Supplementary files for

Birth and death of a phantom

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Methods and seizure

1. rTMS protocol

The experimental session was conducted as follows: JC was sitting in a chair, the head lying back in a holder, and the coil was held by the TMS operator and simultaneously fixed in an articulated arm appended to the chair. A 'figure of eight' MCF-B65 butterfly coil was positioned over the parietal region of the left hemisphere, with the stimulation being delivered by a TMS MagVenture Pro X100. The coil was oriented in the rostrocaudal axis over the M1 hand area[21]. Biphasic pulses were delivered at 100% of the stimulation intensity of the motor threshold, which was determined during a resting condition as the minimal stimulation intensity at which a movement of two intrinsic hand muscles could be visually detected after a single pulse TMS. The primary motor cortex was mapped to identify the most excitable part of the hand area of the primary motor cortex. The mapping consisted in applying 170 single pulses (triggered manually by the experimenter) at an intensity starting at a maximal value of 60% of the maximal stimulator output (MSO) at 14 locations spaced from 1 cm following a 9*9cm grid, the first stimulation site being located 2 cm laterally and 4 cm rostrally to the vertex. After the mapping, a 30Hz continuous Theta Burst Stimulation (cTBS) was applied at the location with the maximal excitability (largest MEP amplitude) with the following parameters: stimulation threshold intensity of 80% of the resting motor threshold and corresponding to 55% of the MSO, 600 pulses in 200 trains of three pulses with 33ms time interval, the tie interval between two trains being 167 ms[22]. Concurrently, electromyographic (EMG) activity of 8 hand, arm and shoulder muscles (first dorsal

interosseus, thenar, extensor carpi ulnaris, palmaris longus, biceps, triceps, anterior deltoïd and trapezius; Fig 1B), including 3-dimensional accelerometers on the extensor carpi ulnaris muscle, were continuously recorded during the experiment.

2. Seizure

Prior to the experiment, the participant reported no transcranial magnetic stimulation (TMS) risk factors such as medication intake or history of closed head injury, loss of consciousness, seizures or febrile seizures, nor family history of epilepsy. However, we learned subsequently that he (unusually) drank 76 ml alcohol between 9 and 11 hours prior to the TMS session and that he had mild sleep deprivation (unfortunately, he was unable to report more exactly on his sleeping time in the previous days).

During stimulation over the left M1 hand area, the TMS operator first noted that the right arm quickly moved upwards after the beginning of the cTBS stimulation and the participant asked to stop the experiment, which was done immediately by removing the coil from the head. The participant then presented typical tonico-clonic movements of the right forelimb (as recorded by the electromyogram), followed by tonic and clonic bilateral arm movements during 1 minute and loss of consciousness without incontinence. Consciousness was progressively regained over the 10 following minutes. The in-house medical doctor confirmed a post-ictal status with quickly regressive confusion and an absence of focal motor deficit. An ambulance was called and arrived 12 minutes later to take the patient to an emergency ward. A general neurologic and mental exam 2 hours after the event showed no neurological or mental deficits, except a mild headache. Laboratory values showed only increased muscle enzymes. Brain MRI and EEG executed in the 24 hours were normal. Two subsequent neurological evaluations, 2 and 11 days after the seizure confirmed an absence of sequellae. The clinical diagnosis of this event was TMS-induced seizure, as evidenced by the concurrent EMG recordings. Seizures in the context of current safety guidelines for TMS experimentation are a rare occurrence, and several causes and mechanisms have been proposed both to explain such situations and to prevent them[23]. However, we were unable to pinpoint the exact facilitating factors of the seizure in the present case, except perhaps a mild sleep deprivation and an unusual amount of alcohol intake the previous night (5 units). The present report is, to our knowledge, only the second account of a cTBS induced seizure: the previous case involved a healthy 33 year-old

participant who came back, 2 days prior to the event, from a Trans-Atlantic flight, perhaps suggesting a sleep pattern alteration[24]. Many rTMS studies are run on young participant and data indicate age-dependent decline in cortical excitability and sensorimotor integration within the human motor cortex, suggesting a stronger cortical excitability in young adults[25]. This event was reported to the local ethical committee. This report illustrates the necessity of a perfect anamnestic control, including recent alcohol intake and sleep-deprivation, particularly when stimulation amplitude is at 55% of MSO.

3. Interview transcription

Experimenter: Can you tell us with your own words what happened?
Participant: At first - that was when they were looking for the stimulation area, in the motor cortex, the hand area. This made light electrical shocks, very light, it caused no pain, it just made a sort of "click" [snaps fingers]. At the same time, the hand was stimulated [shows his right hand contracting], then it was a little on the side [shows the left side of the head], it was the face, the left part, on the side of stimulation, which reacted more.
E: So these were just movements at that point, were there any sensations ?
P: No pain, but a movement, the eye closed when it was mainly on the face, and the hand reacted when it was the hand area, I guess.
E: Yes.
P: So when the correct area was found [shows his right hand contracting], they diminished stimulation intensity, so that there were only two fingers moving [shows thumb and index contracting]…
E: Mh mh.
P: And at that moment, they were ready to do the rTMS. I was asked whether I was ready and I said yes, and so it started [short pause]. And they started the stimulation and [short pause] rather quickly, I'd say after 2-3 seconds – but apparently it was more like 6 seconds [the participant learned later] – but say after 2-3 seconds I had the impression that the hand was really shaking [shows his right forearm shaking], strongly shaking, and then more generally, more or less the whole upper body was clenched [short pause], and then a little bit later I really felt the hand clenching really strong

[shows his clenched right arm moving towards his face] and come towards me, I couldn't do anything about it, and by the way it's at that point that I said "stop!" I guess [short pause]. And right at that moment, I had the feeling that [short pause], a second hand was [short pause], a second virtual hand was there [shows a "second hand" appearing behind the right hand, still clenched and close to the face, using his left hand] and it "went out" in that direction [shows the "virtual hand" moving away from his face, "out" of the right arm], so it almost reached the original position of my hand, I'd say [now shows the right arm laying down, representing the "virtual hand" recovering the initial position of the physical arm], like an "excorporation" like that [shows same movement again], and still with a mounting tension [short pause]. And that hand that was virtual, which was here [shows the distinction between "both" hands now, one clenched near his face, the other lying supine, as he watches "both" in front of him], it began to dis… disintegrate like [short pause], starting from the tip of the fingers, as if the fingers were opening, and it spread along that virtual hand [short pause], the picture was pretty violent [short pause], and it went up along the shoulder, along the arm towards the shoulder, but when it arrived at the shoulder, I think I, well at that point I, I lost consciousness.

E: Mh mh.

P: I'd say it's a rather violent reminiscence.

E: So, you saw flesh, you saw… you had the virtual hand that was, then, in a rather extended posture ?

P: Yes.

E: As compared to the hand, the real hand.

P: Absolutely, yes [shows again the position of "both" hands]

E: You could *see* both at the same time ?

P: [thinks] Yes, yes [very affirmative]

E: You remember seeing both at the same time ?

P: I remember seeing the one that was [shows how the physical clenched hand was near his face] very tended towards me…

E: Yes…

P: And the other one which was here [shows using left hand how the "virtual" hand was in the supine position], and I couldn't understand what was going on, it happened so fast…

E: Yes.

P: So, really both hands, together.

E: Right. And so, the hand that was there, the virtual hand, it was first in a normal situation? And only then, it started “opening” starting from the fingers ?

P: Yes, I’d say it’s…

E: Or was it during the movement ? Did it started “opening” while it was changing place?

P: [hesitates] Hard to say, maybe a bit at the same time.

E: Hard to say uh ?

P: It went out, and here it start…

E: To burst.

P: Right, to burst like that.

E: Yeah.

P: And then it quickly, quickly went up to the shoulder, and it’s then that I [pause]…

E: You said you saw the fingers, the muscles, the skin, the skin disappearing, or “opening”?

P: [hesitates] That’s right, something like that, but it really started at the fingers, like that [shows right hand fingers “exploding”]…

E: From the fingers.

P: …as if they opened, so I think I saw some flesh, it was all very violent, like that.

E: You said like a banana?

P: Right, like a banana, really “opening” like that [makes opening gesture with both hands, like a banana peeling].

E: This started at the fingers, or was it more specifically the more, the more « far away » part…

P: It really was the more distal part [shows distal direction] and…

E: Okay…

P: … back to the proximal direction [gesture showing progression from distal hand to right shoulder], but mainly the reminiscence is strongest with the fingers, then I mostly had the impression I was losing my arm [shows arm as if sent away] and then…

E: You felt you were losing your arm…

P: Well, it really was as if it was caught in… in some kind of gears [gesture of a rotating machine]…

E: Like ripped away ?

P: …it was being taken away from my body, and yet I could still see the other arm here

[shows right clenched fist near the face, the physical arm].

E: Okay.

P: After that… I quickly passed out.

E: Did you feel any pain ? During…

P: Absolutely not, no.

E: No pain, this was only visual ?

P: It was psychologically difficult, because [short pause]…

E: And so what did you think at the time…

P: [interrupts] I was losing my arm.

E: You lose your arm, you're afraid ?

P: [pause] Yeah.

E: And then… so you had time to be afraid you might lose your arm…

P: That it was too late, that it was over, that my arm was gone.

E: Right. Does all this make a reference to something you might have seen previously, like something in a movie, a gore movie ?

P: I'd say no, I don't think so. No.

E: So this was the first time you saw that kind of image ? Can you still see it, if you think about it, if you…

P: Not really, no.

E: No.

P: It's more like a visual sensation. Something sensitive… But kind of both at the same time… It was more like a feeling my self had to interpret the way I told you [short pause], still it was more like a feeling.

E: You have a feeling that you transform into something visual, actually, it's like that ?

P: Rather like that, yeah.

E: So something like a sensation… a modification of the normal sensation of your arm…

P: Right.

E: … that you, that was interpreted as if you were losing your skin, as if it « opened »…

P: Right, and then it was also like some kind of pressure over the entire arm, that was coming up towards the shoulder. I really remember that it came up until here [shows right shoulder], when I was really clenched I guess [shows right arm straight and rigid in from of him, slightly turned towards the left side], and then I passed out.

E: Before that, the arm stayed in the same position, there was no more movement ?

P: Yes it was still there. The virtual hand was here [shows right arm extended and supine] and the other was still clenching like that [now right arm clenched and near the face] and the shoulder went up, I guess.

E: Okay.

P: And… that's it. [pause] (…)

E: Was it disgusting, did you feel any nausea at the sight ?

P: No, no no, it wasn't physical like that, but I thought… I thought I was losing my arm and it was all over…

E: Did you try to remove the arm, did you try to do something, to avoid…

P: Yes, I'd say yes. But… at the same time [shows again both right arms in their respective positions]… all this happened so fast, but… at the same time, I had my arm that was there, the virtual one [uses left arm to display the position of the virtual arm, while the right arm displays the clenched position of the physical right arm], the other was here, I couldn't do anything, I was clenching all over [all his body tensed and rising from the chair], increasingly, also the face…

E: Right.

P: I couldn't speak anymore… I felt powerless, and oppressed, anxious.

E: Right.

P: I'm not claustrophobic at all, but I think someone claustrophobic would feel the same thing when… as if he saw the walls approaching, something alarming like that.

E: Did you feel that your arm still belonged to you, was it clear that it was yours, or did you sense that it might belong to someone else ?

P: Yes, it was clearly mine. You know, I feared I might lose it, so it was mine. (…)

E: (…) Do you still fear for your arm, now ?

P: No.

E: Did you have « visions » of the scene afterwards, like flashbacks or nightmares ?

P: [Thinks] No. (…) But at the time, I got scared, I thought I was going to die.

E: When was that : when you saw the [virtual] arm, or just before you passed out ?

P: It was just before I passed out, I thought it was over. (…) I thought [extends his right arm], if it starts from the hand [holds his right hand], goes up to the shoulder [follows the arm to shoulder], why should it stop there… It was as if I was sucked into a grinder [shows rotating movement].

E: Right.

P: Or something like that. What came after the shoulder, if not the rest of the body…

so I thought I was done. (…) And then I passed out, and I don't remember what came next. When I woke up, in fact, I didn't even think about that [the virtual hand episode], that wasn't the first thing I remembered.

E: You were confused at first, for about 20 minutes or so, that was in the ambulance, but you recognized people around you there.

P: Yes that I remember, I knew some people (…) Actually, my very first memory, real memory, when I woke up was you [EC], next to me at my right, and MK at my left, (…) but I still thought we were doing the experiment, that it was about to start.

E: Right.

P: It was pretty clear to me that we were continuing the experiment and that… So I put aside that story [the virtual hand episode] and I couldn't understand why we had to go to the hospital (…), but then I was pretty much okay with it.

Supplementary references

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