Corticospinal properties are associated with sensorimotor performance in action video game players

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ABSTRACT

Notwithstanding the apparent demands regarding fine motor skills that are required to perform in action video games, the motor nervous system of players has not been studied systematically. In the present study, we hypothesized to find differences in sensorimotor performance and corticospinal characteristics between action video game players (Players) and Controls.

We tested sensorimotor performance in video games tasks and used transcranial magnetic stimulation (TMS) to measure motor map, input-output (IO) and short intra-cortical inhibition (SICI) curves in the first dorsal interosseous (FDI) muscle of Players (n = 18) and Control (n = 18).

Players scored higher in performance tests and had stronger SICI and higher motor evoked potential (MEP) amplitudes. Multiple linear regressions showed that Players and Control differed with respect to their relation between reaction time and corticospinal excitability. However, we did not find different motor map topography or different IO curves for Players when compared to Controls.

Action video game players showed an increased efficiency of motor cortical inhibitory and excitatory neural networks. Players also showed a different relation of MEPs with reaction time.

The present study demonstrates the potential of action video game players as an ideal population to study the mechanisms underlying visuomotor performance and sensorimotor learning.

1. Introduction

Elite athletes and professional musicians can easily be distinguished from ordinary people on the behavioral level. The reason is that they have acquired specific skills over years of practice. It seems intuitive to expect that neural plasticity associated with numerous hours of practice should induce neural changes, making athletes and musicians interesting models to study the long-lasting effects of sensorimotor training on the central nervous system (CNS) (Yarrow et al., 2009). Unfortunately, elite athletes and musicians are scarce and often hesitant to participate in scientific experiments. Recently, it has been suggested that action video gaming might be an excellent model to study the limits of human sensorimotor performance as well (Pluss et al., 2019). With a talent pool of nearly 100 million players, esports athletes need exceptional sensorimotor skills to dominate competition, and esports practitioners from all levels should be easy to recruit for experiments. However, even though differences in the motor part of the central nervous system between action video game players and non-players are likely to be expected, most of the studies focused on perceptual and cognitive capacities (Bavelier et al., 2012; Bavelier and Green, 2019) whereas studies on sensorimotor performance and underlying neural mechanisms are scarce (Gozli et al., 2014).

To the best of our knowledge only few studies looked at neural differences of action video game players (Players) or changes as a result of action video game practice in the sensorimotor system. Imaging (fMRI) cross-sectional studies showed differences in brain motor regions between video game players and control (Gong et al., 2015; Zhang et al., 2015; Benady-Chorney et al., 2018; He et al., 2020), and a longitudinal study showed neural plasticity in motor regions induced by action video game training (Kuhn et al., 2014). Furthermore, a study using Transcranial Magnetic Stimulation (TMS) over the hand motor cortex showed a higher increase in corticospinal excitability of Players compared to

Abbreviation: EMG, electromyography; FDI, first dorsal interosseous; IO, input-output; ISI, inter stimulus interval; MEP, motor evoked potential; Mmax, maximal peak to peak amplitude of the M-wave; MSO, maximal stimulator output; PNS, peripheral nerve stimulation; rms, root mean square; RMT, resting motor threshold; SICI, short intra-cortical inhibition; TMS, transcranial magnetic stimulation; CoG, centre of gravity; SOA, sum of all MEP amplitude that contributed to the motor map.

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Controls immediately after the learning of a new visuomotor task, suggesting a more pronounced neuroplasticity in Players (Morin-Moncet et al., 2016). Together, these studies underpin the intuitive notion that playing action video games is associated with sensorimotor plasticity, but are still far from painting a conclusive picture on how long-term video gaming affects the sensorimotor system and how these adaptations are linked to measures of sensorimotor performance.

We know that playing action video games requires precise and fast control of the arm and fingers and it has been reported that professional esport athletes perform on average 350 actions per minute with the mouse and keyboard whilst playing action video games (https://en.wikipedia.org/wiki/Actions_per_minute). It is well established that fast and precise hand and finger movements in humans rely mainly on the integrity of corticospinal pathways and especially of the direct connections between the primary motor cortex (M1) and the motoneurons (Lemon, 2008; Isa et al., 2013). Thus, it can be expected that long-term Players, even at low level of competitiveness, have different corticospinal characteristics compared to non-players (Controls).

To detect such differences, the size and site of a cortical motor map as well as the excitability of neuronal networks that constitute the map of a finger muscle seems to be an appropriate object of investigation, since the properties of cortical motor maps might be related to the capacity to acquire a new skill (Monfils et al., 2005). Studies performed with TMS have shown that during skill training, the cortical motor map of the relevant muscles expanded, and got easier to activate (Pascual-Leone et al., 1994; Pascual-Leone et al., 1995; Liepert et al., 1998). Interestingly, the cortical map and cortical excitability returned to baseline once the skill had been mastered (Pascual-Leone et al., 1994) or the training ended (Molina-Luna et al., 2008). However, in professional athletes or musicians, who need to master complex motor skills over years, several studies showed distinct differences of the cortical motor map (Pearce et al., 2000; Tyé et al., 2005; Schwenkreis et al., 2007).

Besides differences between Players and Controls in motor map characteristics, differences in the modulation of excitatory and especially of inhibitory cortical networks (Isomura et al., 2009) might be expected as well. To estimate the modulation in these intracortical circuits different TMS protocols are available. The input-output (IO) curve estimates the modulation of excitatory and inhibitory networks at corticospinal level (Ridding and Rothwell, 1997), and reflects changes in glutamatergic activity with increasing stimulation intensity over M1 (Stagg et al., 2011). The short-latency intracortical inhibition (SICI) paired pulse paradigm evaluates the activity of intra-cortical GABAergic inhibitory networks and also entails the modulation of both, excitatory as well as inhibitory circuits (Ilic et al., 2002; Chen, 2004). Both, IO curves and SICI might be of functional relevance for sensorimotor performance as they have been related to changes in the motor function in previous studies. For example, abnormal regulation of SICI can be seen in stroke or dystonia patients (Gilio et al., 2003; Hummel et al., 2009), and amputees present different IO curves in the intact and amputated side (Ridding and Rothwell, 1997). On the other hand, professional musicians display different SICI and IO curves than control participants, possibly partly explaining their better dexterity (Rosenkranz et al., 2007).

Thus, in the present study, we hypothesized that Players have larger FDI motor maps, larger peak to peak motor evoked potentials (MEPs) in the IO curves, and stronger SICI than Controls. Moreover, we expected to find group differences in the relationships between neurophysiological variables and video game related visuomotor performance.

2. Methods

2.1. Data and code availability statements

All the data required to reproduce the present results is available on Figshare Link: https://figshare.com/s/8690c4bcda4a2b4defde.

2.2. Participants

Thirty-eight individuals were recruited at the University Konstanz and at a local esport club. The study was specifically approved by the ethics committee of the University Konstanz (no. IRB 07/2019) and conducted in accordance with the latest revision of the Declaration of Helsinki. All subjects signed the informed consent form before the start of the study. Exclusion criteria were: safety issues related with TMS as defined by the questionnaire from Rossi et al. (2009) (see Supplemental Materials), uncorrected vision problems, dexterous activities (drawing, painting or playing a music instrument given as examples) of more than two hours per week during the last 2 years or using the computer mouse with the left hand. In the control group, in addition to the aforementioned criteria, participants were excluded if they were playing action video games for more than 2 h per week during the last 6 months. In contrast, action video game players (Players) were only included in this group if they had at least 2 h per week of action video game practice over the last 2 years. For the definition of an action video game we used the criteria established by Bavelier and Green (2019), Bavelier and Green (2019). Eighteen participants met the criteria for action video game players and were included in the Players group, eighteen participants met the criteria for the non-action video game players and were included in the Control group. The anthropometric data and the action video game history of both groups are summarized in Table 1.

2.3. Overall procedure

Participants took part in two experimental sessions separated by at least one day. All participants were asked to abstain from caffeine and alcohol use during the two days of the experiments. During the first session, participants filled a questionnaire about their video game history and handedness, and then their height and weight were measured. The participants were then prepared for the electromyography (EMG) measurement, peripheral nerve stimulation (PNS) and TMS. After the preparation, the participants were comfortably placed on a desk chair with head support. Both arms rested on a desk, so that the elbow of the right arm formed an angle of 150°. We verified the elbow angle with a goniometer and marked the position of the arm on the desk to ensure its position throughout the whole experimental session. The course of experiments was as follows: First, we determined the maximal M-wave (Mmax) in the FDI muscle, then assessed the hotspot and the resting motor threshold (RMT) with TMS, followed by the motor map measurement and ended up with the IO and SICI recruitment curve measurements. In the second session, participants performed 4 different sensorimotor performance tests, one related to keyboard typing skills and the other three related to action video game skills.

2.4. Handedness

Preferred handedness was determined with the modified Edinburgh Handedness Inventory (Oldfield, 1971) from Brainmapping.org (http://www.brainmapping.org/shared/Edinburgh.php). The score consists in a laterality index. When 48 ≤ laterality index ≤ 100, the participant is considered right handed. When −28 ≤ laterality index < 48, the participant is considered as middle handed, and when −100 ≤ laterality index < −28, the participant is considered as left handed.

2.5. EMG

We prepared the skin (cleaned with sandpaper and with alcohol) of the right hand FDI muscle and then taped EMG electrodes (Bagnoli Desktop EMG, Delsys, Natick, MA, USA) on the belly of the muscle. EMG signals were amplified (× 1000 for motor evoked potentials elicited by TMS and × 100 for measuring the maximal M-wave), high-pass- and low-pass-filtered (20 Hz ± 10% and 450 Hz ± 10%, respectively), sampled with a Power 1401 interface (Cambridge Electronic Design, Cambridge,
UK) at 4000 Hz and stored on a computer using the Signal software (Version 5.08, Cambridge Electronic Design).

2.6. Peripheral Nerve Stimulation (PNS)

We stimulated the ulnar nerve with bipolar electrodes placed on the anterior surface of the forearm around 5 cm proximal to the wrist to assess the Mmax in the FDI (with the cathode placed proximal in regard to the spinal cord). We performed stimulations with 1 ms duration (stimulator: DS7A; Digitimer, Welwyn Garden City, UK). The current of the stimulation was progressively increased until an increase in current produced no increase in the M-wave any more. We analysed the peak to peak amplitudes and considered the highest value as Mmax.

2.7. Transcranial Magnetic Stimulation (TMS)

Stimulations were elicited with an inter stimulus interval (ISI) of at least 7 s (Kleim et al., 2007). TMS were delivered as biphasic pulses (current flow in the coil in anterior-posterior/posterior-anterior direction) through a figure of eight shaped coil (MC-B70, MagVenture) connected to a MagPro R30 Stimulator (MagVenture, Inc, Denmark). The coil was positioned at 45° to the sagittal plan with the handle in posterior direction. We used stereotaxic neuronavigation (Brainsight TMS Neuronavigation, Brainbox Ltd) with a MNI space calibrated to the head of the participant throughout all experiments with TMS to ensure the exact positioning of the coil.

2.8. Resting Motor Threshold (RMT)

We used the procedures described by Kleim et al. (2007) to determine first the most responsive location of the TMS coil for the FDI muscle (hotspot) and thereafter the RMT. We used a stimulator output intensity of 50% maximal stimulator output (MSO) which always elicited a distinct MEP in the FDI and searched for a “temporary hotspot” with 30 stimulations. We stored this “temporary hotspot” position on the navigation system and aligned a 1 cm by 1 cm spaced grid (11 by 11 cm) to the head of the participant with its centre on the “temporary hotspot”. Additionally, we marked the location of the vertex, defined as the upper point of the head, and stored it on the computer for later off-line analysis. With the coil placed over the “temporary hotspot”, we searched for the coil position with the highest muscle response by modifying the coil plane carefully while maintaining the 45° coil orientation toward the sagittal plan. In this position, we measured the RMT and finally located the hotspot according to the procedure described in detail by Kleim et al. (2007): We started the procedure with the coil placed on the “temporary hotspot”. The experimentee used an arbitrary stimulation intensity that he estimated according to the MEPs observed during the stimulations with 50% MSO. Per stimulation intensity we always analyzed 10 MEPs at maximum. If less than six out of ten MEPs were of smaller peak to peak amplitude than 50 μV, we increased the stimulation intensity by 2% MSO. We then repeated this procedure until at least six MEPs out of ten were of bigger peak to peak amplitude than 50 μV. After that, we reduced the stimulation intensity in steps of 1% until less than six out of ten MEPs were of larger peak to peak amplitude than 50 μV. Based on this stimulation intensity we again increased the stimulation intensity in steps of 1% until six out of ten MEPs were of bigger peak to peak amplitude than 50 μV. With this procedure we determined RMT stimulation intensity given in MSO. In order to determine the actual hotspot we moved the coil on the anterior node, with a squared grid of 1 cm between nodes and repeated the procedure to determine RMT on this location. In case RMT on this node was higher, we checked RMT for all other nodes next to the previous determined hotspot. In case RMT was lower, this node was defined as the new “temporary hotspot” and the RMT procedure was repeated. The whole iteration cycle was repeated until the node was completely surrounded by nodes with higher RMT. This node was then defined as the hotspot.

2.9. Motor map

We followed the procedure described by Kleim et al. (2007) to determine the motor map. We ensured with stereotaxic neuronavigation that the orientation of the coil in space was maintained stable during the mapping procedure. We kept the stimulation intensity at 110% RMT. We started the mapping over the hotspot and then included systematically the neighboring nodes. Over each node we stimulated ten times and continued with the procedure until the resulting area was completely surrounded by non-responsive nodes (nodes with less than six out of ten MEPs ≥ 50 μV).

2.10. IO and SICI curves

We assessed IO curves with the coil positioned over the hotspot with 4 blocks of 10 stimulations. TMS intensity differed between each block (90% RMT, 110% RMT, 130% RMT and 150% RMT) (Kleim et al., 2007). To limit the amount of stimulations performed, the MEPs obtained from the motor map procedure at the hotspot location were used to define the 110% RMT block. The blocks were performed in a pseudo random order to avoid cumulative effects on MEP amplitude induced by a progressively increasing stimulation intensity (Kleim et al., 2007). The pseudo-random order was different between participants but matched between groups. We used the procedure described by Kujirai et al. (1993) with paired pulses consisting of a conditioning subthreshold TMS followed by a test TMS after 2 ms (Kujirai et al., 1993). The stimulation intensity for the test MEP was set to 120% RMT, as this intensity is known to be the most sensitive to inhibition (Garry and Thomson, 2009). We created a SICI curve by 3 blocks of stimulations, with each block performed at a different conditioning stimulation intensity (60%, 70% and 80% RMT). In each block, we measured 10 test MEPs (single pulse TMS) and 10 conditioned MEPs (double pulse TMS), separated in 4 sub-blocks of 5 TMS (all 5 being single or double pulse). The order of intensity blocks and stimulations sub-blocks was pseudorandomized between individuals but matched between groups. For one participant of the control group we were not able to measure SICI, as the subject started to feel drowsy during the measurement. Examples of IO and SICI curves are plotted in Fig. 1.

### Table 1

| Groups     | N  | Age  | Weight | Height  | Gender | Latersity Index | Years AVGP | Hours AVGP |
|------------|----|------|--------|---------|--------|-----------------|------------|------------|
| Players    | 18 | 22.6 | 80.1   | 179.3   | 7.5    | 2 women         | 76.7 ± 40.7| 10.7 ± 4.6 | 13.7 ± 7.1 |
| Control    | 18 | 23.9 | 79.1   | 178.2   | 9.9    | 2 women         | 75.4 ± 38.2| 2.75 ± 4.1 | 0.29 ± 0.8 |

Latersity index corresponds to handedness, with latersity index > 47 indicating that the participant is considered as right handed. Years action video game play (AVGP) corresponds to the life-time exposure to action video game playing (in years), and hours AVGP corresponds to the number of hours spent to play action video games over the last 2 years per week.
2.11. Skill tests

All tests were performed on a laptop (MSI GE60 0ND-288NL (MicroStar INTL Co, 2019), Graphics Card: NVIDIA GeForce GTX660M 2 GB GDDR5 (NVIDIA corporation, 2019)) connected to a standard screen, mouse and keyboard. The participants were seated at a distance of 70 cm from the screen. The full test procedure was explained to the participants before starting the whole test-battery and details on each test were given at the beginning of the specific tests. The mouse sensitivity was adjusted to the comfort of each participant. The session always started with the typing test and was then followed by the three video games tests, which were performed in a pseudo-random order for individuals, but matched between groups. For each test, the participants performed exactly 3 trials, no familiarization trials were allowed. For the keyboard typing test subjects used both hands, for all other tests subjects used only their dominant hand. In all experiments the FDI of the dominant hand was tested with TMS. The keyboard typing test https://www.keyhero.com/free-typing-test/) consisted in typing as fast and as accurate as possible a short random text. The number of words per minute and the typing accuracy were used to score this test. For the video game specific performance tests, we used the following three tests: “Bigger then Smaller”, “Reflex” and “Reaction Time” (Aimtastic video game, Pixel Pointer Studio, http://aimtasticgame.com). In all three tests, the default difficulty level was used. In “Bigger Then Smaller”, participant had to point and click targets that appeared at random locations on the screen (one new target every 0.9 s). The targets appeared at random position on the screen, first big and then got smaller until they disappeared after 3 s. The participants were instructed to click on every target before it disappeared. Over time the targets appeared at more frequent time intervals and the attempt ended if three targets in a row disappeared without the participant being able to click on one of them. The test-score was calculated according to hits and misses (1000 points for hitting a target, -250 points for missing the target). The “Bigger then Smaller” test is considered to estimate the general visuomotor accuracy of a player. During the “Reflex” test, only one target was present at a given time on the screen. The participant was instructed to point and click the target as fast as possible. Each target appeared for 0.45 s and every 0.45 s a new target appeared at a random position on the screen. The attempt ended always after 30 s. The test-score was calculated according to hits and misses (1000 points for hitting a target, -250 points for missing the target). The “Reflex” test is considered to estimate the visuomotor speed and accuracy of a player. During the “Reaction Time” test a black target was presented always in the middle of the screen. The participants were instructed to perform a mouse click as fast as possible when the target color changed from black to red (no accuracy was required for this test). The time between the target presentation and the change of color was random. Each trial consisted of five reaction time tests. The test-score was the measured time between the change of color of the target and the mouse click. It must be noted that only two participants, one from each group, were not naive to the video game tests.

2.12. Analysis

For the “Reaction Time” test, we have removed values over 1000 ms (2 values removed) as they did not correspond to a reaction time but were a result of a misunderstanding regarding the start of the test.

For the analysis of MEPs of the motor map measurements, only the MEPs from the active nodes were included. We checked the preceding background EMG activity of FDI for all MEPs. In case of an EMG activity, defined as the root mean square (rms) of the EMG activity [105,5] ms preceding the TMS, being above the averaged rms EMG + 2 SD per subject, per measurement, i.e. during the motor mapping or IO or SICI, we removed these stimulation from further analysis (Jonker et al., 2019) (motor map: 9 out of 2339; IO curves: 7 out of 1439; SICI curves: 0 out of 2046). The MEPs were first normalised to Mmax and afterwards summed up to calculate the sum of all MEP amplitudes that contributed to the motor map (SOA) (Schwenkreis et al., 2007). We then calculated the amplitude weighted centre of gravity (CoG) of the motor map of each participant, with its coordinates x and y = Σ (x_i * y_i) / Σx_i, with x_i and y_i being the coordinates of the ith node and z_i the averaged MEP amplitude at the ith node (Liepert et al., 1999). Additionally, we calculated the mean coordinates of the hotspot for the two experimental groups. For the IO curves, MEPs amplitude were normalised to Mmax. For the SICI curve, all test MEP amplitudes were averaged within each

Fig. 1. Example of MEP traces. A) Averaged MEP traces of one subject during the IO curves experiment expressed in % Mmax (10 traces per TMS intensity level). B) Averaged MEP traces in another subject during the SICI curves experiment expressed in % Mmax (30 traces per subject for the Test MEPs and 10 traces per subject and TMS conditioning intensity level).
participant. Then, each conditioned MEP amplitude was expressed in % of the mean test MEP amplitude.

2.13. Statistics

For a complete description of the statistic procedures, please refer to the Supplement Material section. We used Bayesian generalized linear mixed models and linear mixed models for statistical analysis since these models provide several advantages when analysing TMS and PNS measurements. For a detailed discussion please see (Boisgontier and Cheval, 2016; Kruschke and Liddell, 2018; Nalborczyk et al., 2019; Giboin et al., 2020). The distribution of MEP amplitudes residuals was often not normal, and in such cases we used generalized linear mixed models instead of linear mixed models (Bolker et al., 2009). We used the brms R package (Bürkner, 2017) to perform the statistical analyses. We had no a priori of the prior distribution of the dependent variables and used the brms package pre-set priors to reduce the influence of priors on the statistical results as much as possible. For all models, we maximized the random error structure to limit type I errors by adding random intercepts by subject and random slopes across independent variables by subject (Barr et al., 2013). We made contrast analyses (e.g., is the SICI higher or lower in Players compared to Control) by comparing posterior distributions with two-sided hypothesis (e.g. Control = Players).

12.13.1. Sensorimotor performance

First, for all tasks, we tested if Players were overall better than Controls (by clustering all trials per subject). Then, to assess if differences occurred at one particular trial, we used a model with effects of group, number of trials (as factors) and the interaction between groups and number of trials.

12.13.2. Motor map

We compared the difference between groups in RMT, number of active nodes, SOA, CoG (x and y coordinates), and hotspot location (x and y coordinates). We compared MEP peak to peak amplitudes between groups, with MEPS from all active nodes clustered within subjects. Furthermore, we compared the excitability spread across the motor map between groups by comparing the MEP peak to peak amplitude from the hotspot onward in the x and y axis of the motor map.

12.13.3. SICI curves

First, we tested whether there was a difference in all the test MEP peak to peak amplitude clustered by subjects between groups. Then, we tested whether there was an overall difference of SICI between groups by comparing all the conditioned MEPs clustered by subjects, whatever the conditioning intensity. Finally, we compared SICI between groups at each conditioning intensity with a model with effect of group, conditioning intensity and interaction between group and conditioning intensity.

12.13.4. Relationship between behavioral performance and neural correlates

We averaged per subject the “Reflex” test score, the “Bigger than Smaller” test score, the reaction time test score, the overall MEP peak to peak amplitude obtained during the motor map and IO curves, as well as the peak to peak amplitude of the conditioned MEP obtained during the SICI procedure. Then, we performed Bayesian multiple linear regressions with the behavioural performance as dependent variable and interactions between group and MEP amplitude of motor map, IO and SICI (the subject who did not perform the SICI experiment was removed). Because of the differences of units between variables can influence the multiple regression results, we scaled all variables (minus the mean and divided by the standard deviation). To prevent the effect of potential outliers, we used a model with a Student distribution for errors (Kruschke, 2013; Bürkner, 2017). The variables number of hours played and years of playing were tested with another multiple regression model and only for Players as in Controls these variables contained many zeros which didn’t fit the linear regression model. We repeated the same analysis on the improvement of performance in the “Bigger Then Smaller”, “Reflex” and reaction time tasks (improvement = performance in Trial 3 / performance in Trial 1 × 100).

For all models, the control group was set as the baseline. Therefore, the intercept given by the model corresponds to the estimate of the control group, and the slope coefficient represents the effect of the Players on the dependent variable, e.g. the difference from Controls to Players in a group comparison. All descriptive results are given as follow: mean ± standard deviation. Statistical test results are presented as follows: Mean of the posterior distribution [upper and lower 95% credible interval boundaries of the posterior distribution]. The 95% credible interval can be interpreted as the boundaries that has 95% of chance to contain the population estimate. In general, if the 95% credible interval contains zero, we assume that the estimate is not credibly different from zero. However, since results are given as a probability distribution and not as a point estimate, the credibility/non-credibility of a result should not be assumed only because a given threshold is reached or not (e.g. in the present study the threshold for the CI was defined at 95%).

3. Results

3.1. Sensorimotor performance

The results of the performance tests are displayed in Fig. 2. Overall (i.e. when pooling all the data from each trial together and just comparing groups), Players typed more words per minute than Controls (beta coefficient = 11.33 [0.86, 21.67] words per minute, which indicates that on average, Players typed 11.3 more words per minute than Controls), but there was probably no difference in typing accuracy between groups (−1.19 [−7.48, 2.38] %). Players were way better than Controls for the “Bigger then Smaller” (27073 [14060, 40457] score points) and “Reflex” games (10082 [5689, 14576] score points). Players also had faster reaction times than Controls (−19.64 [−35.20, −3.73] ms, indicating that Players were on average 19.6 ms faster than Controls).

For a more precise analysis, we have used models including the effects of trials. The model outputs are given in Table 2 and here we describe the contrast between groups for each trial level. To perform these contrasts, we subtracted the posterior distribution of Players from the posterior distribution of Controls (a negative posterior estimate indicates that Players have a higher estimate than Controls). Players may have written more words per minute than Controls during Trial 1, and clearly wrote more words per minute at Trial 3 (difference of performance at trial 1, corresponding to Controls – Players = −11.23 [−22.44, 0.07] words per minute; trial 2 = −8.29 [−19.7, 3.52] words per minute; trial 3 = −14.91 [−29.05, −1.08] words per minute). There was no difference in typing accuracy between groups at any trials (although a difference at Trial 2 may potentially exist): trial 1 = 0.47 [−5.54, 6.33]%; trial 2 = 4.7 [−0.55, 9.94]%; trial 3 = −1.9 [−10.1, 6.08]%. For the “Bigger then Smaller” test, Players were clearly superior than Controls for all trials (trial 1 = −30.395 [−45.787, −15.006]; trial 2 = −23.198 [−38.465, −8000]; trial 3 = −27.034 [−46.458, −7235]). This result was similar for the “Reflex” test (trial 1 = −6709 [−10.914, −2539]; trial 2 = −11.272 [−15.949, −6554]; trial 3 = −11.138 [−17.311, −4956]). Regarding reaction time, Players were clearly better than Controls for the first set of 5 trials. Given the small overlap of the 95% CI under zero, a potential difference may also exist for the second set of 5 trials (set 1 = 40.43 [5.86, 74.09] ms; set 2 = 15.85 [−6.06, 37.52] ms, set 3 = 12.07 [−22.5, 46.49] ms).

3.2. Motor map

The motor maps, CoG and hotspot locations as group means including data of all participants are plotted against the vertex coordinates in Fig. 3A. Motor maps were also plotted against the hotspot coordinates in Fig. 3B as a way to discount the effect of map location variability
between subjects against the vertex. Players showed higher MEP amplitudes than Controls over the whole active motor map (Players = 3.97 ± 5.93 % Mmax, Controls = 2.75 ± 3.84 % Mmax, beta coefficient = 1.37 [0.89, 2.01] % Mmax). However, there was no clear difference between groups in how excitability was spread across the motor map starting from the hotspot (see curves in Fig. 3C and D). There was no difference between groups in the RMT (Controls = 31.1 ± 8.4, Players = 30.8 ± 5.6 % MSO, beta coefficient = -0.26 [-5.23, 4.7] % MSO), number of active nodes (Controls = 6.89 ± 3.34, Players = 6.11 ± 2.62 active nodes, beta coefficient = -0.78 [-2.84, 1.29] active nodes), hotspot location (beta coefficient $x = 0.0$ [-0.63, 0.64] cm, beta coefficient $y = -0.33$ [-1.40, 0.77] cm), CoG coordinates (beta coefficient $x = -0.24$ [-0.91, 0.42] cm, beta coefficient $y = -0.44$ [-1.64, 0.76] cm), and SOA (Controls = 189 ± 128, Players = 232 ± 213 % Mmax, beta coefficient = 52.6 [-64.6, 169.5] % Mmax).

### 3.3. IO curves

IO curves are displayed in Fig. 4. When clustering all MEPs per subject irrespective of the TMS intensity, Players had higher MEPs than Controls (Control = 6.41 ± 7.95 % Mmax or 0.89 ± 1.28 mV, Players = 9.51 ± 13.6 % Mmax or 1.27 ± 1.76 mV; beta coefficient = 1.42 [0.9, 2.15] % Mmax). However, when incorporating TMS intensity levels, we found no clear differences between groups in the MEP amplitude at each TMS intensity level (statistical output displayed in Table 3, marginal effects are depicted in Fig. 4A, and group comparison of distributions at each intensity level using the model estimates are displayed in Fig. 4B, C, D and E).

### 3.4. SICI curves

Players had higher test MEP amplitude than Controls (Controls = 6.19 ± 5.94 % Mmax or 0.84 ± 0.94 mV; Players = 10.6 ± 12.9 % Mmax or 1.38 ± 1.59 mV; beta coefficient = 1.56 [0.9, 2.48] % Mmax). Despite the difference between groups in the test MEP size, SICI was still analysed by expressing the conditioned MEPs in percentage of the mean test MEP because the test MEP difference between groups remained small. Overall, i.e. when clustering all MEPs per subject irrespective of conditioning intensity level, SICI was stronger in Players than in Controls, since the conditioned MEP peak to peak amplitude was larger in Controls (39.7 ± 63.9 % test MEP) compared to Players (24.2 ± 33.2 % test MEP; beta coefficient = -0.51 [-0.9, -0.12] % test MEP). The SICI results for each group at each conditioning stimulus intensity level are displayed in Fig. 5. The output of the statistical model is given in Table 3 and marginal effects are plotted in Fig. 5. As displayed in Fig. 5B, C and D, Players had a stronger SICI than Controls at conditioning intensity levels of 60 % RMT and 80 % RMT but not at 70 % RMT. It must be noted that for Controls, SICI at 70% and 80% RMT conditioning intensity was stronger than at 60% RMT, while there was no clear difference for SICI between conditioning intensity level for Players.

### 3.5. Relationship between behavioural performance and neural correlates

Important results from the multiple linear regressions are plotted in Fig. 6. MEP size from the IO curves explained the reaction time performance in Controls ($-1.37 [-2.45, -0.19]$ scaled units) but not in Players ($0.16 [-0.21, 0.55]$ scaled units). This relationship was clearly different.
between groups (i.e. groups have different slope coefficients), with a higher slope in Players than Controls (difference between groups = 1.53 [0.31, 2.67] scaled units; see Fig. 6A). This means that, for Controls, participants with a small MEP had longer RT. It must be noted that when performing this analysis without an influential point from Controls (top left point in Fig. 6A), the difference between group is less obvious (1.05 [−0.28, 2.30]).

MEP size from the IO curves also explained changes in reaction time (from Trial 1 to Trial 3) in Controls (1.43 [0.18, 2.69]), but not in Players (−0.24 [−0.71, 0.21]), and this relationship was clearly different between groups, with a much smaller slope for Players compared to Controls (difference between groups = −1.67 [−3.01, −0.32] scaled units, Fig. 6B). A negative change indicates a faster RT at Trial 3 than Trial 1. This means that, for Controls, participants who decreased RT over the three trials had a smaller MEP. Without the same influential participant mentioned above, the difference between groups remains similar (−1.88 [−3.39, −0.43]).

The only effect of number of years or hours played found in Players was a strong positive effect of number of hours played per week on the “Reflex” task (0.81 [0.26, 1.36] scaled units).

4. Discussion

We found that Players clearly outperformed Controls in sensorimotor performance tasks linked to computer specific skills, i.e. typing and video game related visuomotor tasks. Players had slightly higher MEP amplitudes during the measurements of motor maps, IO curves and SICI test stimulations. Players had a stronger SICI than Controls, particularly with conditioning TMS intensities of 60% and 80% of RMT. There was no difference between groups in MEP size at each TMS intensity level for the IO curves and in the topographic properties of the motor map. Finally, we found that Players and Controls had clear difference in the relationship between MEP obtained during the IO curves and reaction time.

According to our hypothesis and in line with the literature (Griffith et al., 1983; Borecki L et al. 2013), Players outperformed Controls in the tested action video game related visuomotor tasks and in reaction time (Green et al., 2010; Morin-Moncet et al., 2016). It must be noted that these tasks were new for all but one subject from each group. These results suggest that Players, probably due to their past training or predispositions, were able to transfer their skills to new visuomotor tasks, even at the first trial. These differences at behavioral level were also accompanied by neurophysiological differences in the motor cortex and/or the corticospinal pathway. Overall, but keeping in mind that the present study is cross-sectional and not longitudinal, these observations suggest that Players could potentially be used as model to study long term effect of visuomotor training on the neural system, and to study the role of the different part of the neural system in visuomotor performance.

Players, compared to Controls, had a higher level of corticospinal excitability over the whole FDI motor map. However, the topographical properties (size, hot-spot, center of gravity, etc.) were not different. Previous experiments testing the relationship between long-term skill practice and motor map excitability and topography couldn’t provide a clear consensus. Indeed, in elite racquetball players, compared to non-players, the stimulation of the cortical representation of the FDI muscle elicited MEPs with a larger amplitude, indicating a higher cortical excitability. The motor map area was not larger compared to controls, but was spatially shifted laterally, suggesting a task-related functional reorganization (Pearce et al., 2000). In professional volleyball players, the medial deltoid cortical map was larger but not spatially shifted compared to control participants (Tye et al., 2005) and in professional violinists, TMS over the FDI motor map elicited MEP with larger amplitude and the motor map was found to be larger and spatially shifted when compared to the FDI representation of the non-dominant hand, but

### Table 2

| Dependant variable | Effect       | Estimate | SE  | Lower 95% CI | Upper 95% CI |
|-------------------|--------------|----------|-----|--------------|--------------|
| Words per minute  | Intercept    | 36.71    | 4.06| 28.79        | 44.78        |
|                   | Group Players| 11.23    | 5.7 | −0.07        | 22.44        |
|                   | Trial 2      | 6.07     | 2.52| 1.07         | 10.94        |
|                   | Trial 3      | 5.1      | 2.59| 0.06         | 10.1         |
|                   | Group Players: Trial 2 | −2.93 | 3.53 | −9.87 | 4 |
|                   | Group Players: Trial 3 | 2.71 | 3.68 | −4.54 | 9.97 |
| Typing accuracy (%) | Intercept   | 88.43    | 2.15| 84.31        | 92.74        |
|                   | Group Players| −0.47   | 3.01| −6.33        | 5.54         |
|                   | Trial 2      | 5.02     | 2.37| 0.38         | 9.75         |
|                   | Trial 3      | 4.65     | 2.55| −0.33        | 9.7          |
|                   | Group Players: Trial 2 | −4.23 | 3.31 | −10.79 | 2.35 |
|                   | Group Players: Trial 3 | 2      | 3.57 | −4.91 | 9 |
| Bigger then Smaller (score) | Intercept | 36.992   | 5605 | 28.231      | 48.016       |
|                   | Group Players| 30.395  | 7916| 15.006       | 45.787       |
|                   | Trial 2      | 9154     | 4539| 196          | 18.081       |
|                   | Trial 3      | 9388     | 4639| 125          | 18.379       |
|                   | Group Players: Trial 2 | −7196 | 6485 | −19.883 | 5749 |
|                   | Group Players: Trial 3 | −3127 | 6628 | −16.185 | 10.029 |
| Reflex (score)    | Intercept    | −7.749   | 1531| −10.815      | −4.782       |
|                   | Group Players| 6709    | 2152| 2539         | 10.914       |
|                   | Trial 2      | −994     | 1054| −3087        | 1033         |
|                   | Trial 3      | 125      | 1183| −2182        | 2438         |
|                   | Group Players: Trial 2 | −40.43 | 17.29 | −74.09 | 5.86 |
|                   | Group Players: Trial 3 | −35.96 | 10.31 | −56.47 | −15.83 |
| Reaction time (ms) | Intercept   | 340.97   | 12.43| 316.45       | 365.68       |
|                   | Group Players| −40.43  | 17.29| −74.09       | 5.86         |
|                   | Trial 2      | −35.96   | 10.31| −56.47       | −15.83       |
|                   | Trial 3      | −36.29   | 14.88| −65.38       | −7.09        |
|                   | Group Players: Trial 2 | 24.58 | 14.67 | −4        | 53.41 |
|                   | Group Players: Trial 3 | 28.03 | 20.8 | −13.53      | 67.92 |

Intercept corresponds to the baseline, i.e. group Control and Trial 1. Effects with a “∗” correspond to interaction estimates (SE = standard error, CI = credible interval). To obtain, for example, the posterior estimate of Players at trial 2, one has to add up Intercept + Group Players + Trial 2 + Group Players: Trial 2.
Fig. 3. Motor map results. A) Aggregate of the motor map of each subject from the Control and Players groups. The x and y coordinates refer to the distance in cm from the vertex (0,0). A smaller x corresponds to a lateral shift from the vertex, and a higher y corresponds to an anterior shift. Only the active nodes are considered here. A larger point indicates a higher number of MEPs (and therefore a higher number of participants with active nodes). The colour indicates the averaged MEP amplitude in % Mmax at a particular node. The point and error bars correspond to the group mean and standard deviation of the CoG (brown colour) and of the hotspot (black colour). B) Same as A), but this time with the motor maps of each subject centred on their hotspot (0,0). C) and D) Model result display the effect of the interaction between groups and distance from the hotspot (0 on the x axis) and on the MEP amplitudes in the x and y directions respectively. The thick lines represent the mean and the areas the 95% credible interval.
Fig. 4. *IO curves results.* A) The “violin plots” correspond to the distribution of MEPs (in % Mmax) between groups and at different level of stimulation intensity. The wider the “violin”, the denser the distribution at a given point on the y axis. The violin points are constructed with the whole data set, i.e. with all MEPs measured and kept for the analysis. Diamonds correspond to the mean of MEPs. Large points and associated error bars correspond to the exponentiated marginal effects and their credible interval calculated by the model. B), C), D) and E) Distribution obtained after subtracting the posterior distribution of Players from the posterior distribution of Control MEPs at stimulation intensities of 90%, 110%, 130% and 150% respectively. The x axis represents the difference of MEPs amplitude in % Mmax. The vertical dashed line corresponds to 0 on the x axis and the vertical blue line corresponds to the mean of the distribution. The red area corresponds to the 95% credible interval. Please note that at 90% RMT, most of the distribution is located around zero, clearly indicating that there was no difference between groups in MEP amplitudes at this intensity.
not when compared with the FDI representation of control participants (Schwenkreis et al., 2007). The difference of results between studies may stem from the different muscles and populations studied, the very small samples used for the expert groups (n = 5, 3 and 10 respectively), and for some, inadequate use of statistics (Nieuwenhuis et al., 2011). Our results suggest that long-term skill training can increase the overall excitability of the FDI motor map, without modifying its topographical properties when measured at rest. It must be noted that skill training most probably induces task-specific adaptations, which are observable only during the trained task preparation or execution (Giboin et al., 2018; Giboin et al., 2019; Giboin et al., 2020). Further research should therefore consider exploring the dynamics of motor map topographical properties during the execution of trained and untrained tasks in long-term skill trained subjects.

As expected, MEPs elicited during the IO curves were larger with the higher intensities used (Ridding and Rothwell, 1997; Chen et al., 1998; Kleim et al., 2007). Furthermore, and in coherence with motor map MEPs results, we detected larger MEPs in Players compared to Controls. This is in line with a large body of evidence relating higher corticospinal excitability at rest in long-term skilled population (Pearce et al., 2000; Rosenkranz et al., 2007; Schwenkreis et al., 2007). However, unlike previous studies, we were not able to detect credible differences in MEP size when making comparisons at a given intensity level. It is not clear if this lack of difference is a methodological issue or a relevant physiological observation, i.e. long-term skill training is poorly reflected in IO curves measurements. For example, it can be hypothesized that measurements with higher TMS intensities (e.g. 170% RMT) would have allowed the clear observation of higher MEPs in Players at these high intensities (but see Rosenkranz et al., 2007) who find differences at low intensities). Nevertheless, the observation of overall higher MEPs in Players suggests that motor learning induced changes at intracortical but also possibly at spinal level (Reis et al., 2008; Vahdat et al., 2015). Although changes in corticospinal excitability associated with short-term skill training are well documented (Pascual-Leone et al., 1994; Pascual-Leone et al., 1995; Reis et al., 2008), it still remains quite obscure how a long-term increase in corticospinal excitability is mechanistically associated with long-term motor skill training. It can be speculated that the higher MEP size is due to an increase in intracortical neurons synchronisation, a phenomenon that has been observed after long term (> 5 years) skill training in monkeys (Schieber, 2002).

In line with previous research, SICI in Controls was stronger with an increasing intensity of the conditioning stimulation (Chen et al., 1998; Rosenkranz et al., 2007). We found a clear difference between groups, with Players displaying stronger SICI with conditioning stimulation given at an intensity of 60% and 80% RMT. It must be noted that, contrarily to Controls and previous reports from the literature (e.g. Rosenkranz et al., 2007), SICI was not stronger with an increasing conditioning intensity up to 80% RMT in Players, suggesting a possible ceiling effect. These results support the need to use SICI curves instead of only one conditioning stimulation to better depict GABAergic systems (Stagg et al., 2011; Ibáñez et al., 2020). It has been shown in a previous study that professional musicians had a lower SICI in the ab-

![Fig. 5. SICI curve results. A) The “violin plots” corresponds to the distribution of the conditioned MEP (expressed in % of mean test MEP). The wider the “violin”, the denser the distribution at a given point on the y axis. The violin points are constructed with the whole data set, i.e. with all MEPs measured and kept for the analysis. 76 MEPs out of 1023 were not displayed in the figure as they were > 100%. Diamonds correspond to the mean of conditioned MEPs. Large points and associated error bars correspond to the marginal effects and their credible interval calculated by the model. B), C) and D) Distribution obtained after subtracting the posterior distribution of Players from the posterior distribution of Control conditioned MEPs at intensities of 60%, 70% and 80% respectively. The vertical dashed line corresponds to 0 on the x axis indicates the amplitude of the MEPs in % Mmax and the vertical blue line corresponds to the mean of the distribution. The red area corresponds to the 95% credible interval.](image-url)
Table 3: Statistical model output for the IO and SICI curves.

| Dependent variable | Effect | Estimate | SE   | Lower 95% CI | Upper 95% CI |
|--------------------|--------|----------|------|--------------|--------------|
| log transformed MEP in % Mmax (IO curves) | Intercept | -1.86 | 0.16 | -2.18 | -1.54 |
| Group Players | 0.09 | 0.23 | 0.14 | -0.54 | 0.36 |
| Intensity 110 % RMT | 2.43 | 0.27 | 1.9 | 2.95 |
| Intensity 130 % RMT | 3.52 | 0.24 | 3.04 | 3.99 |
| Intensity 150 % RMT | 4.04 | 0.29 | 3.46 | 4.62 |
| Group Players: 110 % RMT | 0.35 | 0.38 | -0.41 | 1.1 |
| Group Players: 130 % RMT | 0.42 | 0.35 | -0.28 | 1.11 |
| Group Players: 150 % RMT | 0.46 | 0.42 | -0.37 | 1.29 |
| log(cond MEP in % test MEP) (SICI) | Intercept | 3.81 | 0.17 | 3.46 | 4.11 |
| Group Players | -0.74 | 0.26 | -1.29 | -0.23 |
| Cond 70 % RMT | -0.52 | 0.22 | -0.98 | -0.1 |
| Cond 80 % RMT | -0.47 | 0.21 | -0.93 | -0.07 |
| Group Players: Cond 70 % RMT | 0.23 | 0.32 | -0.12 | 1.17 |
| Group Players: Cond 80 % RMT | 0.11 | 0.35 | -0.62 | 0.76 |

Intercept corresponds to the baseline. For the IO curves, Intercept refers to Control and a stimulation intensity of 90 % RMT. For the SICI, Intercept refers to Control and a conditioning intensity of 60 % RMT. Effects with a “+” correspond to interaction estimates (SE = standard error, CI = credible interval). Please note that for IO curves data was log transformed and that for SICI the estimates are given with their log link. For an easier interpretation of the statistical output (due to the transformed data or the log link), the exponentiated marginal effects are plotted in Figs. 3 and 4.

Fig. 6. Multiple linear regression plots. A) Mean peak to peak amplitudes of MEP size obtained during the IO curves versus mean reaction time (both units are scaled). B) Mean peak to peak amplitudes of MEP size obtained during the IO curves versus changes in mean reaction time from Trial 1 to Trial 3 (both units are scaled). For both, the thick line represents the posterior mean estimate and the filled area the 95% credible interval.

...ductor pollicis brevis muscle at a conditioning intensity of 70% active motor threshold but a higher SICI at 90% compared to non-musicians (Rosenkranz et al., 2007) (but see Nordstrom and Butler, 2002 who find different results). This observation, when combined and compared with the present results, suggests that GABAergic systems are not affected as a whole by the long-term training, and are affected in a task-specific way. These suggestions are in line with the large functional diversity of GABAergic neurons found in the neocortex (Tremblay et al., 2016). For example, GABAergic activity is related with skill learning and neural plasticity. A reduction in GABAergic activity favours neural plasticity and skill learning (Ziemann et al., 2001; Kolasinski et al., 2019), and baseline GABAergic levels correlates negatively with motor performance (Stagg Charlotte et al., 2011). Therefore, the present observations, i.e. stronger SICI and better performance and learning rate in the new video game tasks tested for Players versus Controls, is in contradiction with the literature related to GABAergic activity and motor skill learning. However, the effect of long term skill training on such mechanisms remain unknown. In any cases, we suggest that action video game players could be used as an interesting model to study the interactions between GABAergic activity, neural plasticity, motor learning and long term skill training. GABAergic activity is also a mediator of surround inhibition, a mechanism that increases the selectivity of motor activity (Beck and Hallett, 2011), especially useful for the fine and fast movements required for action video games. A stronger surround...
inhibition could partly explain the higher dexterity of Players, but also their capacity to display fast and accurate movements for long durations (Bächtiger et al., 2019). We suggest that Players could also be used as model to study surround inhibition mechanisms.

Interestingly, SICI was the strongest neurophysiological difference observed between groups, suggesting that playing action video games has possibly a stronger long-term effect on inhibitory than excitatory circuits. This observation would contradict the idea that long-term skill training maintains a balance between excitatory and inhibitory networks (Dai et al., 2016). However, it must be noted that, in Players, this balance may still be maintained at physiological level, but may not be observable with the means of TMS given that strong inhibitory networks could potentially mask stronger excitatory networks. Indeed, the MEP is a result of both excitatory and inhibitory postsynaptic potentials that occur simultaneously at M1 level, with a possible gating of EPSP by IPSP. Additionally, it has been shown that lorazepam, a drug that increases the excitability of inhibitory intracortical networks, increases SICI on the one hand and decreases single pulse MEP amplitudes on the other hand (Di Lazzaro et al., 2000). Based on this consideration, and given the stronger GABAergic inhibitory system in Players as observed with SICI, the physiological difference between groups in the excitatory systems may be larger than what has been observed here with TMS during the motor map and IO curves procedures. Similarly, this stronger inhibition may also mask difference in the motor map size (which could potentially be larger in Players).

It must be noted that only a few associations between neural correlates and performance were observed (reaction time and MEPs size from the IO curves measurements), and these associations may be driven by an “influential participant”. The interpretation of these results should thus be done with care. The visuomotor tasks tested presently required high-level of sensorimotor skills and perceptual and cognitive processing, each in proportion that cannot be estimated with any certainty (Gozli et al., 2014). Therefore, because of their multifactorial performance structure neither the “Bigger then Smaller” nor the “Reflex” test offer themselves as tests that can easily be associated with very restricted neurophysiological assessments, like e.g. SICI in the FDI muscle during rest. Keeping this in mind, it is not surprising that we didn’t find any correlations between these complex visuomotor gaming tasks and the TMS measures in the present study. With the simpler tests, like the “Reaction Time” test the differentiation between Players and Controls became more difficult compared to the more complex tasks, but the association with the neurophysiological measures, like the MEPs from the IO curves, more straightforward. Controls, but not Players, had a shorter reaction time correlated with a higher MEP size at rest, which is in line with previous work (Greenhouse et al., 2017). The functional explanation that associates MEP size and reaction time is still unclear but could be related to different neural characteristics all along the corticospinal pathway (e.g. higher cortical and spinal excitability, better descending connectivity, etc.) (Greenhouse et al., 2017). Interestingly, the absence of such relation in Players may indicate that the effect has been saturated, possibly due to their long-term training (i.e. an increase in excitability has an effect on reducing reaction time only up to a certain point at individual level, and this ceiling has probably been reached by all Players).

To sum it up, from a functional perspective both adaptations, stronger inhibitory as well as stronger excitatory networks appear useful to increase sensorimotor performance in e.g. a reaction time task. Whereas a higher excitatory output might be comparable with a more powerful engine, a higher inhibitory output might constitute a stronger braking system. It must be noted that the correct inhibition of antagonist muscles is possibly more crucial for a rapid and precise movement than the strong activation of synergists, possibly explaining the stronger difference between Controls and Players for the SICI than the IO curves. The present study is absolutely in line with the notion that long term skill training may increase both the excitatory and inhibitory capabilities of intracortical networks projecting to trained muscles, most probably in a task-specific way (Pearce et al., 2000; Nordstrom and Butler, 2002; Rosenkranz et al., 2007; Schwenkreis et al., 2007; Hirano et al., 2014).

The present results also offer interesting clinical perspectives. Indeed, many motor afflictions (e.g. stroke and amyotrophic lateral sclerosis) seem to be related with SICI dysfunction (Hummel et al., 2009; Menon et al., 2014), and rehabilitation programs including action video game training could potentially help to regain motor functionality by acting on dysfunctional cortical networks. It must be noted that physiological therapies using action video games are not new and seem to be relatively successful (Bonnehère et al., 2016). In the present context, among many issues, the main difficulty of such process may reside in the dynamic adjustment of the games difficulty to the patient motor capability across recovery.

4.1. Limitations

One of the biggest limitation lies in the small number of TMS per level used (10 TMS), which can clearly limit the reliability of our results (Goldsworth et al., 2016). This number was maintained low as a compromise between the requirement of limiting the overall number of stimulations and the amount of measurements to perform (Kleim et al., 2007).

Control and Player had different test MEP size during the SICI experiment. This difference in MEP size could have influenced SICI and partly explained why Player have stronger MEP inhibition (Lackmy and Marchand-Pauvert, 2010). However, in the present study, the absence of difference between groups in SICI induced with conditioned TMS at 70% RMT indicates that the difference observed with 60% and 80% RMT are most probably not driven entirely by the test MEP difference, but also by group differences at neural level.

In general, SICI level is probably better correlated with active motor threshold (AMT) than RMT, and using AMT may reduce results variability compared to RMT (Ort et al., 2003). However, in the present case, we believe that using RMT is more controlled than using AMT. Indeed, Player, given their extensive action video game practice, have most probably “fitter” muscles involved in visuomotor tasks, meaning different level of maximal force due to adaptations at muscle and neural level, e.g. better capacity of recruiting motor unit and/or affecting their firing rate. Thus, at a given level of AMT (absolute or relative), it is not clear whether the same proportion of the motoneuron pool is observed between both groups. Because of these adaptations, the state of the corticospinal pathway may be more different between groups during AMT than RMT (and thus less comparable or controlled). Additionally, it must be mentioned that we used biphasic TMS to assess SICI, while it has been shown that SICI may have (Sale et al., 2016; Davila-Pérez et al., 2018) or may have not (Wessel et al., 2019) different sensitivity to current directions (e.g. monophasic anterior-posterior versus monophasic posterior-anterior currents). The SICI characteristics of Player could be further investigated using different TMS current directions.

It must be noted that, in general, the visuomotor tasks performed by action video game players are complex and involve a large set of muscles. For example, the flexor digitorum superficialis (FDS) may have a more important role than the FDI to achieve task precisions. Considering this, and considering how neural adaptations are task-specifically shaped by training (Giboin et al., 2020), different corticospinal adaptations than the one presently observed for the FDI may occur for the other involved muscles.

It could be speculated that, unlike for example professional musicians, the training level of Players was not high enough to discriminate them clearly from Controls. Although Players are not elite esport players, we believe that such supposition is unlikely. Indeed, Players had a clear skill superiority in the complex visuomotor tasks, even at the first trial, and they have been playing action video games for an average of 13 years. If such exposure level is not enough to clearly assess neurophysiological differences with TMS, it may indicate that these TMS methods
are not sensitive enough, or that these neurophysiological markers are not that relevant for long-term skill training related brain changes.

Finally, it is important to keep in mind that the present study is cross-sectional and not longitudinal, which of course limit our interpretations regarding the neural difference observed here. Many studies have shown that playing action video games can induce neural plasticity after a few weeks of training (Bavelier et al., 2012), suggesting that a part of the present difference was induced by the training. However, predisposition and selection effects could also explain partly the observed differences, e.g. a high initial performance and a fast progression may increase the probability that one continues to play action video games compared to someone with rather low initial aptitudes (Georgiades et al., 2017).

5. Conclusion

We have shown that long term action video games players have better visuomotor skills than non-players. Additionally, Players depicted stronger excitation and especially stronger inhibitory corticospinal function. Players and Control had different relationships between corticospinal excitability and reaction time performance, suggesting a possible training-induced saturation effect in Players. Amongst the mechanistic insights into effects of long term skill training, the present study demonstrates the potential of video games and in particular of action video games as an ideal tool to study sensorimotor function and opens up the potential of video gaming as a treatment of pathologies associated with the dysregulation of intracortical networks.

Credit Author Statement

Louis-Solal Giboin: Conceptualization, Methodology, Formal Analysis, Investigation, Writing - Original Draft, Visualization, Supervision, Project Administration, Funding Acquisition.
Tom Reunis: Investigation, Formal Analysis, Conceptualization.
Markus Gruber: Funding Acquisition, Conceptualization, Resources, Writing – Review & Editing.

Declaration of Competing Interest

None.

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Data and code availability statements

All the data required to reproduce the present results is available on Figshare (with a private link until acceptance of the article, it will be made publicly available after publication). Link: https://figshare.com/s/8690c4bcda4a2b4ede.

Supplementary materials

Supplementary material associated with this article can be found in the online version, at doi:10.1016/j.neuroimage.2020.117576.

References

Bächer, M., Lehner, R., Thomas, F., Hanimann, S., Balsters, J., Wendroth, O., 2019. Human motor fatigability as evoked by repetitive movements results from a gradual breakdown of surround inhibition. eLife 8, e46750.
Barr, D.J., Levy, R., Scheepers, C., Tily, J.H., 2013. Random effects structure for confirmatory hypothesis testing: keep it maximal. J. Mem. Lang. 68, 255–278.
Bavelier, D., Green, C.S., 2019. Enhancing attentional control: lessons from action video games. Neuron 104, 147–162.
Bavelier, D., Green, C.S., Pouget, A., Schrater, P., 2012. Brain plasticity through the life span: learning to learn and action video games. Annu. Rev. Neurosci. 35, 391–416.
Beck, S., Hallett, M., 2011. Surrounded inhibition in the motor system. Exp. Brain Res. 210, 165–172.
Benady-Chorney, J., Yau, Y., Zeigami, Y., Bobbott, V.D., West, G.L., 2018. Habitual action video game players display increased cortical thickness in the dorsal anterior cingulate cortex. NeuroReport 29, 393–396.
Bogontjier, M.P., Cheval, B., 2016. The anova to mixed model transition. Neurosci. Biobehav. Rev. 68, 1004–1005.
Bolker, B.M., Brooks, M.E., Clark, C.J., Geange, S.W., Poulsen, J.R., Stevens, M.H.H., White, J.-S.S., 2009. Generalized linear mixed models: a practical guide for ecology and evolution. Trends Ecol. Evol. 24, 127–135.
Boncchio, B., J., Besni, B., Omeina, L., Van Sint Jan, S., 2016. The use of commercial video games in rehabilitation: a systematic review. Int. J. Rehabil. Res. 39, 277–290.
Borecki, L., Tolsky, T., Pokorski, M., 2013. Computer games and fine motor skills. Respiratory Regulation - Clinical Advances 39, 243-348. doi:10.1007/s10938-007-9456-9.
Bürkner, P.C., 2017. BRMS: an R package for Bayesian multilevel models using stan. J. Stat. Softw. 80, 1–28.
Chen, R., 2004. Interactions between inhibitory and excitatory circuits in the human motor cortex. Exp. Brain Res. 154, 1–10.
Chen, R., Tam, A., Bütteich, C., Corwell, B., Ziemann, U., Rothwell, J.C., Cohen, L.G., 1998. Intracortical inhibition and facilitation in different representations of the human motor cortex. J. Neurophysiol. 80, 2870–2881.
Dai, W., Pi, Y.-L., Ni, Z., Tan, X.-Y., Zhang, J., Wu, Y., 2016. Maintenance of balance between motor cortical excitation and inhibition after long-term training. Neuroscience 326, 114–122.
Davila-Pérez, P., Jannati, A., Fried, P.J., Cudeiro Mazaira, J., Pascal-Leone, A., 2018. The effects of waveform and current direction on the efficacy and test–retest reliability of transcranial magnetic stimulation. Neuroscience 393, 97–109.
Di Lazzaro, V., Oliviero, A., Meglio, M., Cioni, B., Tamburini, G., Tonali, P., Rothwell, J.C., 2000. Direct demonstration of the effect of lorazepam on the excitability of the human motor cortex. Clin. Neurophys. 111, 794–799.
Garry, M.I., Thomson, R.H., 2009. The effect of test TMS intensity on short-interval intracortical inhibition in different excitability states. Exp. Brain Res. 193, 267–274.
Georgiades, E., Klissouras, V., Bauch, J., Wang, G., Pinlailis, Y., 2017. Why nature pre- vails over nurture in the making of the elite athlete. BMC Genom. 18, 835.
Giboin, L.-S., Loewe, K., Hassa, T., Kramer, A., Dettmers, C., Spiteri, S., Gruber, M., Schoenfeld, M.A., 2019. Cortical, subcortical and spinal neural correlates of skillline training-induced balance performance improvements. NeuroImage 202, 116061.
Giboin, L.-S., Tokuno, C., Kramer, A., Henry, M., Gruber, M., 2020. Motor learning induces time dependent plasticity that is observable at the spinal cord level. J. Physiol. n/a.
Giboin, L.-S., Weiss, B., Thomas, F., Gruber, M., 2018. Neuroplasticity following short-term strength training occurs at supraspinal level and is specific for the trained task. Acta Physiol. (Oxf) 222, e12998.
Gillo, F., Curra, A., Inghilbert, M., Lorenzana, C., Suppa, A., Manfredi, M., Berardelli, A., 2003. Abnormalities of motor cortex excitability preceding movement in patients with dystonia. Brain 126, 1745–1754.
Goldstein, M.R., Hordacre, B., Ridding, M.C., 2016. Minimum number of trials required for within- and between-session reliability of TMS measures of corticospinal excitability. Neuroscience 320, 205–209.
Gong, D., He, H., Liu, D., Ma, W., Dong, L., Luo, C., Yao, D., 2015. Enhanced functional connectivity and increased gray matter volume of insula related to action video game playing. Sci. Rep. 5, 9763.
Göstl, D.G., Bavelier, D., Pratt, J., 2014. The effect of action video game playing on sen- sorimotor learning: evidence from a movement tracking task. Hum. Mov. Sci. 38, 152–162.
Green, C.S., Pouget, A., Bavelier, D., 2010. Improved probabilistic inference as a general learning mechanism with action video games. Curr. Biol. 20, 1573–1579.
Greenhouse, I., King, M., Noah, S., Maddock, R.J., Irvy, R.B., 2017. Individual differences in resting corticospinal excitability are correlated with reaction time and GAIA content in motor cortex. J. Neurosci. 37, 2686–2696.
Griffith, J.L., Voloshin, P., Gibb, G.D., Bailey, J.R., 1983. Differences in eye-hand motor coordination of video-game users and non-users. Percept. Motor Skills 57, 155–158.
He, Q., Turel, O., Wei, L., Bechara, A., 2020. Structural brain differences associated with extensive massively-multiplayer video gaming. Brain Imaging. Behav. Hirano M., Kubota S., Morishita T., Uehara K., Fujimoto S., Funae K. 2014. Long-term practice induced plasticity in the primary motor cortex innervating the ankle flexor in football juggling experts. 18:310.
Hummel, F.C., Steven, B., Hoppe, J., Heise, K., Thomalla, G., Cohen, L.G., Gerloff, C., 2009. Deficient intracortical inhibition (SCI) during movement preparation after chronic stroke. Neurology 72, 1766–1772.
Ibáñez, J., Spampinato, D.A., Pararseethanan, V., Rothwell, J.C., 2020. SCI during changing brain states: differences in methodology can lead to different conclusions. Brain Stimul. 13, 353–356.
Illic, T.V., Meintzsche, F., Cleff, U., Ruge, D., Kessler, K.R., Ziemann, U., 2002. Short-in-
terval paired-pulse inhibition and facilitation of human motor cortex: the dimension of stimulus intensity. J. Physiol. 545, 153–167.

Isa, T., Kinoshita, M., Nishimura, Y., 2013. Role of direct vs. indirect pathways from the motor cortex to spinal motoneurons in the control of hand dexterity. Front. Neurrol. 4.

Ismoru, Y., Harakuni, R., Takekawa, T., Aizawa, H., Fukai, T., 2009. Microcircuitry coordination of cortical motor information in self-initiation of voluntary movements. Nat. Neurosci. 12, 1586–1593.

Jonker, Z.D., van der Vliet, R., Hauwert, C.M., Gaiser, C., Tulen, J.H.M., van der Geest, J.N., Donchín, O., Ribbers, G.M., Frens, M.A., Selles, R.W., 2019. TMS motor mapping: comparing the absolute reliability of digital reconstruction methods to the golden standard. Brain Stimul. 12, 309–313.

Klein, J.A., Klein, E.D., Cramer, S.C., 2007. Systematic assessment of training-induced changes in corticospinal output to hand using frameless stereotaxic transcranial magnetic stimulation. Nat. Protoc. 2, 1675–1684.

Kolasinski, J., Hinson, E.L., Divanjibghiz Zand, A.P., Rizov, A., Amir, U.E., Stagg, C.J., 2019. The dynamics of cortical GABA in human motor learning. J. Physiol. 597, 271–282.

Kruschke, J.K. 2013. Bayesian estimation supersedes the t test. J. Exp. Psychol. Gen. 142, 573-603.

Kruschke, J.K., Liddell, T.M. 2018. Bayesian data analysis for newcomers. Psychonom. Bull. Rev. 25, 155–177.

Kuhn, S., Gleich, T., Lorenz, R.C., Lindenberger, U., Gallinat, J., 2014. Playing super mario induces structural brain plasticity: gray matter changes resulting from training with a commercial video game. Mol. Psychiatry 19, 265–271.

Kujirai, T., Caramia, M.D., Rothwell, J.C., Day, B.L., Thompson, P.D., Ferbert, A., Wroe, S., Asselman, P., Marsden, C.D., 1993. Corticospinal inhibition in human motor cortex. J. Physiol. 471, 501-519.

Lackmy, A., Marchand-Pauvert, V., 2010. The estimation of short intra-cortical inhibition depends on the proportion of spinal motoneurons activated by corticospinal inputs. Clin. Neurophysiol. 121, 612–621.

Lemon, R.N., 2008. Descending pathways in motor control. Annu. Rev. Neurosci. 31, 195–218.

Lieberp, J., Milner, W.H.R., Bauder, H., Sommer, M., Detmers, C., Taub, E., Weiller, C., 1998. Motor cortex plasticity during constraint-induced movement therapy in stroke patients. Neurosci. Lett. 250, 5-8.

Lieberp, J., Terborg, C., Weiller, C., 1999. Motor plasticity induced by synchronized thumb and foot movements. Exp. Brain Res. 125, 435–439.

Menon, P., Kiernan, M.C., Vucic, S., 2014. Cortical dysfunction underlies the development of the split-hand in amyotrophic lateral sclerosis. PLoS One 9, e87124.

Molina-Luna, K., Hertler, B., Buitrago, M.M., Luft, A.R., 2008. Motor learning transiently changes cortical somatotopy. Neuronale 40, 1748–1754.

Monti, M.-H., Plauth, E.J., Klein, J.A., 2005. In Search of the motor engr apartments: motor map plasticity as a mechanism for encoding motor experience. Neuroscience 117, 471–482.

Morin-Monet, O., Therrien-Blanchet, J.M., Ferland, M.C., Theoret, H., West, G.L., 2016. Action video game playing is reflected in enhanced visuomotor performance and increased corticospinal excitability. PLoS One 11, e0169013.

Nabórzyck, L., Batalier, C., Lovenbruck, H., Vilain, A., Bürker, P.-C., 2019. An introduction to bayesian multilevel models using BRMS: A case study of gender effects on vowel variability in standard Indonesian. J. Speech, Lang. Hear. Res. 62, 1225–1242.

Nieuwenhuis, S., Forstmann, B.U., Wagenmakers, E.-J., 2011. Error analyses of interactions in neuroscience: a problem of significance. Nat. Neurosci. 14, 1105–1107. Nordström, M.A., Butler, S.L., 2002. Reduced intracortical inhibition and facilitation of corticospinal neurons in musicians. Exp. Brain Res. 144, 336–342.

Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9, 79–113.

Orth, M., Snijders, A.H., Rothwell, J.C., 2003. The variability of intracortical inhibition and facilitation. Clin. Neurophys. 114, 2362-2369.