inverse efficiency scores (IES) (Townsend & Ashby, 1983) which provides a validated measure that gauges the average energy consumed by the system over time.

$$IES = \frac{RT_s}{1 - error\ rate}$$

The IES of each tasks was then analyzed in the statistical package for the social sciences (SPSS) software version 20 (IBM Corp, 2011) using a repeated measures ANOVA with a (between subjects) factor “GROUP” (2 levels: Gaming; 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 gaming 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  $2 \times 2$  ANOVA were long-lasting or not. The critical  $p$ -value was then adjusted using Bonferroni correction to account for multiple comparisons ( $*0.05$  Bonferroni corrected;  $^{\wedge}0.05$  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 S1.

## 2.8.2 | Longitudinal morphometric MRI changes

The smoothed, normalized gray matter images were analyzed using a  $2 \times 3$  flexible factorial design with a (between subject) factor "GROUP" (2 levels: Gaming; Controls) as well as a (within subject) factor "TIME" (3 levels: T0; T1) in SPM12. Then – only for gaming group – another  $1 \times 3$  flexible factorial design with "Time" (3 levels: T0; T1; T2) as within-subject factor was performed, in order to verify whether the significant effects found in the  $2 \times 2$  ANOVA were long-lasting or not.

Total intracranial volume (TIV) was estimated in order to correct for different brain sizes and entered as nuisance covariate, together with age and gender. A permutation test for peak-cluster level error correction (AlphaSim) was applied for whole brain analysis (Song et al., 2011), by taking into account the significance of the peak voxel (threshold  $p < 0.01$ ) along with a stringent cluster size (71 voxels).

## 2.8.3 | Morphometric predictors of response to FPS exposure

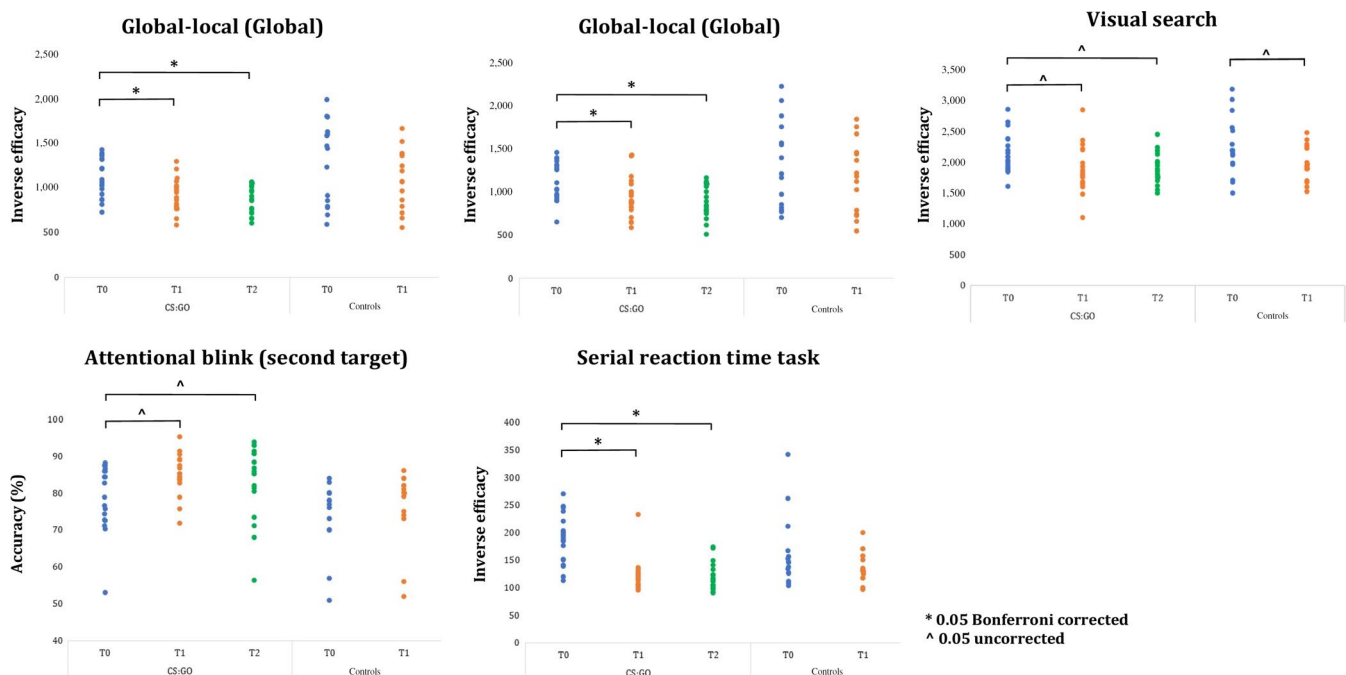
We aimed at determining whether gray matter volume (GMV) at T0 could explain longitudinal changes in gaming performance. A voxel-wise multiple regression analysis was implemented to identify potential brain regions associated with more or less pronounced gains in in-game performance after the fifteen 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.

## 3 | RESULTS

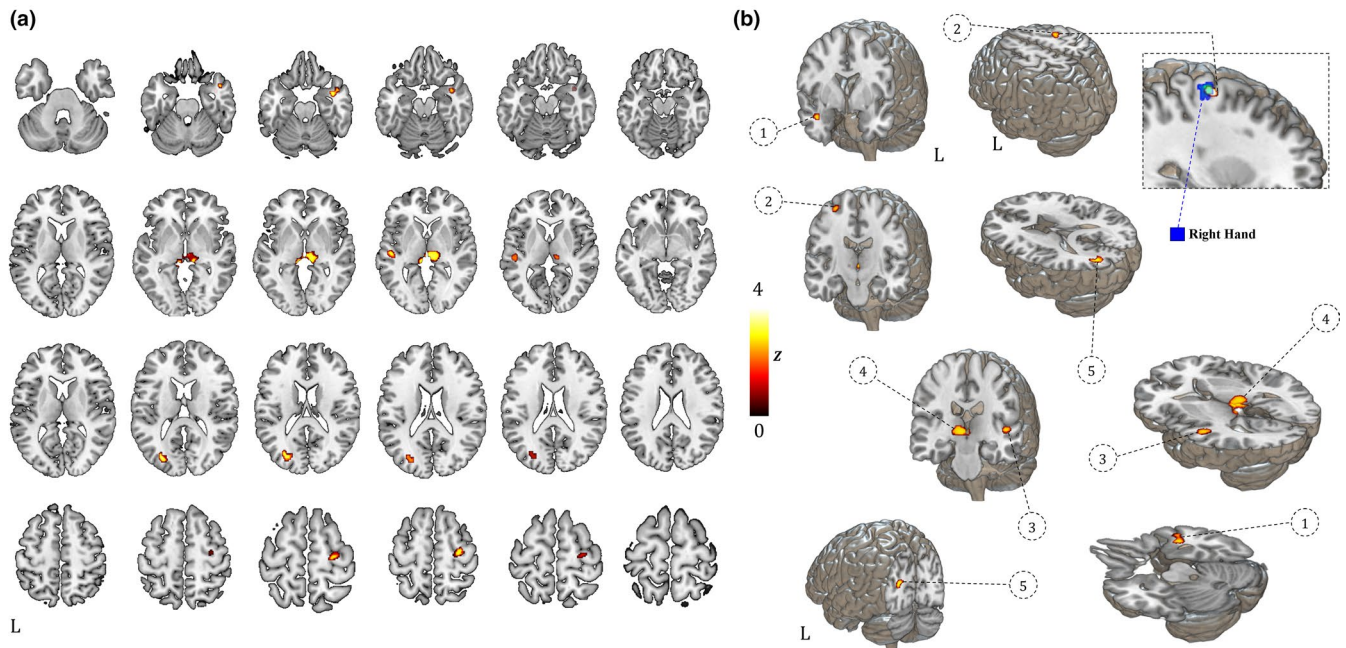
### 3.1 | Cognitive effects

As shown in Figure 2, a significant interaction Time\*Group was found in the  $2 \times 2$  ANOVA for: GL Global ( $F_{(1,14)} = 11.17$ ,  $p < 0.0001$ ), GL Local ( $F_{(1,14)} = 12.38$ ,  $p = 0.001$ ), AB Second Target ( $F_{(1,14)} = 5.81$ ,  $p = 0.03$ ), SRTT ( $F_{(1,14)} = 51.33$ ,  $p < 0.0001$ ).

As for CS:GO group, the results of  $1 \times 3$  ANOVA has shown significant differences corrected via Bonferroni (at the post-hoc level) for: GL Global ( $F_{(2,38)} = 20.13$ ,  $p < 0.0001$ , T1 > T0: energy decrease: 205.09,  $p = 0.001$ ; T2 > T0: energy decrease: 237.85,  $p = 0.0002$ ), GL Local ( $F_{(2,38)} = 17.58$ ,



**FIGURE 2** Immediate and long-lasting behavioral changes after gaming. Improvement in test scores for CS:GO and CONTROL groups. Individual Inverse Efficacy Scores for T0 (blue), T1 (orange), and T2 (green) are reported.  $*0.05$  Bonferroni corrected;  $^{\wedge}0.05$  uncorrected. [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]



**FIGURE 3** Volumetric changes after gaming (T1 > T0). Axial slices (a) and 3D visualization (b) showing significant increase in voxel-level gray matter volume in the right STG (1), right MC (2), left STG (3), bilateral pulvinar (4) and left MOG (5) ( $p < 0.05$ ; cluster size correction  $< 0.01$ , permutation-based correction). The top right inset represents the overlap between gray matter volume changes in the motor cortex and the motor representation of the right hand obtained using meta-analytic data ([www.neurosynth.org](http://www.neurosynth.org)). STG: superior temporal gyrus, MC: motor cortex, MOG: middle occipital gyrus, L: Left; R: Right. [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

$p = 0.001$ , T1 > T0: energy decrease: 180.09,  $p = 0.001$ ; T2 > T0: energy decrease: 211.86,  $p = 0.001$ ), AB Second Target ( $F_{(2,38)} = 4.21$ ,  $p = 0.02$ , T1 > T0: accuracy increase: 6.12%,  $p = 0.003$ ; T2 > T0: accuracy increase: 4.27%,  $p = 0.01$ ), SRTT ( $F_{(2,38)} = 32.83$ ,  $p < 0.0001$ , T1 > T0: energy decrease: 66.99,  $p < 0.0001$ ; T2 > T0: energy decrease: 69.39,  $p = 0.00002$ ).

Moreover, an uncorrected significant change was also found for VS ( $F_{(2,38)} = 11.79$ ,  $p = 0.003$ , T1 > T0: energy decrease: 263.38, uncorrected  $p = 0.009$ ; T2 > T0: energy decrease: 249.03, uncorrected  $p = 0.003$ ). Notably, none of the participants reported significant changes in the amount of time spent playing videogame between T1 and T2.

For further details see Supporting Information Table S1 and Supporting Information Figure S2 (no significant results).

### 3.2 | Immediate morphometric changes

Figure 3 displays GMV clusters showing a significant increase in volume at T1 ( $p < 0.05$ ) as compared to T0. Significant changes were present in left ( $x = -9$ ,  $y = -33$ ,  $z = 0$ ; with  $Z = 3.36$ ) and right ( $x = 2$ ,  $y = -21$ ,  $z = 2$ ; with  $Z = 3.36$ ) posterior thalamus, left ( $x = -51$ ,  $y = -21$ ,  $z = 3$ ; with  $Z = 3.25$ ) and right superior temporal gyrus (STG;  $x = 39$ ,  $y = 2$ ,  $z = -23$ ; with  $Z = 3.34$ ), right motor cortex (MC;  $x = 27$ ;  $y = -17$ ;  $z = 62$ , with  $Z = 3.24$ ), and left middle occipital gyrus (MOG;  $x = -27$ ,  $y = -77$ ,  $z = 17$ ; with  $Z = 3.56$ ). Given the anatomical localization of the results on the motor cortex, a further

investigation was conducted testing the overlap with the hand representation. A meta-analysis of 80 studies was carried out using the software Neurosynth ([www.neurosynth.org](http://www.neurosynth.org)) and an average fMRI activation for the right hand was obtained. Results were exported as a nifti.nii file and overlaid with the MC cluster, suggesting a significant overlap (Figure 3).

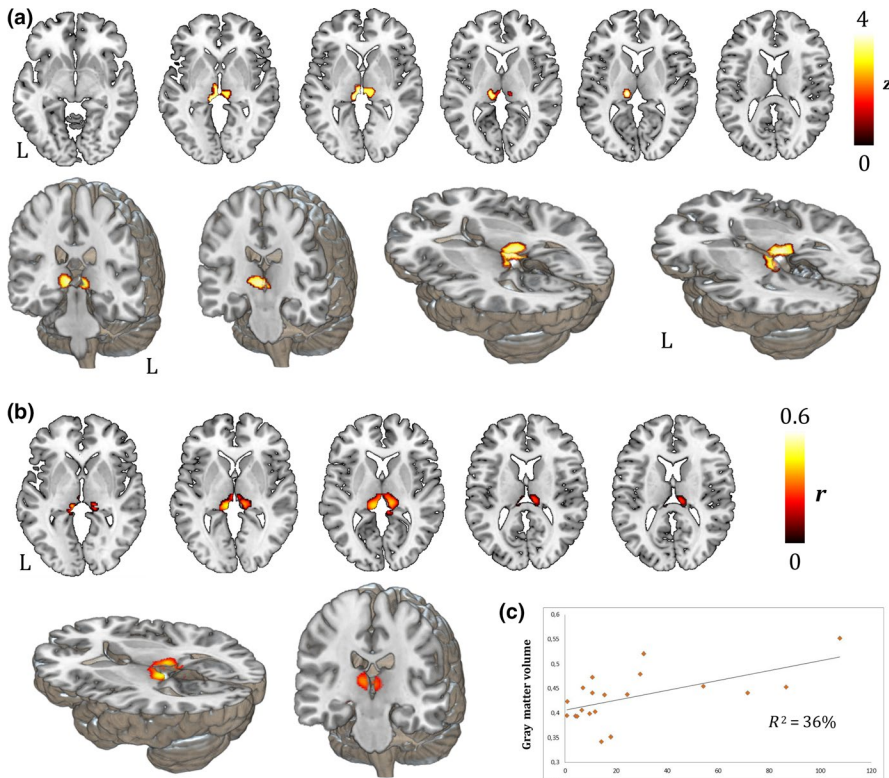
### 3.3 | Long-lasting morphometric changes

As shown in Figure 4a, a cluster located in the left and right pulvinar showed a significant change in volume even 3 months (T2) after exposure to the FPS game when compared to pre-gaming (T0) (left hemisphere:  $x = -12$ ,  $y = -25$ ,  $z = 9$ ;  $Z = 3.79$ ; right hemisphere:  $x = 15$ ,  $y = -35$ ,  $z = 5$ ;  $Z = 4.05$ ), resembling the finding observed at T1. None of the other regions showing significant changes at T1 reached statistical significance at T2.

Individual gray matter values are reported in Supporting Information Figure S3 for both videogaming and a control group.

### 3.4 | Morphometric predictors of response to FPS practice

Whole brain regression analysis identified a significant predictor closely resembling the thalamic nuclei modulated by game practice at T1 and T2. As shown in Figure 4b–c, the predictive model included the bilateral pulvinar region,



**FIGURE 4** Long-lasting changes and prediction of response. (a) Distribution of significant increase in gray matter volume 3 months after the end of the CS:GO training ( $p < 0.05$ ; cluster size correction  $p < 0.01$ , permutation-based correction). (b) Voxel-wise prediction of gain in game performance based on baseline morphometry. Axial slices and 3D rendering of significant correlation between the volume of posterior thalamic nuclei (specifically bilateral pulvinar region) and changes in in-game performance. Scatter plot showing (c) correlation of in-game performance (T1–T0) and bilateral pulvinar volume ( $R^2 = 0.36$ ,  $p = 0.05$ ). L, Left; R, Right. [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

showing a positive correlation with changes in CS:GO performance ( $p < 0.05$ ;  $R^2 = 0.36$ ).

### 3.5 | Anatomical mapping

Given the heterogeneity of thalamic nuclei structure and function, a previously validated parcellation atlas was used to characterize the voxel-level results related to T1 > T0, T2 > T0 and prediction of response to gaming. Significant clusters were mapped on the anatomic-functional thalamus parcellation by Morel et al. (Figure 5a) (Morel, 2007). Overall, significant changes were exclusively related to medial and posterior thalamic nuclei. Immediate effects involved posterior and medial thalamic nuclei, specifically the bilateral habenular nucleus (Hb), bilateral limitans nucleus (Li), bilateral mediodorsal nucleus (MD), bilateral medial pulvinar (PuM), right central median nucleus (CM), right anterior pulvinar (PuA; Figure 5b, red). Long-lasting changes showed a more pronounced effect on left medial pulvinar (PuM; Figure 5b, green), while prediction of response also involved right medial pulvinar and the parvocellular part of bilateral mediodorsal nuclei (MDpc; Figure 5b, blue). A quantification of the overlap is reported in Figure 5.

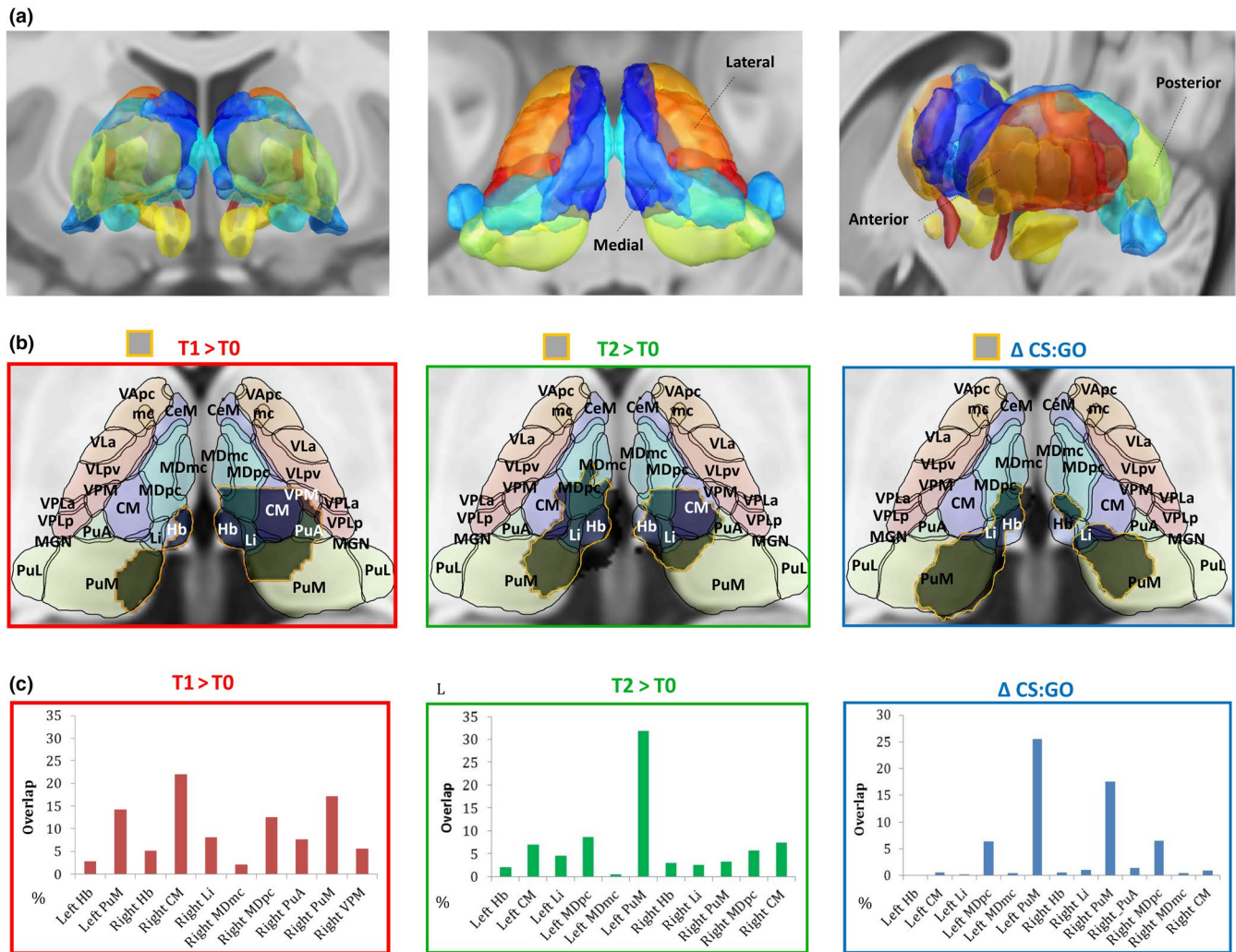
## 4 | DISCUSSION

Morphometric data showed how even a relatively intensive but short gaming practice is able to induce structural

changes in brain regions related to attention and perception, with subcortical modifications lasting up to 3 months after exposure. Moreover, individual differences in the volume of bilateral medial-posterior thalamus were identified as a predictor of changes in gaming performance, suggesting a pivotal role for posterior thalamic nuclei in FPS gaming. Such specificity of gaming-induced neuroanatomical changes might point to the possibility of using FPS training for rehabilitation purposes, especially in the attention domain.

### 4.1 | Immediate and long-lasting thalamic changes

Our most prominent structural change was evident in the bilateral thalamic nuclei. According to anatomic-functional criteria, the thalamus can be divided into five major clusters: lateral, medial, posterior, anterior nuclei and the reticular nucleus (Morel, 2007). From a functional point of view, the anterior part of the thalamus is mainly linked to the modulation of alertness and is involved in learning and episodic memory, while receiving afferents from the mammillary bodies and subiculum, and projecting to the cingulate gyrus (Child & Benarroch, 2013). Medial and posterior nuclei, i.e., the regions showing changes in the present study, project to the occipital, parietal, somatosensory and temporal cortices and are thought to play a pivotal role in attentional as well as perspective processing (Zhang, Snyder, Shimony, Fox, & Raichle, 2010). More specifically, changes induced by CS:GO practice mainly



**FIGURE 5** Anatomical mapping of thalamic nuclei. (a) Coronal (left), axial (center) and sagittal (right) 3D visualization of thalamic nuclei according to the Morel atlas (Morel, 2007). (b) Overlap between changes in gray matter volume (black cluster, orange contour, see Figure 3) for T1 > T0 (left, red line), T2 > T0 (center, green line, see Figure 4a) and significant predictor of increase in-game performance (right, blue line, see Figure 4b-c). Quantitative similarity scores between Morel parcellation scheme and significant clusters are shown in (c) for each nucleus. VApc, ventral anterior nucleus (parvocellular part); VL<sub>a</sub>, ventral lateral nucleus (anterior); VL<sub>pv</sub>, 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; VPL<sub>a</sub>, ventral posterior lateral nucleus (anterior); VPL<sub>p</sub>, Ventral posterior lateral nucleus (posterior); MGN, medial geniculate nucleus; PuA, anterior pulvinar; PuM, medial pulvinar; PuL, lateral pulvinar. [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

involved the pulvinar (i.e., bilateral medial pulvinar and right anterior pulvinar), which have been shown to play key roles in attention control for peripheral discrimination (Coull, 1998), selective attention (Shipp, 2004), spatial-seeking (Fischer & Whitney, 2009), movement detection (Berman & Wurtz, 2011), visually guided eye–limb coordination movements toward the contralateral space (Schneider, 2011) and multisensory integration processes (Stein & Stanford, 2008).

These abilities are well-captured by demands of FPS games, where the core ability resides into performing high-precision visually guided saccades in order to identify, select and target enemies within a sub-millisecond

timeframe. The ability to identify salient targets (e.g., opponents) among distractors (e.g., teammates, neutral players), while constantly filtering irrelevant information is a crucial and constant component of FPS gaming experience. Moreover, stimuli suddenly move along the vertical and horizontal midline, continuously varying in speed and direction, thereby strongly engaging hand-eye coordination mechanisms.

In addition to the pulvinar, morphometric increase in bilateral habenular and mediodorsal nucleus was found. Both structures play pivotal roles in functions relevant for FPS gaming performance; specifically, the habenula is connected to reward prediction (Schultz, Dayan & Montague, 1997),

reward-based action selection (Matsumoto & Hikosaka, 2007), spatial reference memory (Lecourtier, Neijt, & Kelly, 2004), and attention (Lecourtier & Kelly, 2005). The medial dorsal nucleus exchanges projections with the prefrontal cortex and the limbic system, playing a crucial role in attention, learning, inhibition, decision-making, and memory (Mitchell, 2015).

The increase in GMV observed in the medial and posterior thalamic nuclei was still significant three months after the gaming days, even with no further exposure to CS:GO. So far, structural brain changes outlasting the duration of the training period (by weeks or months) have been reported only for meditation (Hernández, Suero, Barros, González-Mora, & Rubia, 2016), juggling (Driemeyer, Boyke, Gaser, Buchel, & May, 2008), and cognitive training (Ceccarelli et al., 2009), making our results provide the first evidence of macrostructural changes following exposure to FPS videogame. Most importantly, longitudinal changes in thalamic volume following exposure to any kind of stimulation (e.g., visual, motor) have not been documented so far. Based on these observations, future investigations could employ FPS games as rehabilitative strategy to induce neuroanatomical changes in diseases where an alteration of posterior thalamic nuclei functioning has been reported, such as schizophrenia (Byne et al., 2007; Mileaf & Byne, 2012; Zhang, Chu, Teague, Newmark, & Buchsbaum, 2013), depression (Hamilton et al., 2012; Tadayonnejad et al., 2016), anxiety disorder (Pacheco-Unguetti, Acosta, Marqués, & Lupiáñez, 2011; Sladky et al., 2012), attention-deficit/hyperactivity disorder (Ivanov et al., 2010; Li et al., 2012), Alzheimer's disease (Zarei et al., 2010), neglect (Barron, Tandon, Lancaster, & Fox, 2014; Ward, Danziger, Owen, & Rafal, 2002), epilepsy (Chatzikonstantinou, Gass, Förster, Hennerici, & Szabo, 2011; Ohe et al., 2014; Rosenberg, Mauguière, Catenoix, Faillenot, & Magnin, 2009; Tschampa, Greschus, Sassen, Bien, & Urbach, 2011), and Lewy Body Disorders (Delli Pizzi et al., 2014, 2015). However, it is important to notice that subcortical fMRI changes (e.g., involving the ventral striatum) following intensive videogame training have already been reported (Lorenz et al., 2015), and interpreted as an unspecific reward-related response that could be independent from the videogaming experience itself. We cannot entirely discard this hypothesis, although we did not observe any significant change in the ventral striatum; so, future studies should explore the impact of FPS games as compared to a reward-based cognitive training with no gaming component.

## 4.2 | Cortical changes and cognitive enhancement

Additional immediate morphometric changes were found in the bilateral STG and left MOG. In line with the observed behavioral results, structural changes were restricted to low-level cortical areas specialized in visual and auditory-spatial

processing (Lovden et al., 2010). While changes in mid-temporal regions have already been documented in response to visuomotor training (Draganski et al., 2004; Driemeyer et al., 2008), numerous studies have shown the involvement of the MOG in a wide range of visuospatial attentional processes responsible for the interpretation of images, such as detection of light intensity (Richards, Kozak, Johnson, & Standish, 2005), pattern recognition (Fokin et al., 2007), visuomotor tracking (Dieterich, Bauermann, Best, Stoeter, & Schindwein, 2007), sustained attention to color and shape (Le, Pardo, & Hu, 1998), and feature-based attention (Kamitani & Tong, 2006). Interestingly, MOG and STG have also been associated to the ventral auditory stream. While FPS games obviously load on perceptual system implicated in a finer discrimination of visual stimuli, auditory processing (e.g., footsteps, gunshots) represents an equally important component. For instance, activity in the MOG and STG have been associated to the discrimination of location and azimuth eccentricity of a sound source (Lewald, Riederer, Lentz, & Meister, 2008), pitch and sound intensity discrimination for nonverbal sounds (Bernal, Altman, & Medina, 2004), as well as numerous memory and visual processes such as color attribution relative to structural judgments (Kellenbach, Hovius, & Patterson, 2005) and multimodal memory retrieval (Takashima et al., 2007). Changes in these structures might reflect enhanced ability to extrapolate and elaborate visual and acoustic information providing tangible in-game advantages like the ability to estimate opponents' number and position based on their footsteps or the echo of their gunshots.

Finally, structural changes in the right motor cortex corresponding to the (left) hand operating the keyboard were also found. Studies have stressed a possible role for the precentral gyrus in learning and planning of complex coordinated movements (Bischoff-Grethe, Goedert, Willingham, & Grafton, 2004) and visuomotor attention (Tanaka, Honda, & Sadato, 2005). Increase in GMV has been previously documented in professional musicians (i.e., piano players) and linked to planning and control of finger movements (Bermudez, Lerch, Evans, & Zatorre, 2009; Gaser & Schlaug, 2003). In the present study, participants were asked to perform a high number of coordinated keyboard movements over the one-month gaming period (estimated at around 50 key strokes per minute, equal to ~80,000 total key strokes). These movements, all contributing to moving the avatar in the 3D environment (while e.g., aiming, umping, crouching, strafing), might have led to the observed gray matter changes.

Remarkably, gray matter increase has been already reported both in the right hippocampal formation (HC) and in the DLPFC following 2 months exposure to a third-person view, 3D platform game (i.e., Super Mario). However, videogame player's perspective in FPS is different and might also lead to a higher level of engagement (Petras, Ten Oever, & Jansma, 2016). This aspect might explain

the specificity of the results related to both the pulvinar and cortical regions belonging to sensorimotor integration pathways (right motor cortex, STG and left MOG). Indeed, differently from arcade platform games like Super Mario, where the avatar is viewed from an aloft camera, FPS is played with player's avatar viewpoint where the position and the volume of the ambient sounds is also varied depending on their position with respect to the player's avatar. This provides players a more realistic game experience involving mostly low (e.g., sensorimotor) than high level cortical regions (e.g., DLPFC).

As for cognitive performance, FPS gaming also induced changes in visual and attention tasks. Cognitive improvements were restricted to low level functions, accounting for near and moderate transfer. Cross-sectional evidence in healthy individuals demonstrated how videogaming are able to enhance several cognitive domains measured with Enumeration (Green & Bavelier, 2006a), Flanker (Dye, Green, & Bavelier, 2009), Attentional Blink (Li, Ngo, & Levi, 2015), Useful Field of View (Green & Bavelier, 2003), Mental Rotation (Feng et al., 2007), Serial Reaction Time Task (Bergstrom, Howard, & Howard, 2011), Digit Span (Toril, Reales, Mayas, & Ballesteros, 2016). Interestingly, we were able to replicate some of those effects (e.g., Attentional Blink, Serial Reaction Time Task), with a novel findings of improved performance at two executive functions tasks, i.e., Visual Search and Global-Local features, respectively measuring the ability to filter irrelevant information (Treisman & Gelade, 1980) and inhibition/flexibility (Navon, 1977). Importantly, a crucial role for activity in the pulvinar and occipito-temporal regions has been reported using fMRI for both tasks (Fairhall, Indovina, Driver, & Macaluso, 2009).

However, no transfer effects were observed for other tasks (e.g., UFOV, Flanker, Mental Rotation, Enumeration, Sandia) demonstrating how human cognitive and perceptual enhancement following a videogame exposure might not be straightforward (Oei & Patterson, 2014).

Indeed, replication of videogame effects on cognition in the case of both cross-section and longitudinal designs has been reported for many of the aforementioned tasks (Boot et al., 2008; Irons, Remington, & McLean, 2011; Murphy & Spencer, 2009). A number of methodological issues might contribute to this inconsistency, including the use of unspecified recruiting methods targeting less or more experienced gamers, the differential impact of placebo effect in training studies involving active or passive control groups, as well as the impact of different videogame genre (Boot, Blakely, & Simons, 2011; Dobrowolski et al., 2015).

Nevertheless, it must be noticed that a few tasks (i.e., AB, VS) showed significant changes also in the control group, questioning the nature of such results in the CS:GO group as well in previous cross-sectional reports suggesting such differences between AVGPs and NAVGPs.

### 4.3 | Morphometric predictors of response to gaming exposure

Apart from estimating the impact of a given intervention, identifying specific features 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 volume of bilateral pulvinar. Apart from its predictive values, the overlap between regions predicting "neuroanatomical response" to FPS gaming exposure and those showing the strongest and longer lasting change after gaming is intriguing and deserves further investigations. Prospective studies including a predefined assignment to a low and high pulvinar volume group are needed to causally validate this hypothesis.

### 4.4 | Study limitations and future directions

Our results must be interpreted within the debate about the nature of morphometric changes as those measures via VBM, which cannot be attributed to neurogenesis processes restricted to the perinatal period or to the hippocampus during adult life (Pereira et al., 2007). The observed increase in gray matter volume possibly reflects, among other interpretations, increase of spine and synapse turnover (Trachtenberg et al., 2002), glial cell genesis or changes in blood flow or angiogenesis (Kempermann, Kuhn, & Gage, 1997). An investigation based on novel techniques for the quantification of neurite morphology (e.g., NODDI)(Jespersen et al., 2010) and perfusion MRI (e.g., ASL) should be considered in order to disentangle the real contribution of neural and cerebrovascular changes induced by FPS.

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 dynamic of artificial intelligence was systematically modulated in order to provide a challenging experience for any player. However, FPS games, and CS:GO in particular, are thought as online games. Future efforts should be put in monitoring brain structural and functional changes of a team of five players playing together on competitive online server.

## 5 | CONCLUSION

Our findings extend over the notion that videogame playing might impact cognitive and brain functioning in a beneficial way, showing for the first time long-term brain structural

changes even months after gaming practice. The specific involvement of posterior thalamic structures, both in response to training and as a predictor of response, suggest a novel anatomo-functional link between FPS gaming and thalamo-cortical structures related to attention and multisensory integration.

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## CONFLICT OF INTEREST

The authors report no conflicts of interest.

## DATA ACCESSIBILITY

Data are available upon request from the corresponding author, Emiliano Santarnecchi (esantarn@bidmc.harvard.edu).

## AUTHOR CONTRIBUTIONS

CS and ES designed the study; DM collected and analyzed the data and wrote the first draft of the paper; GS, FN and GDL actively participated in collecting the data and revising the manuscript; ES, AR and SR revised the manuscript. All authors critically reviewed the manuscript for content and approve the final version for publication.

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