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Supporting Online Material for

Movement Intention After Parietal Cortex Stimulation in Humans

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SUPPORTING ONLINE MATERIAL

MATERIALS AND METHODS

The protocol was approved by the local ethics committee (CPP, Lyon Sud-Est IV, Centre Léon Berard, Lyon) and sponsored by CNRS (CNRS n° 07011). Before surgery patients were informed about the surgical procedure and gave a formal consent.

<u>Stimulation</u>: Methods for direct electrical stimulation (DES) under local anesthesia have been described in details elsewhere (S1-S3). In brief, following opening of a large bone flap, a bipolar electrode with 5 mm spaced tips delivering a biphasic current was placed on the brain of awake patients (pulse frequency 60 Hz, pulse phase 1 ms, amplitude from 2 to 8 mA; duration 1 to 4 s). Up to four replications were performed for each stimulation site. Replications were delivered non-consecutively to avoid provoking seizures. Duration of the stimulation was controlled visually by the surgeon via a digital clock placed in front of him. Functionally, DES has been shown to propagate only along the stimulated white matter pathways (S4, S5) and to induce a marginal amount of cortical spreading (S6). Note that current propagation along white matter pathways is inevitable, even for single pulse stimulations (S7). However, it does not occur randomly. It follows physiologically meaningful pathways (S8-S10). The normal function of the stimulated region depends on these pathways. Based on these observations, it has been suggested that the spread of signal through the network should be seen "as a necessary part of the technique rather than as something to control or avoid" (S11).

For the present study, stimulations were performed in the following way: (i) the surgeon informed the patient that a stimulation was about to start ("we are going to stimulate"); (ii) the surgeon counted aloud to provide the patient and the experimenter standing next to the patient, with a feedback about the onset and the end of the stimulation (e.g. for a 4 s stimulation: "One, two, three, four"); (iii) at the end of the stimulation, the experimenter asked the patient whether he/she felt something and whether he/she moved, except when the patient commented spontaneously on his/her feelings.

As part of a clinical testing other stimulations were made to uncover: (i) areas potentially eloquent for movement, while the subjects were performing simple limb movements (e.g. touch each individual finger successively, with the thumb); (ii) areas potentially eloquent for

language, while subjects were performing naming and counting tasks (only for patients with left hemisphere lesion). These stimulations are not considered in the present paper. Finally, a number of sham stimulations, i.e., the surgeon made *as if* he was going to stimulate but no stimulation actually occurred, were intermingled with the real stimulations, in order to test patients' behavior for false positives responses. No responses were found for these fake stimulations.

Localizing stimulation sites: A neuronavigation system was used for all patients. During surgery, coordinates of the stimulation sites were recorded on individual high resolution MR images, via the neuronavigation system (Fig. S1 below). Spatial normalisation of preoperative MR images into the standard MNI space was performed using the dedicated non-linear registration procedures provided by SPM5 (Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm/). Lesion areas were manually defined from preoperative MR images and masked to be excluded from the normalization transformation (S12). Transformation from MNI to Talairach coordinates was performed using the icbm2tal procedure (S13). Assignment of Brodmann area labels from Talairach coordinates was then performed using the *Talairach Client* tool (http://www.talairach.org/) (S14). 3D surface rendering images were generated from MR images using the Brainvisa software (http://www.brainvisa.info/).

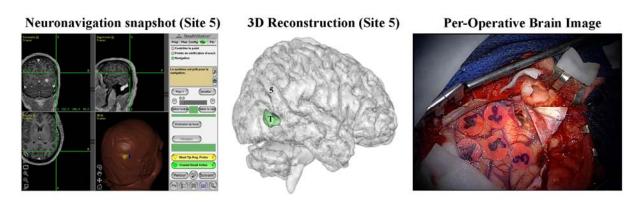


Fig. S1: Illustration of the site localization procedure. Each stimulation site was localized on a preoperative high resolution MR image of the subject, using the neuronavigation tool (snapshot, left panel). 3D rendering images of the brain surface and stimulation sites were then generated from MR images (middle panel). Neuronavigation coordinates were afterwards confronted with number-tags positioned during surgery on the cortical surface (right panel).

<u>Electromyography (EMG)</u>: The method for EMG recording has been described in details in previous publications (S15, S16). In brief, disposable surface Ag/AgCl electrodes were used to record EMG continuously at a 1,000 Hz frequency, in the contralesional hemibody in 12 muscles covering the face, hand, wrist, elbow, ankle and knee. EMG signals were differentially amplified (gain = 1,000 to 10,000), band pass filtered (30–1000 Hz) and full wave rectified.

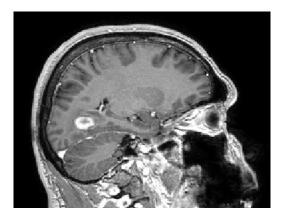
PATIENTS

Patients with postcentral lesions (N = 3), who were stimulated in the posterior parietal (PP) areas, are designated PP1 to PP3 hereafter. Patients with precentral lesions (N = 4), who were stimulated in the premotor (PM) areas, are designated PM1 to PM4 hereafter.

Some patients exhibited motor and speech deficits immediately after surgery. These deficits disappeared within weeks. After six months, all patients had resumed a normal social life, as is the case in most individuals with slow growing lesions (S17). At this time, they had no debilitating deficits when evaluated with classical clinical procedures.

Patient PP1

Male, 42 years old.Cavernoma in the right temporo-parietal region.5 sites stimulated.



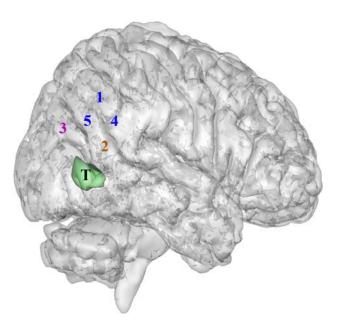


Fig. PP1. MRI and 3D image of the patient brain and stimulations sites (sites were stimulated from 1 to 5). Color code:

Conscious Intention;
Conscious Intention + Illusory Movement;

Visual Illusion (background movement). T: Tumor.

Evoked movements.

Body Part	Stimulation Sites
Foot	1
Arm / Hand	3
Hand	4;5

Verbatim samples of patient's report. Experimenter (E), Patient (P).

Site 1:

<u>5 mA / 4s</u>
E: Did you feel something?
P: Yes... It felt like I wanted to move my foot. Not sure how to explain
E: Which foot?
P [showing the left leg]: This one.
E: How did you want to move it?
P: I don't know, I just wanted to move it.

8 mA / 4s E: Did you feel something? P: A movement of the foot E: You moved your foot? P: Yes. E: Are you sure? P: Yes.

Site 3:

<u>8 mA / 4s</u>

P [spontaneously at the end of the stimulation]: My arm, maybe my hand

E: Did you move them?

P: No, I wanted to.

Site 4:

5 mA / 4 s

E: Did you feel something?

P: Yes, yes, in my hand, like I wanted to close it

E: Which hand?

P: This one [closing and opening the left hand].

8 mA / 4 s

P [spontaneously at the end of the stimulation]: My hand moved

E: Are you sure?

P: Yes, sure.

Site 5:

2 mA / 4s
P [spontaneously at the end of the stimulation]: Same, a desire to move my hand
E: Did you move it?
P: No
8 mA / 4s
P [spontaneously at the end of the stimulation]: My hand, my hand moved.
E: Your hand?
P: Yes, the fingers
E: Are you sure?

P: Yes, I think. Did it not move?

Patient PP2

Female, 41 years old.

Oligodendroglioma in the right posterior parietal region.

11 sites stimulated.

Note that positive functional responses were found in the tumoral region for this patient. This is a common observation which can be explained by the nature of the tumor (S17). Indeed, oligodendrogliomas are primary glial brain tumors that do not prevent the neurons from functioning.

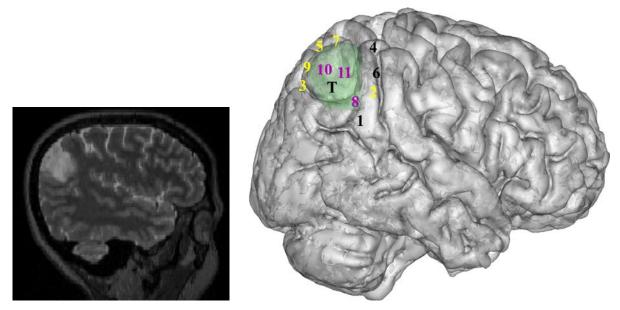


Fig. PP2. MRI and 3D image of the patient brain and stimulations sites (sites were stimulated from 1 to 11). Color code: • Conscious Intention ; • Itching and tingling sensations ; • No response. T: Tumor.

Evoked movements.

Body Part	Stimulation Sites
Chest	8
Hand	10
Arm	11

Verbatim samples of patient's report. Experimenter (E), Patient (P).

Site 8:

8 mA / 4 s

E: Did you feel something?

P: I had a desire to do something

P [showing her chest]: Here I have a desire to do...

E: In the chest?

P: Yes

E: And what did you feel?

P: Like a, like a will to move

E: What did you feel?... Tinglings?

[in french "picotement"-tingling- can be mistaken with "mouvement" –movement-]

P: I felt like a will to move.

Site 10:

<u>8 mA / 4s</u>

- E: Did you feel something?
- P: I had a desire to move my right hand
- E: You wanted to move your right hand?

P: Yes

E: Do you know what kind of movement you wanted to do?

P: No, I don't know.

Site 11:

8 mA / 4 s

- E: Did you feel something?
- P: Like a will to move
- E: You had a desire to move?

P: Yes

- E: And where, what kind of movement did you want to do?
- P: I wanted to raise my arm.

Patient PP3

Male, 76 years old.

Glioblastoma in the left fronto-temporo-parietal region.

9 sites stimulated.

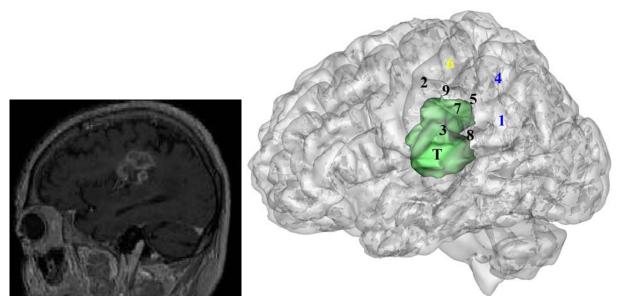


Fig. PP3. MRI and 3D image of the patient brain and stimulations sites (sites were stimulated from 1 to 9). Color code: • Conscious Intention + Illusory Movement ; • Itching and tingling sensations ; • No response. T: Tumor.

Evoked movements.

Body Part	Stimulation Sites
Mouth / Lips	4
Mouth	1

Verbatim samples of patient's report. Experimenter (E), Patient (P).

Site 1:

<u>5 mA / 4s</u>
E: Did you move?
P: No... I had a desire to roll my tongue in my mouth
E: To roll what, your... ?
P: To roll my tongue in my mouth.

8 mA / 4s E: Did you move? P: Yes, yes, a corner of the mouth E: You did move the mouth? P: Yes

Site 4:

<u>5 mA / 4s</u>
E: Did you move?
P: No, I had something in my mouth
E: In your mouth?
P: Yes, in my mouth
E: What did you feel, tinglings?

P: No, it was something elseE: What was it? What did you feel in the mouth?P: I felt a desire to lick my lips.E: A desire to lick your lips?P: Yes, yes that's it.

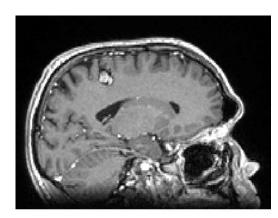
<u>8 mA / 4s</u>
E: Did you move?
P: Yes, Yes, I moved my mouth
E: You moved your mouth?
P: Yes, I moved my mouth, I talked, what did I say?

Patient PM1

Male, 31 years old.

Melanoma in the right central sulcus.

3 sites stimulated. Functional mapping was interrupted before its completion, due to the occurrence of a seizure after stimulation of M1 (BA 4).



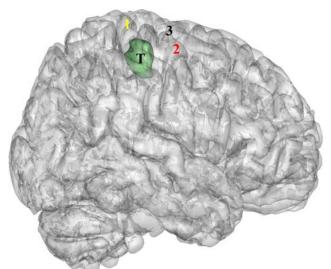


Fig. PM1. MRI and 3D image of the patient brain and stimulations sites (sites were stimulated from 1 to 3). Color code: • Unconscious Movement ; • Itching and tingling sensations ; • No response. T: Tumor.

Evoked	movements.

Body Part	Stimulation Sites
Hand / Arm	2

Verbatim sample of patient's report. Experimenter (E), Patient (P).

Site 2:

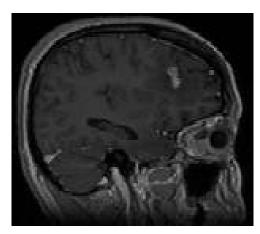
8 mA / 4s E: Did you feel that you moved? P: Here? No... No E: No? P: No.

Patient PM2

Female, 43 years old.

Nodular lesion consecutive to the treatment of a brain nocadia abscessus in the right prefrontal region.

3 sites stimulated. Functional mapping was interrupted before its completion, due to the occurrence of a seizure after stimulation of the premotor region (BA 6).



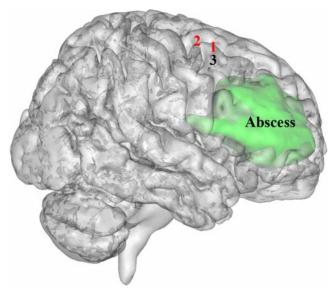


Fig. PM2. MRI and 3D image of the patient brain and stimulations sites (sites were stimulated from 1 to 3). Color code: • Unconscious Movement ; • No response.

Evoked movements.

Body Part	Stimulation Sites
Hand / Arm	1;2

Verbatim sample of patient's report. Experimenter (E), Patient (P).

Site 2:

2 mA / 2s E: Did you feel something? P: No. E: Why did you move your hand? P: I did not move.

Patient PM3

Male, 52 years old.

Meningioma in the left lower frontal circonvolution.

17 sites stimulated.

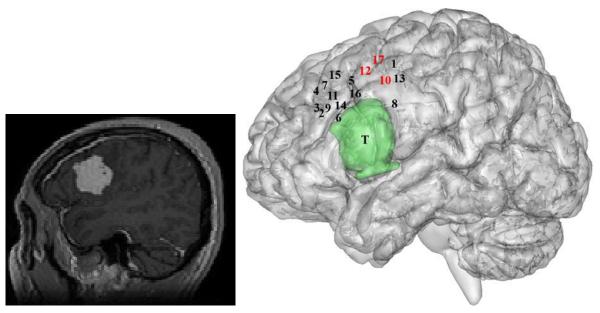


Fig. PM3. MRI and 3D image of the patient brain and stimulations sites (sites were stimulated from 1 to 17). Color code: • Unconscious Movement ; • No response.

Evoked movements.

Body Part	Stimulation Sites
Hand / Arm	17
Mouth	10 ; 12

Verbatim sample of patient's report. Experimenter (E), Patient (P).

Site 17:

5 mA / 2s E: Did you move? P: No, I don't think so.

Patient PM4

Female, 54 years old.

Oligodendroglioma in the right prefrontal region (tumoral recurrence).

9 sites stimulated.

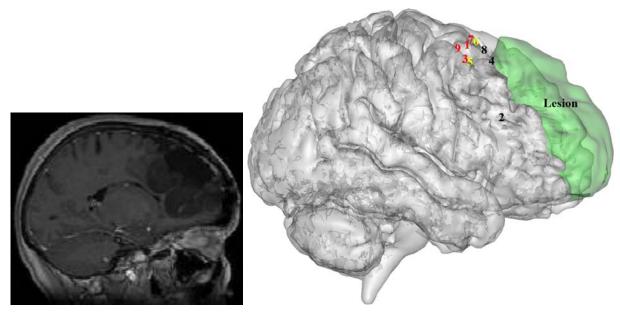


Fig. PM4. MRI and 3D image of the patient brain and stimulations sites (sites were stimulated from 1 to 8). Color code: • Unconscious Movement; • Itching and tingling sensations ; • No response.

Evoked movements.

Body Part	Stimulation Sites
Foot	1;7;9
Hand	3

Verbatim sample of patient's report. Experimenter (E), Patient (P).

Site 1:

8 mA / 1s E: Did you move? P: No

RESULTS

Distribution of the stimulation sites:

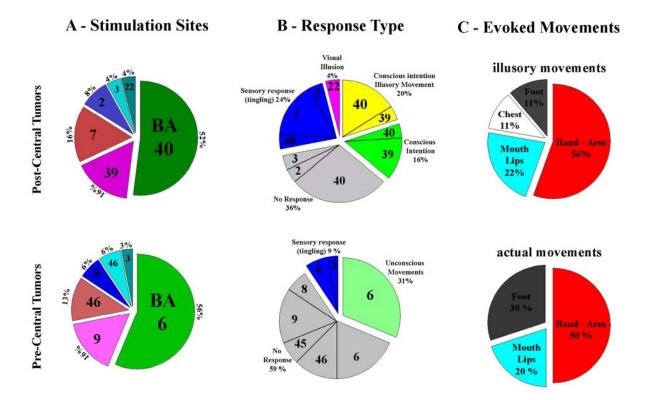


Fig. S2: Summary of the stimulation data: (A) anatomical distribution of the stimulation sites (numbers refer to Brodmann areas); (B) functional distribution of the DES-related responses (total is not exactly 100% for the bottom panel due to roundings); (C) type of movements evoked by the stimulation (bottom row: actual evoked movements, pre-central stimulation sites ; top row: illusory evoked movements, post-central stimulation sites). BA: Brodmann Area.

It may be worth noting that no stimulation was performed in M1. This raises the question whether movements evoked from M1 stimulation would be consciously perceived by the subjects, in contrast to the movements evoked from the preomtor cortex. We could not address this issue because no patients with lesions in the peri-central region could be recruited. This region is not a common location for most types of tumors in adults (S18-S20). In 3 of our 4 patients, the tumors were too anterior to allow access to M1 or to make stimulation of this region clinically relevant. In the fourth patient, the rolandic area was partially uncovered. However, the first stimulation of M1 at the lowest possible intensity produced a seizure, thus preventing further investigation.

<u>LEGENDS FOR VIDEOS</u> (available for download at http://www.isc.cnrs.fr/sir/article/videos_desmurget.zip)

PM1.avi: This video shows a large multijoint movement triggered by direct electrical stimulation of the premotor cortex (8 mA, 4s), in patient PM1. This movement was not consciously perceived by the patient. Stimulation was delivered over the site numbered 2 in the 3D figure of patient PM1 (see above).

PM4.avi: This video displays finger, hand and wrist movements triggered by direct electrical stimulations of the premotor cortex, in patient PM4. It is shown that higher currents recruit more muscles and trigger larger movements. Intensity of the stimulation had no effect on the ability of the subject to consciously perceive the evoked movements. Stimulations were delivered for 1 s at 2, 5 and 8 mA, over the site numbered 3 in the 3D figure for patient PM4 (see above).

PP2.avi: This video shows a "pure intention" following stimulation of the posterior parietal cortex. The patient reported that she felt "like a will to move" her chest. Stimulation (8 mA, 4s) was delivered over the site numbered 8 in the 3D figure for patient PP2 (see above).

PP3.avi: This video displays a "pure intention" after stimulation of the posterior parietal cortex at median intensity (5 mA, 4s), followed by an "illusory sensation of movement" when the intensity of the stimulation was raised (8 mA, 4s). The patient reported first that he "had a desire to roll his tongue in his mouth" and then that "he had moved the corner of his mouth". Stimulations were delivered over the site numbered 1 in the 3D figure for patient PP3 (see above).

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