Revealing humans’ sensorimotor functions with electrical cortical stimulation

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Direct electrical stimulation (DES) of the human brain has been used by neurosurgeons for almost a century. Although this procedure serves only clinical purposes, it generates data that have a great scientific interest. Had DES not been employed, our comprehension of the organization of the sensorimotor systems involved in movement execution, language production, the emergence of action intentionality or the subjective feeling of movement awareness would have been greatly undermined. This does not mean, of course, that DES is a gold standard devoid of limitations and that other approaches are not of primary importance, including electrophysiology, modelling, neuroimaging or psychophysics in patients and healthy subjects. Rather, this indicates that the contribution of DES cannot be restricted, in humans, to the ubiquitous concepts of homunculus and somatotopy. DES is a fundamental tool in our attempt to understand the human brain because it represents a unique method for mapping sensorimotor pathways and interfering with the functioning of localized neural populations during the performance of well-defined behavioural tasks.

1. Electrical stimulation: a unique approach for probing brain functions

One of the most important discoveries in modern neuroscience can indisputably be attributed to Luigi Galvani, who showed that electrical stimulation of the sciatic nerve in a severed frog leg caused the attached muscle to contract [1]. This finding sparked a flurry of research activity that has persisted up to the present. In animals, the first systematic use of direct electrical stimulation (DES) was conducted by Gustav Fritsch and Eduard Hitzig in Germany [2] and David Ferrier in England [3]. These authors showed that stimulating the cerebral cortex of dogs and monkeys evoked topographically organized muscle contractions in the contralateral hemibody [4]. They also established that lesions of the regions from which a movement was evoked caused a deficit in the realization of this movement and even, sometimes, a total paralysis. In the following years, DES was progressively generalized to human patients with various levels of success and ethical concerns [5]. However, this technique only reached its apogee in the 1930s with the well-known work of Wilder Penfield [6]. Since then, the approach has remained roughly unchanged, beyond minor technical and procedural adaptations [7,8].

Of course, in humans, the unique raison d’être of DES is (and has to be) clinical. If neurosurgeons now use this mapping procedure almost universally, it is with the purpose of identifying cerebral areas, resection of which could cause major functional deficits [9,10]. Consistent with this goal, it has been shown that the surgical use of DES dramatically reduces the occurrence of permanent post-operative sequelae in patients with brain tumours, while significantly improving long-term survival [11–15]. However, the pre-eminence of clinical goals is not inconsistent with the existence of fundamental inquiries. Obviously, the behavioural and neurophysiological observations collected in per-operative contexts can also be of major interest for fundamental research and, in particular, for understanding the organization of the human brain.
Certainly, this does not mean that DES is devoid of limitations. In particular, the range of questions it allows us to address is strongly restricted by clinical demands and per-operative constraints. This is why the results obtained with this technique have to be interpreted in light of a more general knowledge, generated by other approaches [16]. Consider, for instance, neuroimaging (functional magnetic resonance imaging—fMRI, positron emission tomography—PET) and electrophysiology (electro and magneto encephalography—EEG, MEG). During the past three decades these methods have obviously played a major role in improving our understanding of the sensorimotor organization of the human brain. However, it should not be forgotten that they too bear important limitations [17–19]. In particular, they do not allow us to neatly determine whether a responsive area is truly critical for the expression of an investigated function and whether an activated region receives afferent information, sends efferent signals to the muscles or suberves computational processing. DES opens a window to this type of knowledge. Of course, nobody would seriously argue that this technique recruits neural populations as autogeneous processes do. It should be evident that DES produces unnatural patterns of cellular activation. However, such a limitation does not, by any means, call into question the usefulness of the method. Indeed, even if it relies on unnatural patterns of neural activation, DES remains unparalleled in its ability to: (i) drive descending pathways for identifying cortical regions with outputs to motoneurons (e.g. [6,20]); (ii) elicit positive sensorimotor effects through the recruitment of neural populations associated with the expression of high- (e.g. motor intention; e.g. [21,22]) or low-level (e.g. sensory feelings; e.g. [6,20]) functions; (iii) elicit negative sensorimotor effects through disruption of an endogenous neural activity involved in the realization of an ongoing task (whether motor or cognitive; e.g. [23,24]). It is true that interpretative biases related to a possible spread of the electrical current have always been a subject of concern for researchers [25,26]. However, during the past two decades solid evidence has been gathered, at least for the high-intensity/high-frequency stimulation parameters typically used in surgical protocols, that DES effects are typically mediated by the cell population being stimulated [27–29]. In other words, DES does not spread in a meaningless jumble. It operates primarily at a local level and, doing so, offers an invaluable way to investigate the anatomo-functional organization of the human brain. Among the multiple elements supporting this conclusion (see [27,28] for detailed reviews), the most convincing evidence comes probably from the successful use of DES for mapping brain functions in per-operative contexts. If, as is sometimes claimed [26], DES effects were reflective of an artificial spread of current at distant sites, then this method should be ineffective at preventing post-operative deficits in neurosurgical contexts. As reported above, this is clearly not what the clinical literature demonstrates [11–15].

This being said, in the present review, we will focus on the specificity and fundamental importance of DES. At a first level, we intend to show that if this technique had not been exploited in the past decades, several of our pillar concepts and much of our knowledge on the anatomo-functional organization of the sensorimotor system would be dramatically undermined. At a second level, we plan to emphasize recent studies and technical developments to demonstrate that DES remains a major approach for understanding brain functions.

2. Mapping the sensorimotor system

At a time when the theory of brain localization was still strongly questioned [30,31], Penfield’s work proved ground breaking. As is the rule (see above), this neurosurgeon used DES for clinical reasons ‘to define the motor area of the hemisphere so that an infiltrating tumour could be removed as widely as possible without producing paralysis [and . . .] as a preliminary to radical extirpation of an epileptogenic focus’ [6, p. 396]. However, using this approach he also reported results of great fundamental interest. In particular, he was the first to show, in humans, that functional specialization existed not only across brain areas, but also within them.

In his main pioneering work, Penfield used DES in 163 patients, among whom 126 provided useful results [6]. He observed that movements could be triggered from only a limited number of cortical regions, including the primary motor cortex (M1), the primary somatosensory cortex (S1), the premotor cortex (PM) and the supplementary motor area (SMA). Sensations were mostly evoked from the same regions. It is unclear, however, whether stimulations (and how many) were performed in non-central regions including the prefrontal or posterior parietal cortices. Penfield found that more movements were triggered from the precentral gyrus, while more body sensations were evoked from the post-central gyrus, although sensory and motor responses were identified in both of these two regions. He also reported that different cortical loci triggered movements and sensations in different body parts. These observations led to the key idea that sensorimotor regions are somatotopically organized in such a way that each part of the body is represented within a different cortical space in the pre- and post-central gyri. To formalize this finding, Penfield introduced the now famous concept of the homunculus. According to him, within the central area, ‘toes begin at the top and the members follow in order as though representing a man hung upside down, but that thumb is followed by the head as though the head and neck were erect and not inverted (. . .) The homunculus may be said to be both motor and sensory as the sequence pattern is roughly the same, although there are differences’ [6, pp. 431–432]. Most major biology textbooks still mention Penfield’s idea and display a version of his drawing of the human homunculus (e.g. [32,33]).

The idea that M1 and S1 are somatotopically organized is probably one of the very few proposals that have withstand the test of time in modern neuroscience. The concept of the homunculus has seen its general validity supported by numerous neuroimaging and electrophysiological studies in humans [34–41]. However, recent evidence has started to suggest that this consensus may rely, when carefully considered, on a rather weak ground [42–45]. According to this view, the concept of the homunculus would mainly be an emerging artefact of inter-individual averaging. It would have no validity at the intra-individual level, where major organizational differences are observed. In other words, the homunculus as we know it would not represent a biological reality but rather a statistical construct that ‘does not appear to exist’ [44, p. 292]. The same kind of criticism has been raised with respect to neuroimaging data which ‘can produce the illusion of a localized process by emphasizing fortuitous regions of overlap to the exclusion of the more widely distributed active regions in the individual subjects’ [46, p. 197].

Clearly, these claims are consistent with the observation that the synoptic, regularly ordered sequence of body...
movements and sensations described by Penfield on the basis of the responses he recorded [6] is almost never observed at the individual level. Although initial evidence came from electrophysiological studies in monkeys [47–49], recent data have confirmed that this is also true in humans, where sensory and motor maps are typically organized as an intermingled mosaic of neural populations related to different body parts [43,44,50,51]. Major violations of Penfield’s regular ordering are commonly found. It happens, for instance, that mouth and face responses are represented above finger or leg responses [43]. Moreover, both monkeys [52] and humans [44] exhibit large variations of the sensorimotor cortical organization from individual to individual and between hemispheres. More generally, recent data have also suggested that the functional segregation between M1 and S1 might not be as strict as initially postulated by Penfield [53]. In humans, in particular, it was found that the hand ‘hot spot’, defined as the cortical area that evokes hand or finger responses at the lowest electrical intensity, was located in the post-central gyrus in a significant fraction of subjects [54,55]. At a first level, this puzzling result highlights the necessity of considering Penfield’s anatomical maps with caution. Indeed, 100 years ago, neuronavigation tools were not available and localizing stimulation sites was not easy. For instance, as acknowledged by Penfield & Boldrey, there was a strong bias toward associating motor response with M1 stimulation because ‘the Rolandic fissure can hardly be recognized until after stimulation has identified it’ [6, p. 398]. However, the idea that the hand hot spot is commonly localized in S1 was recently contradicted by clinical observations showing, in a large population of 165 patients, that motor responses were scarcely evoked from the post-central gyrus [20]. This conclusion is consistent with monkey data showing that the level of current required to trigger overt movements is almost systematically lower in M1 than S1 [56,57]. In fact, as shown by a study aiming at comparing the output properties of these two regions, the motor responses evoked from S1 are rare, weak and often inhibitory [58]. Strikingly, in monkey experiments, the lowest motor threshold is consistently identified in regions located within the bank of the central sulcus for both M1 (Brodmann area 4) and S1 (Brodmann area 3a). In humans, however, these intrasulcal areas are not accessible and DES is only performed over the convexity of the pre- and post-central gyri. Together with the limited number of sites that can be stimulated in each subject, this may explain why the hand hotspot has sometimes been reported in S1 in humans.

The recent questioning of Penfield’s homunculus does not seem surprising. In truth, what appears to be really puzzling is the ubiquity of this schematic representation and how it became so universally accepted. Indeed, looking at Penfield’s own data, it seems quite clear that the nice arrangement of body parts he described along the pre- and post-central gyri is functionally deceitful, although, of course, graphically convenient. This can be seen in figure 1 for a few representative examples. The left side of the three first panels (figure 1a–c) shows the individual stimulation sites identified as eloquent by Penfield [6]. The right side displays the classical homunculus he constructed from these data.

Figure 1a investigates the claim that an ordered somatotopy exist for the fingers. Really, considering the actual stimulation data, it seems hard to see any justification for this hypothesis. Thumb contractions (coloured in blue), for instance, are observed along the whole extent of the central sulcus; they are not clustered in the medio-lateral region and do not appear to be consistently medial with respect to the responses recorded for other fingers, including the little one (coloured in red). In fact, rather than observing independent contractions for each finger, Penfield reported, in most cases, motor responses that involved all fingers together without individual segregation (black dots). Recently, this combined activation has been reproduced in monkeys, where microstimulation was found to trigger organized patterns of finger synergies [60]. Also, data gathered in these animals have clearly challenged the idea of a sequential representation of each individual finger along a medio-lateral axis going from the little finger to the thumb [49,61].

Figure 1b displays, on the same plot, upper limb (shoulder, elbow, wrist, hand, undissociated by Penfield, coloured in red) and finger responses (coloured in blue). Eloquent sites for these two segments exhibit a major level of overlap and redundancy. It is hard to figure out how Penfield went from these intermingled responses to the nice sequential ordering presented on the right panel, where upper limb representations are located more medially than finger representations.

Data from the third panel (figure 1c) are even more disconcerting. They show face and neck representations. Placing the neck above the face from these recordings really seems questionable considering that all neck responses except one are represented more laterally than face responses.

From a scientific point of view, the logic that led Penfield to identify a precisely ordered homunculus on the basis of his scattered data is hard to infer. However, a plausible hypothesis might be that he got, at some point, the idea of an inverted body map lined up over the cortical surface. This map, drawn by Penfield himself in his pioneering work [6], is shown on figure 1d. It implies, for instance, that the neck should be represented more medially than the face. Based on these remarks, it is tempting to speculate that Penfield did not go from the data to the model, but was rather biased toward forcing his clinical observations into a predetermined map of representations.

In summary, DES has been a key approach for understanding the organization of the primary sensorimotor regions. The early work of Wilder Penfield, in particular, proved fundamental for establishing the central idea that brain functions are localized and that the sensorimotor system is organized somatotopically in such a way that specific cortical sites control specific muscles. Nevertheless, Penfield also went too far in his attempt to describe a nicely ordered map of sensorimotor representations within the central regions. Both recent results [42–44,50] and a re-evaluation of his original observations show that sensorimotor representations are not organized in a sequential rigidly ordered way, but rather in a mosaic of intermingled representations where body parts overlap in multiple non-contiguous areas. Such a fractured arrangement (a term coined by Welker and his co-workers for describing the somatosensory organization of the cerebellum [62]) has been claimed to favour the production of complex motor responses by making it easier to combine elemental body movements within coordinated muscle synergies [59,61,63–65].

3. Mapping complex sensorimotor synergies

From the data above, it appears that DES typically evokes simple meaningless movements in humans. Nevertheless,
Figure 1. The nicely ordered homunculus constructed by Penfield is not consistent with the individual data actually collected by this neurosurgeon. (a) (Left part.) Evoked responses identified by Penfield for the different digits; (right part) corresponding homunculus. (b) (Left part.) Evoked responses identified by Penfield were reported on the same graph for the arm (including shoulder, elbow, wrist, hand; red colour) and the digits (blue colour); (right side) corresponding homunculus. (c) (Left part.) Evoked responses identified by Penfield were reported on the same graph for the face (green colour) and the neck (red colour); (right side) corresponding homunculus. (d) (Left part.) Penfield’s idea of an inverted homunculus; (right side) corresponding formalization of this idea. Adapted from [6,59], with permission.
following cortical stimulation some studies have reported the development of relatively complex, apparently purposeful actions, including joint hand–mouth responses, coordinated arm–eye–head aversive synergies and organized reach-to-grasp gestures [6,22,43,66,67]. Unfortunately, when observed, these movements were generally not described in detail. Also, they were often said to be artefactual and reflective of the unspecific recruitment, through current spread, of body parts having contiguous cortical representations [43].

Technically, a reason why complex movements have not been more commonly observed in response to DES could be related to the tendency of clinicians (in humans) and experimenters (in animals) to use short trains of stimulations. As noted by Penfield & Welch [67, p. 310], for instance, it is plausible that some of the simple motor responses they found in their patients ‘would, with more prolonged stimulations, have gone on to become more elaborate and to have approached the full synergic employment of all extremities and the trunk. The stimulating electrode has frequently been removed at the first evidence of response, and thus the opportunity of producing more of the elaborate synergic responses may have been missed’. Michael Graziano et al. were the first to investigate this possibility in awake macaque monkeys [68]. These authors stimulated the precentral gyrus using stimulation trains of long duration. They found that some motor responses that would have had the form of simple muscle twitches in the context of short train stimulations, unfolded into complex coordinated actions when the duration of the stimulation lasted long enough. These actions included, for instance, self-feeding movements in which the hand closed into a grip while moving toward the opening mouth; reach-to-grasp synergies in which the arm extended while the fingers opened progressively; defensive gestures in which the facial muscles squinted while the head turned sharply to one side and the arm flung up; etc. Interestingly, as shown in figure 2a, each of these categories of action was evoked from different, well-localized, zones of the precentral gyrus.

Recently, Graziano’s pioneering observations were reproduced in New World monkeys and prosimian galagos by John Kaas and his co-workers [70,71]. Also, they were generalized to human subjects in a study aiming to investigate whether hand–mouth synergies, a prominent example of human behaviour with high ethological value, were represented as motor primitives in the precentral gyrus [69]. In this study, electromyographic activity evoked by cortical stimulation was recorded from the face and upper-limb muscles in patients undergoing brain surgery. As shown in figure 2b (top panel), this allowed identification of an integrated motor primitive resembling self-feeding, in which DES caused the closing hand to progressively approach the opening mouth. Of course, not all responses evoked by long train stimulations evolved into complex movements and coordinated hand–mouth synergies intermingled with simpler isolated movements over the whole surface of the precentral gyrus. This anatomical dispersion contrasted with the more clustered pattern found in monkeys (figure 2b). Two main hypotheses may account for this difference. First, it is possible that this cortical region is differently organized in humans and monkeys [72,73]. Second, the pioneering data reported by Graziano et al. in monkeys [68] could be biased toward intra-individual variability (multiple replications in few animals), while the data gathered in humans could be rather slanted toward inter-individual variability (few replications in multiple subjects).

Figure 2. (a) Action zones in the precentral gyrus of the monkey where complex movements are evoked in response to long-train electrical stimulations (adapted from [65], with permission). (b) Sites where complex hand/mouth synergies are evoked by electrical stimulation in the human precentral gyrus. The top panel of the figure displays motor sites (black squares) evoking hand-to-mouth synergies resembling self-feeding, in which DES causes the closing hand to progressively approach the opening mouth. The bottom panel of the figure displays multimodal sites (black squares) that evoke hand/arm actions when stimulated while receiving mouth sensory inputs. Adapted from [69], with permission.
Notably, the true ethological nature of the complex synergies evoked through DES was recently questioned by Cheney and colleagues. In monkeys, these authors provided evidence that postural synergies evoked through cortical stimulation were not produced by natural patterns of EMG activity but instead resulted from an unnatural co-contraction of numerous ‘hijacked’ muscles that forced the limb to an equilibrium point [74,75]. However, the generality of these observations remains debatable for at least three reasons. First, muscle hijacking was not observed in several studies where evoked-EMG and kinematic responses were found to be strikingly similar to the responses seen in natural behaviours [60,68,76]. Second, the non-telemetric nature of the ‘hijacking’ hypothesis seems hardly compatible with the repeated failure of DES to evoke non-functional synergies where, for instance, the opening hand would approach the closing mouth or the closing hand would move away from the opening mouth [68,69]. Third, beyond its ability to explain the emergence of postural equilibria, the ‘hijacking’ model cannot easily account for the finesse and high functional specificity of some very complex multi-segmental synergies. This includes, for instance, multi-joint defensive postures specifically triggered from bimodal neurons with tactile/visual receptive fields and made of the following complementary elements (in Graziano’s terms): a facial grimace, a squinting of the eye, a turning of the head away from the side of the sensory receptive fields, a hunching of the shoulders, a fast thrusting of the hand into the space beside the head, and a turning of the hand such that the palm faced outward, away from the head (fig. 4 in [77]).

Beyond these observations, it may be worth noting that motor responses involving the coordinated recruitment of distinct body segments were not the only type of complex representation identified in the human precentral gyrus. Combined recording of motor and somatosensory evoked potentials revealed that this region also harbours motor-sensory representations where cross-signal integration is realized at specific cortical sites that generate hand/arm actions while receiving mouth sensory inputs. It is tempting to speculate that these multimodal sites underlie the behavioural process of perioral processing. Indeed, they are shaped as a hardwired feedback loop capable of binding oral sensory inputs with upper limb motor commands or, in other words, capable of guiding hand movements according to mouth sensations. This view is consistent with a recent study on upper-limb reaching movements showing, in humans and monkeys, that M1 contains fast feedback control loops integrating sensory and motor signals [78]. As shown in figure 2b (lower panel), complex hand–mouth sensorimotor sites are not evenly distributed over the precentral surface of the patients. They are clustered in the dorsal sector of the precentral gyrus, where hand/arm movements are most commonly represented.

In summary, using long trains of stimulation, researchers and clinicians have provided convincing (although still disputed) evidence that specific sensorimotor synergies with a high ethological value are represented as integrated motor primitives in the precentral gyrus. This cortical region cannot be seen any more as a sort of keyboard, where segregated populations of neurons can be recruited in a specific spatiotemporal order to form complex symphonies of movements. Overall, the use of DES reveals the complexity of primary sensorimotor structures that can probably accommodate different types of representations with various levels of complexity [79]. This hypothesis fits well with the suggestion that sensorimotor organization has been shaped by primate evolution to optimize the production of ethologically relevant behaviours while preserving the ability to learn new complex synergies [64,65,70].

4. Mapping high-level functions

Per-operative mapping is not only useful for identifying brain areas that evoke movements or sensations when stimulated. This approach can also be used for probing the functional contribution of a given cortical region. In this case, DES is applied while the subject is performing a sensorimotor task such as opening–closing the hand, reading or counting. The effect of the stimulation on the ongoing behaviour is then evaluated. In an alternative approach, the neurosurgeon can also interfere with brain activity at rest and ask the patients to report the thoughts or feelings they have experienced in response to the stimulation.

To date, per-operative evaluations of high-level functions have been mainly conducted for language mapping in awake patients [80–83]. Based on this approach, large amounts of data have been collected and used for producing probabilistic maps of anatomo-functional correlations [13,20]. In other words, using DES in large populations of patients, neurosurgical teams were able to associate specific cortical regions with particular language disorders such as speech arrest (cessation of speech output in the absence of evoked motor response); dysarthria (improper articulation of speech); anomia (inability to name objects while still being able to speak or repeat sentences); alexia (inability to read while still being able to spell words or write); receptive aphasia (fluent but meaningless speech and inability to understand simple sentences); expressive aphasia (impaired speech production); etc.

Together with neuroimaging and lesion observations, these per-operative results proved of major interest for improving our understanding of the neural bases of language comprehension and production [84–88]. A striking example concerns Broca’s area, the long-postulated role of which as a speech output region remains debated in neuroimaging and lesion studies [89–92]. A recent per-operative investigation involving 165 patients provides an important, potentially decisive, contribution to this issue [20]. As reported by the authors, stimulation of Broca’s area only produces speech arrest in 4% of the subjects, compared with 83% when the dorsal premotor cortex (dPM) is targeted. The latter proportion is independent of the localization of the tumour, i.e. of whether Broca’s area is lesioned or not. Based on these results, it is tempting to suggest that Broca’s area should no longer be considered a motor region coordinating speech articulation but should rather be viewed as a cognitive structure involved in high-level functions such as verbal working memory, language comprehension or lexical retrieval [20,93].

However, in the linguistic domain, the identification of well-defined anatomo-functional correlations in response to DES does not seem to be the norm. Indeed, a very striking feature of per-operative evaluations of language abilities lies in the wide distribution of functional sites across brain structures (figure 3). In contrast to the relatively circumscribed networks that sometimes emerge from careful syntheses of the lesion and neuroimaging literature (e.g. [90,94–96]), it appears that highly specific aspects of language production...
can be impaired through stimulations delivered over very different cortical zones. Anomia or alexia, for instance, is consistently found after stimulation of wide (sometimes overlapping) regions in the frontal, temporal and parietal cortices (figure 3). This high level of scattering is not totally surprising. It can have two main origins. On the one hand, it may mirror the multiplicity of the neural processing required for naming an object or reading a word [90]. On the other hand, it may also reflect the existence of a tremendous level of inter-individual variability in the localization of language functional sites [13]. Obviously, part of this variability is owing to the plastic changes that occur in brain organization in response to slow-growing tumoural invasion [97]. Together with the existence of substantial differences in the tasks being evaluated [98], these changes could explain some of the above-mentioned discrepancies between DES, acute lesion and neuroimaging studies.

This being said, language is far from being the only high-level function open to per-operative evaluation [99]. Recently, this approach has been used to study, for instance, visuo-spatial processing [100], action inhibition [23], movement awareness [101,102] and sensorimotor intentionality [103,104]. While reviewing the contribution made by DES to all these fields would be beyond the scope of the present paper, a brief focus on sensorimotor awareness and intentionality should help us provide another example of the unique fruitfulness of this method.

Technically, sensorimotor intentionality has been very difficult to address with classical electrophysiological, clinical and neuroimaging tools given, in particular, the difficulty of separating intentional and attentional processing [105,106]. Fortunately, DES does not have to deal with this ambiguity. This was first shown by Penfield, who reported that some frontal sites evoked a desire to move when stimulated [6]. Subsequent studies were able to confirm this observation, but located the neural source of this desire on the frontal medial wall, in a region encompassing the supplementary and cingulate motor areas [22,107,108]. During stimulation, the subjective experiences of the patients were characterized by an uncontrollable urge to act. For instance, an epileptic woman stimulated in the anterior cingulate sulcus at low intensity through implanted intracerebral electrodes exhibited ‘an irresistible urge to grasp something, resulting in exploratory eye movements scanning both sides of the visual field, and accompanied by a wandering arm movement contralateral to the stimulation side. Then, after the patient had visually localised a potential target, her left hand moved towards the object to grasp it, as if mimicking a spontaneous movement. This irresistible need started and ended with stimulation, and the patient was unable to control it. Yet, the patient was aware of both her inability to resist and of the movement she thus performed and could describe very precisely’ [107, p. 265]. The same type of urge was observed in another study, still in epileptic

Figure 3. Language maps indicating, for the (left) dominant hemisphere, the cortical locations where DES induced speech dysfunctions in two large studies involving, respectively, 250 [13] and 165 [20] consecutive patients with gliomas. (a) Brain sites inducing speech arrest per square centimetre of the cortical surface (reconstructed from [13]). (b) Brain sites inducing anomia per square centimetre of the cortical surface (reconstructed from [13]). (c) Brain sites inducing alexia per square centimetre of the cortical surface (reconstructed from [13]). (d) Brain sites inducing speech arrest (red circles) and anomia (blue circles). Each individual circle represents a positive observation. Adapted from [20], with permission.
patients. In this case, however, the stimulation was located in the supplementary motor area. This caused the participants to experience an ‘urge to move the right leg inward’, an ‘urge to move the right thumb and finger’ or an ‘urge to move the right arm away’ [22, p. 3661]. Although no movement was evoked in response to these subjective feelings, overt motor responses were observed when the intensity of the stimulation was raised. For instance, a patient who reported a ‘strong urge to raise the right elbow’ at 5 mA, experienced a right-arm abduction at 6 mA [22, p. 3661].

Interestingly, the frontal medial wall is not the only cortical area where intentional responses can be evoked. The emergence of a subjective desire to move was also reported following stimulation of the inferior parietal lobule [21]. In this case, however, the subjective feelings reported by the subjects were quite different from the ones observed after stimulation of the supplementary and cingulate motor areas. There was no dimension of urge or irresistibility. Also, the patients were unable to precisely describe the movements they wanted to perform. When prompted to try, they either said that they did not know or provided a very general description of their intentions in terms of action class. Representative exchanges were as follows [21]: electronic supplementary material): (1) (Experimenter) Did you feel something? ; (Patient) 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 ; (2) (E) Did you feel something? ; (P) I had a desire to do something ; (showering 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.

Another striking specificity of the parietal intentional sites lies in the absence of motor response when the intensity of the stimulation was increased. When a higher current was used, the patients experienced illusory movements; they felt that the movements they wanted to make at low intensity had actually occurred in the absence of any overt or electromyographic motor response. A representative exchange was as follows [21]: electronic supplementary material): (5 mA) (Experimenter) Did you move? ; (Patient) No. I had a desire to roll my tongue... ; (E) To roll what? ; (P) To roll my tongue in my mouth. (8 mA, same site) (E) Did you move? ; (P) Yes, yes, a corner of the mouth ; (E) Did you move the mouth? ; (P) Yes. To account for this phenomenon, it was hypothesized that higher currents did not simply prime a motor representation to consciousness (giving rise to motor intention), but also recruited the executive network responsible for movement monitoring through forward modelling, a process that is known to rely on posterior parietal computations [109,110].

In sharp contrast to the illusory movements evoked through parietal stimulation, it was also found that actual motor responses evoked by stimulating the dPM were not consciously perceived by the patients. In other words, although overt mouth and contralateral limb movements were observed following stimulation of this region, the patients firmly denied that they had moved [21]. This result highlights clinical data showing that dPM is the most commonly lesioned region in hemiplegic patients with anosognosia [111]. It also echoes neuroimaging observations showing that the dPM is important for comparing the actual and expected sensory signals [112]. It is tempting to speculate that when dPM is prevented from performing its function, no error signal is generated in response to an unexpected muscle contraction, which causes the ongoing movement to remain undetected [101].

Putting these observations together, a general model of linking conscious motor intention and movement awareness could be proposed that takes into account the functional specificity of the parietal and frontal intentional regions [103,104]. In brief, it was suggested that a general, unspecified intention to act first emerges into consciousness within the inferior parietal lobule. This intention is the neural signal that triggers actual motor preparation. While the movement is being planned, the cingulate and supplementary motor areas exert inhibitory control over the motor output regions. This is done to prevent an early, unwanted, release of the motor command. Once the movement is ready, this proactive inhibition is waived, which amounts to the emission of a ‘go’ signal that gives rise to a compulsive urge to act. After movement onset, parietal control mechanisms monitor action progression independently of sensory inputs, through forward modelling. When an error is detected that cannot be corrected through online control processes (e.g. the arm does not move when it should), dPM emits a warning signal that reaches consciousness. Of course, this model is not only based on the outcomes of DES studies but also on a large array of clinical, neuroimaging and electrophysiological data. However, DES was a key method through which the material generated by each of these approaches could be interpreted and aggregated [16].

5. Concluding remarks

To summarize, the data above show that DES has provided a unique body of knowledge since its pioneering use by Wilder Penfield, in humans, almost a century ago [6]. Had this technique not been employed, our comprehension of the organization of the sensorimotor systems involved in movement execution, language production, the emergence of action intentionality or the subjective feeling of movement awareness would have been greatly undermined. This is not to say, of course, that DES is a gold standard devoid of limitations, nor to deny the major importance of other clinical, electrophysiological, modelling or neuroimaging approaches [27]. This just means that DES represents a unique way to map sensorimotor pathways and interfere with the functioning of localized neural populations during the performance of well-defined behavioural tasks. Recent advances suggest that there is still a lot to learn from this technique. In particular, many structures remain to be carefully investigated including, for instance, the cerebellum [113]. Also, cortico-cortical connectivity continues to be a difficult challenge that DES could help to address in humans [114,115]. Finally, the use of probabilistic maps taking into account inter-individual variability to link structures and functions will allow a better targeting, during per-operative evaluations, of the functions that are at risk for a given lesion. Such a ‘tailored’ approach will favour the development of finer evaluation protocols and lead, potentially, to a much better comprehension of the functional fine-grained organization of the brain.

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