Comissural inter-M1 cortico-cortical evoked potential: A proof of concept report

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Abstract

Intraoperative neuromonitoring of motor functions experienced a dramatical revolution in the last years due to significant advances in anaesthesiology procedures and both preoperative and intraoperative mapping techniques. Asleep, awake and combined intraoperative mapping techniques were responsible for an improvement in the functional outcomes in neurosurgery providing reliable and reproducible mapping of both projection and association fibres involved in motor control. Here, we provide evidence of intraoperative mapping of commissural fibres involved in motor control in a patient with asleep technique as well as a review of the potential tracts involved in the connectivity underlying the motor function.

Introduction

The neurosurgical community has witnessed significant changes in the intraoperative motor mapping paradigms since the first descriptions of Penfield and Boldrey in 1937[16]. Our knowledge about the human motor network has evolved thanks to the advances produced by animal-based studies[11], such as viral tracing, and human-based studies, such as cadaveric, neurophysiological and imaging studies[1, 2, 8]. Such knowledge has now taken us forward beyond the anatomical localization of structures towards understanding the concept of functional reserve[19] and its implication for impairment as well as their connections[14].

Preoperative knowledge of patient-centred anatomy and function of motor network improve surgical planning and enhance the odds of identifying and preserving eloquent structures. The initial developments of intraoperative neuromonitoring (IONM) of the motor network started with awake craniotomy techniques – 1st phase - where the primary motor cortex (PMC, M1) was identified with low-frequency mapping techniques[16]. Improvements in anaesthesiology alongside both surgeon and patient preferences, drove the IONM research towards development of reliable asleep techniques – 2nd phase, using high frequency mapping techniques, a train of 5 and the *classic* rule of 1mA-1mm for corticospinal tract (CST) identification[17]. The emerging 3rd phase of IONM for motor network is focused on a patient-centred approach integrating both awake and/or asleep mapping techniques to preserve not only the M1-CST but also the “higher motor functions”. It is now widely recognized that the human motor function requires more than the preservation of the M1-CST complex.

Intra and interlobar networks in both frontal and parietal lobes are responsible for the fine tune control and fluency of the generated movement, overall perceived as motor cognition[19]. The supplementary motor area (SMA) is involved in the fluency and initiation of the movement – volition - with a potential involvement of the SMA-M1 association fibres, Fronto-Aslant tract and U-fibres from the cingulum[4]. The premotor cortex is in direct connection with the parietal lobe via the superior longitudinal fascicular (SLF) system[20] and the inferior fronto-occipito-fasciculus[12]. The contribution of the U-fibers to this network are of increasing interest. The U-fibers connecting the pre and post central gyri are not uniformly distributed, clustering around the hand-knob area – superior, middle and inferior U-tracts – but also in the paracentral lobe – Paracentral U-tract – and in the functional area of the face – face superior and inferior

U-tracts[3, 4, 7]. Intra-parietal short fiber tracts may also be responsible for multimodal sensory integration as they provide connection between the inferior parietal lobule and the postcentral gyrus: to the areas of the face and hand – Parietal inferior-to-Postcentral Tract – and the lower limb – Parietal Superior-to-Postcentral Tract, providing auditory and visual sensory information to the human motor output[5].

The possible interhemispheric influence on motor function adds a further level of complexity. Clinically, interhemispheric control in the motor network has been established mainly in stroke patients[15]. To the best of our knowledge, no intraoperative report of M1-M1 connectivity has been published. We present here an intraoperative report of cortico-cortico-evoked potentials in an asleep patient between both M1s and M1-SMA bilaterally, providing first-in-human data supporting bilateral connectivity between both primary and supplementary motor areas.

Clinical Report

A 74-year-old female patient presented with progressive headaches and behavioural change over 4 months. The preoperative imaging showed a bilateral extrinsic homogenously contrast enhancing lesion with a biconvexity dural-based and falcine origin in keeping with an anterior third bilateral parassagital meningioma. (Figure 1, A-C) She went on to have a bilateral craniotomy for tumour resection with dural excision. Given the extensive oedema on T2 sequences and tumour location, there was concern about the possibility of brain invasion which prompted the surgical team to use IONM for motor mapping (M1-corticospinal tract complex). An uneventful resection was performed (Simpson Grade 1) and the patient was discharged with no motor deficits. the histopathology confirmed a meningioma WHO Grade 1. At 1 year follow up, she had reverted to her pre-morbid behavioural status, without motor deficits and no evidence of recurrent tumour on imaging (Figure 1, D-F).

Intraoperative Neurophysiology:

Transcranial motor evoked potentials (TcMEPs) were present at baseline from both hemibodies with spread of stimulation. At closure the TcMEPs were present from the left hemibody with no spread, and present from the right hemibody, however when evoking small amplitude responses from the right lower limb there was spread of current to the left hemibody. Somatosensory evoked potentials (SSEPs) were bilaterally present from the upper limbs at baseline and stable throughout the procedure.

Cortical monopolar high frequency stimulation evoked the left upper and lower limbs at 15mA. A subdural strip electrode was placed over the right hemisphere motor cortex (intraoperative guidance according to the best motor response) evoking the left upper limb at 13-15mA throughout the resection. A second strip was placed over the left hemisphere (same intraoperative guidance as above) and evoked responses from proximal right upper limb muscles at 15mA with no changes in motor responses throughout the resection. Subcortical monopolar stimulation evoked no responses up to 15mA.

Cortico-cortical evoked potentials between both M1 cortices were attempted to ascertain the integrity of the commissural fibres connecting both these areas. We proceeded with stimulation of the left

hemisphere SMA and recording from right M1 and followed by stimulation of the right hemisphere SMA and recording from left M1, with train of 5 (high frequency) technique, 500 pulse width, 14mA anodal stimulation. The amplitude of the responses observed (2 peaks identified) were in the range 10.5-11.5 uV amplitude with a latency of 45-55ms for the first peak and 60-75ms for the second peak. On both occasions, a contralateral response was elicited. Both montages produced similar evoked responses (amplitude and latency) (Figure 2).

Discussion

Asleep and awake mapping techniques allow for integrated multilevel motor mapping and monitoring. Projection fibres are reliably assessed with both techniques using both low or high frequency stimulation [19]. A multitude of parameters can be used to assess these fibres, such as the amplitude and latency of the motor evoked potentials and the motor threshold. Association fibres are mapped using awake techniques where complex motor movements can be disrupted using bipolar low frequency stimulation. Novel techniques of cortico-cortical evoked potentials have also been described to assess the integrity of association fibres such as the arcuate fasciculus [13] and a recent renew interest has revisited these concepts [6]. In this paper, we took the opportunity to record cortical-cortical evoked potentials, when both hemispheres were exposed for the purpose of tumour resection, and use the data, for the first time, to study interhemispheric connectivity. Figure 3 provides a summary of the main structural connections assessed in this study with IONM.

Large bifrontal parasagittal meningiomas often require bilateral exposure of bilateral supplementary motor and primary motor areas. Recent evidence supports the use of intraoperative neuromonitoring during meningioma surgery to prevent postoperative motor deficits, particularly if brain invasion was suspected preoperatively [18]. Therefore, in asleep conditions, bilateral motor mapping allows not only the mapping and monitoring of bilateral projection fibres and their cortical terminations – corticospinal tract and PMC – but both intra and interhemispheric connectivity of both PMC and SMA.

Extensive intra and interhemispheric interactions have been shown between both SMAs and PMCs with transcranial magnetic stimulation (TMS), functional MRI (fMRI) and Electroenchephalogram[9]. SMA is involved in the stage of motor preparation of both uni- and bi-manual movements. In general, SMA produces an inhibitory influence on the contralateral hemisphere during unimanual movement via transcallosal inhibition and an excitatory influence on the contralateral hemisphere during bimanual coordinated movement via transcallosal facilitation. It seems that SMA achieves this by regulating M1-M1 interhemispheric connectivity. Both TMS and fMRI studies suggest that the SMA influences the ipsilateral M1 via intrahemispheric connectivity during unimanual movement and contralateral M1.

Advanced tractography and post-mortem dissection studies provide insight into the structural substrates of these interactions. The Frontal Superior Longitudinal Fasciculus and the Fronto-Precentral U-tracts are the likely substrates for the intrahemispheric connectivity between SMA and M1. For the interhemispheric connectivity, the corpus callosum takes the role of the substrate, particularly the anterior two thirds of the

body of the corpus callosum which corresponds to the rostral body and the anterior midbody according to Wilteson's classification [3].

Conclusion

In this paper, for this first time, we present direct physiological evidence of this connectivity between SMA and contralateral PMC. Clearly our data will need to be replicated but the evidence provided here paves the way towards a more complete understanding of human motor pathways. This also has direct clinical relevance with potentially new paradigms to be explored for recovery from neurological damage, not only after a stroke but also for post-operative acquired deficits.

Declarations

Funding: No funding was received for conducting this study

Conflicts of interest: None

Availability of data and material: all the data and materials are included in the manuscript

Code availability: not applicable

Authors' contributions:

JPL, HK, PG, FF collected the data and formatted the manuscript. PG formatted the illustration. RSB, FV, RG reviewed and provided the feedback. KA conceptualised the manuscript. All authors reviewed and approved the manuscript.

Ethics approval: All the data were collected from patient records. Department of Neurosurgery at Kings College Hospital approved the study. All patient data were anonymised. The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Consent to participate and publication: Patient consented to participate and for utilisation of anonymised images for publication

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Figures

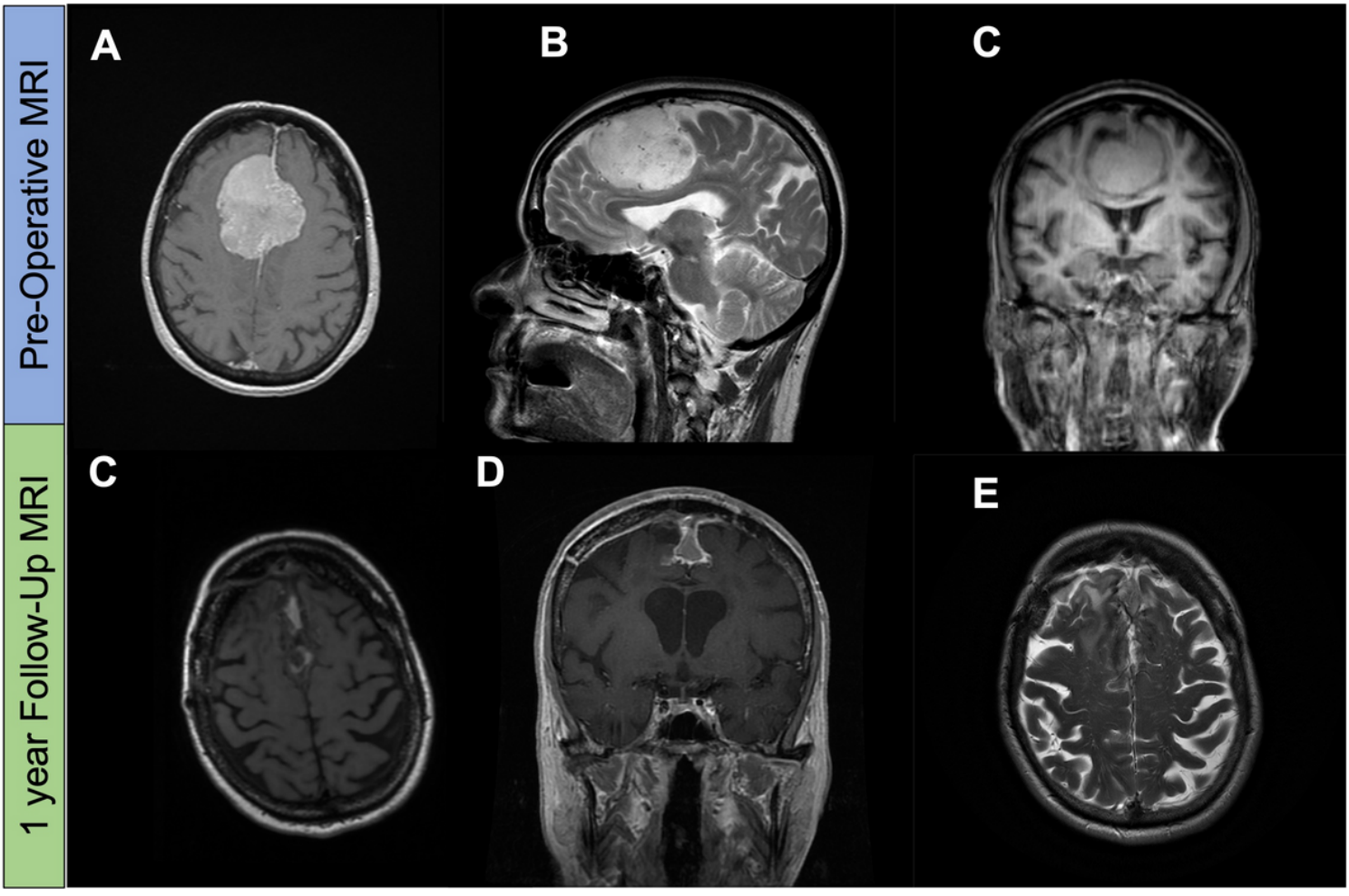

Figure 1

Pre-Operative and 1 year Follow-Up MRI - Axial (A) T1 Gadolinium, Coronal (B) T2 and Sagittal (C) T1 showing a parafalcine extra-axial lesion with mass effect and in close proximity with motor areas bilaterally. Axial (C) and Coronal (D) T1 Gadolinium documenting complete resection with no signs of tumour recurrence and Axial (F) T2 showing no white matter changes in the motor area after tumour resection.

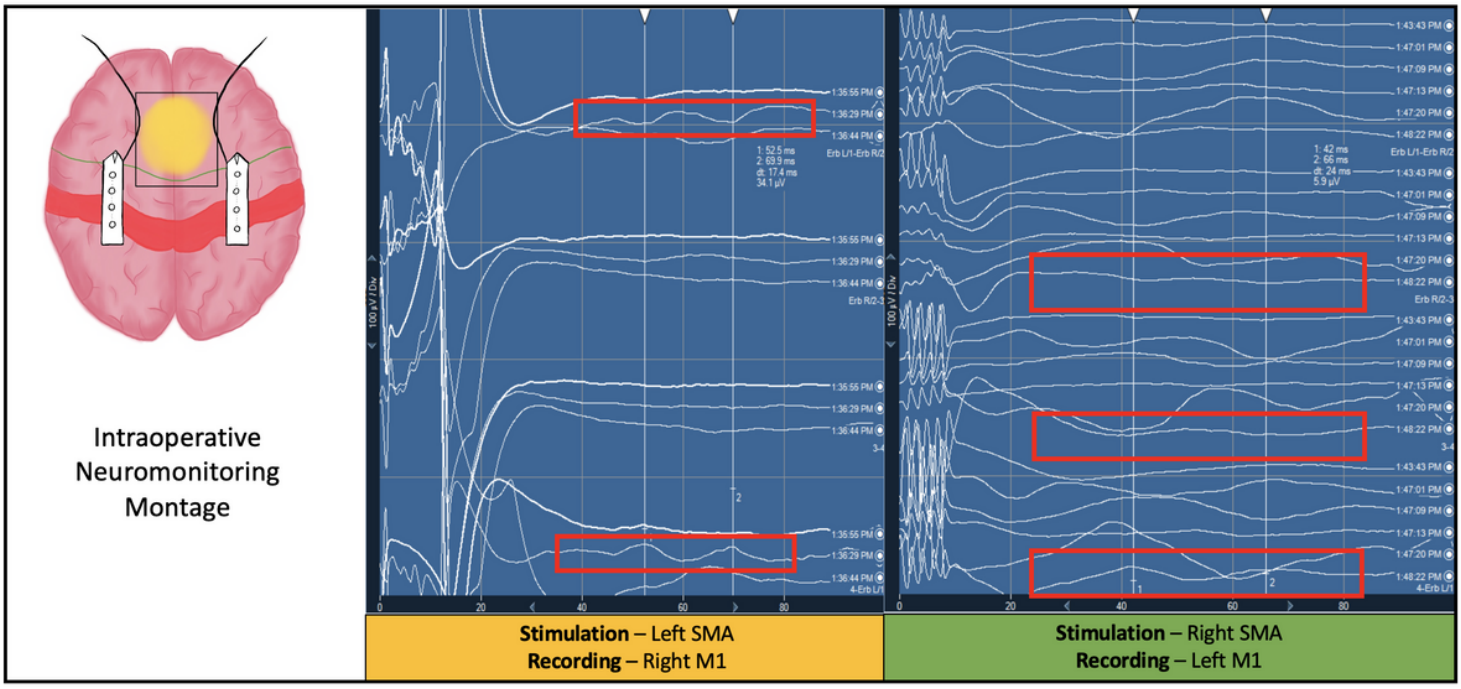

Figure 2

Intraoperative Neuromonitoring documenting interhemispheric connectivity when stimulating in ipsilateral SMA and recording from contralateral M1. Train of 5 (high frequency) technique, 500 pulse width 14mA anodal stimulation. The amplitude of the responses observed (2 peaks identified) were in the range 10.5-11.5 uV with a latency of 45-55ms for the first peak and 60-75ms for the second peak. Red boxes – positive responses

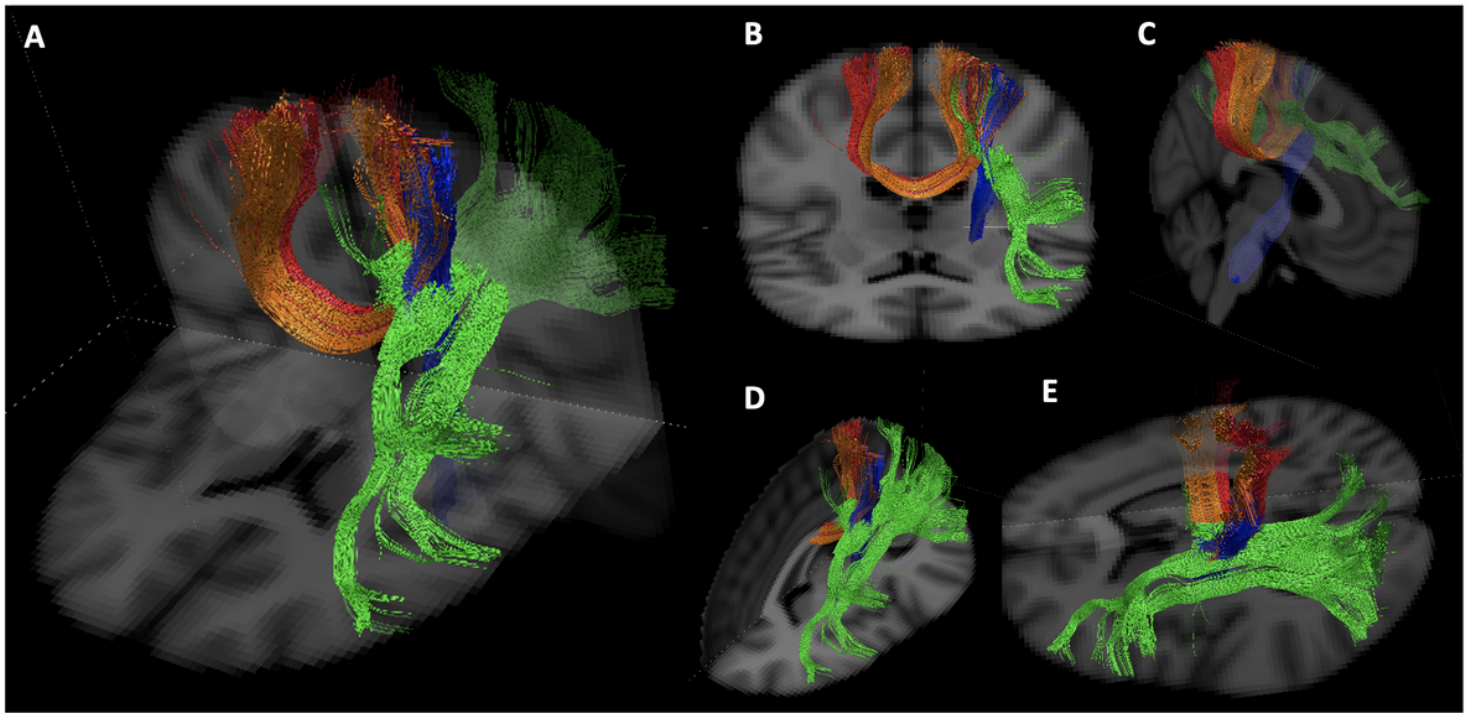

Figure 3

Tractography representation of some of the tracts underlying the connectivity of the primary motor cortex. This representation was performed with TrackViz Software (www.trackviz.com) using spherical deconvolution (SD) tractography performed with StarTrak Software (www.mr-startrak.com). A – Overall View of the model (Superior and Ipsilateral View). B – Anteriro-Superior View. C – Contralateral View. D – Antero-Superior View. E – Lateral-Superior View. The SD model was performed using dRL algorithm (fibre response parameter ALFA=1.5, 200 iterations, regularization n=0.0015, v=8). Deterministic tracking was performed with an angle threshold of 35 degrees, an absolute fODF amplitude threshold of 0.002 and a step size of 1mm. The whole brain tractography was registered to the MNI space. Blue – Projection fibres; Green – Association Fibres ; Orange / Red – Interhemispheric / commissural fibres.