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Pattern of corticospinal projections defined by brain mapping during resective epilepsy surgery in a patient with congenital hemiparesis and intractable epilepsy

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1 **Pattern of corticospinal projections defined by brain mapping during**
2 **resective epilepsy surgery in a patient with congenital hemiparesis**
3 **and intractable epilepsy**

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18 **Disclosures**

19 The authors report no conflict of interest concerning the materials or methods used in
20 this study or the findings specified in this paper.

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1 **Abbreviations:**

2 AEDs, Antiepileptic Drugs; APB, abductor pollicis brevis; AH, CMAP, compound
3 muscle action potentials; DCS, direct cortical stimulation; EEG,
4 Electroencephalography; fMRI, functional magnetic resonance imaging; IONM,
5 intraoperative neurophysiologic monitoring; TCS, transcranial stimulation; TMS,
6 transcranial magnetic stimulation.

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8 **Key words:**

9 congenital hemiparesis; corticospinal projection; intraoperative neurophysiological
10 monitoring; resective epilepsy surgery;

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1 Abstract

2 Background: Congenital or early acquired brain structural lesions often cause
3 contralateral hemiparesis as well as cognitive deficits, developmental delays, and
4 seizures. Among them, seizure is the most debilitating condition, as it greatly impairs
5 the quality of life in both the affected individuals and their caregivers and prevents
6 them from active social participation.

7 Case Description: Here, we present a 34-year-old man with hemiparesis and
8 early-onset seizures since childhood owing to a congenital brain lesion. He developed
9 intractable seizures in the last two years, and was subsequently admitted for resective
10 epileptic surgery. During the operation, we employed an innovative intraoperative
11 neurophysiological monitoring technique. Unlike routine application for transcranial
12 stimulation (TCS), we recorded compound muscle action potentials (CMAPs) over
13 the bilateral limb muscles simultaneously instead of over the contralateral muscles
14 only, to determine the patterns of the corticospinal projections. TCS over the bilateral
15 hemispheres was applied before craniotomy and direct cortical stimulation over the
16 lesioned hemisphere was applied after craniotomy. By integrating both approaches,
17 we could first identify the pattern of corticospinal projections before craniotomy and
18 then accurately define the non-eloquent area, which in turn guided the resection to
19 successfully accomplish the surgical goal.

20 Conclusions: The technique is simple because no patient participation is required.
21 Moreover, we believe that it has the potential to replace conventional preoperative
22 functional magnetic resonance imaging and transcranial magnetic stimulation in
23 resective epilepsy surgery, particularly for young patients. Not only can it improve the
24 safety of surgical procedures, it can help predict the functional outcome as well.

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1 **Introduction**

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3 Many forms of prenatal and perinatal brain injury can lead to congenital
4 hemiparesis. Periventricular white matter injury is the most common lesion type,¹
5 whereas other causes include perinatal arterial stroke, brain malformations, and
6 intracranial haemorrhage. Patients with congenital or early-acquired brain structural
7 lesions present not only with contralateral hemiparesis but also cognitive deficits,
8 developmental delays, and seizures. Among them, seizure is the most debilitating
9 manifestation, which greatly impairs the quality of life in both the affected individuals
10 and their caregivers as well as prevents them from active social participation.²⁻⁴
11 Children with epilepsy may also have cognitive and learning difficulties, leading to
12 low academic performance in school and poor interpersonal relationships with their
13 peers.⁵ Antiepileptic drugs (AEDs), a ketogenic diet, nonspecific interventions, and
14 surgery are the mainstay of the treatment for seizures in childhood. Among them,
15 medication is usually the first-line treatment for confirmed and persistent seizures.
16 Seventy to 80% of epileptic children achieve seizure control with the first or second
17 AED, and about two-thirds of those that take AEDs can be weaned off after two years
18 of being seizure-free.⁶ However, the short-term and long-term adverse effects of
19 AEDs often limit their use. AEDs can cause dose-dependent adverse effects such as
20 cognitive decline, persistent somnolence, and ataxia as well as idiosyncratic responses
21 such as Steven-Johnson disease, or chronic adverse effects including altered hormonal
22 regulation, weight gain, hair loss, and loss of bone density.⁷ Among all the known
23 adverse effects, cognitive decline probably poses the greatest risk on children because
24 they cause long-term developmental impairment.⁸ Thus, early-onset epilepsy disorder
25 as well as its pharmacological management intertwine to create a sub-optimal
26 situation for affected children.

27 If the seizures cannot be managed by AEDs or the adverse effects of the
28 anticonvulsants are intolerable, surgical resection of the epileptogenic focus is the
29 next option to achieve better seizure management. According to a meta-analysis
30 conducted by Cao et al., 71% of epileptic children receiving hemispheric surgery
31 could maintain a seizure-free status in five years, an outstanding long-term
32 prognosis.⁹ Nevertheless, surgical resection of the epileptogenic focus poses the risk
33 of creating new functional deficits. However, it is possible that corticospinal
34 projections of the lesioned hemisphere might migrate to the opposite hemisphere in
35 younger individuals, owing to early onset of the lesions and children's pronounced
36 neuroplasticity.¹⁰ This consideration should affect surgical decision-making and the
37 prognosis of functional outcomes.

1 In the present study, we employed an innovative intraoperative neurophysiologic
2 monitoring (IONM) approach to determine the pattern of corticospinal projections
3 during resective surgery of an adult patient with congenital hemiparesis and refractory
4 epilepsy. We believe that a thorough understanding of the anatomy is essential not
5 only for surgical decision-making but also for predicting functional outcomes
6 following surgery.

8 **Case report**

9 **History and Examination**

10 A 34-year-old man was born full-term via normal spontaneous delivery. His mother
11 denied any abnormality or events during perinatal follow-ups or postpartum. The
12 patient had a history of developmental delay, right hemiparesis since infancy, and
13 seizures starting at the age of six years. He developed dystonia of the right upper
14 extremity in flexor posturing since his adolescence, yet he could still walk a long
15 distance with a hemiparetic gait and was partially independent in activities of daily
16 living. At the time of writing, he was employed at a full-time sheltered job in the
17 housing intermediary industry. In the last two years, the patient developed
18 drug-resistant seizures that significantly impaired his quality of life and prevented him
19 from engaging in active social and vocational activities. The seizures occurred
20 without prodromes or an aura 4–5 times each day, but improved to 1–2 times every 3
21 months under treatment with anticonvulsants. Electroencephalography (EEG) showed
22 a general spike-and-wave complex, 1.5–2.0 Hz over F-C max. A preoperative
23 intelligence test, using the Wechsler Adult Intelligence Scale, indicated borderline
24 mental deficit with a total intelligence quotient of 72. He was admitted to the
25 neurosurgery ward in a tertiary medical centre to undergo resective epileptic surgery.

26 **Imaging**

27 Preoperative brain magnetic resonance imaging (MRI) revealed tissue loss and cystic
28 encephalomalacia in the left parietal and temporal lobes and insular regions, which
29 suggested an old cerebrovascular insult (Fig 1).

30 **Operation and intraoperative neurophysiological monitoring technique**

31 After anaesthesia, a pair of needle electrodes was inserted at the bilateral
32 abductor pollicis brevis (APB) and abductor hallucis (AH) to record compound
33 muscle action potentials (CMAPs). Stimulating electrodes were placed at Cz, C3, and
34 C4 according to the international 10–20 system for transcranial stimulation (TCS).
35 Responses from bilateral APB and AH to multipulse train TCS with either C3/Cz or

1 C4/Cz montages were recorded before incision to define the pattern of corticospinal
2 projections. In this patient, when stimulating with C3/Cz montage (254 V, train of 5,
3 pulse-width 50 μ s), we obtained a motor response from only the right-hand muscle.
4 However, when stimulating with C4/Cz montage (226 V, train of 5, pulse width 50
5 μ s), we obtained compound muscle action potentials (CMAP) over the bilateral hand
6 muscles and AH, which indicated that corticospinal projections from both
7 hemispheres innervated muscles in the paretic limbs (Fig 2). After craniotomy, the
8 central sulcus could not be defined by phase reversal probably owing to severely
9 destructive brain lesions of the left hemisphere. Thus, we used multipulse train direct
10 cortical stimulation (DCS) with a monopolar electrode to help the surgeon confine the
11 resection to the non-eloquent cortex (stimulus parameters--train of 5, 2–4
12 inter-stimulus interval, 0.5 ms pulse width, 0.5–20 mA). The region underneath disc
13 16 was the only area with a motor response from the hand muscle when performing
14 DCS with multipulse train stimulation and stimulus intensity 20 mA, and needed to be
15 preserved (Fig 3). The surgeon then performed a left frontal corticectomy and the
16 extent of resection was defined by pre-operative epilepsy survey (semiology,
17 video-EEG, positron-emission tomography, and MRI) and tailored by
18 electrocorticography. The postoperative course was uneventful and there was no
19 postoperative motor functional deterioration. Moreover, pre- and post-operative
20 linguistic tests, both graded as with mild degree of deficits, did not reveal any
21 significant interval change, although no linguistic mapping was performed during the
22 surgical procedure. The patient had remained seizure-free six months after the
23 operation.

24 **Discussion**

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27 Children with congenital or early onset brain lesions frequently experience
28 contralateral hemiparesis, mental deficits, and seizures, which have a tremendous
29 impact on their development. Among those effects, seizures increase caregivers'
30 burden and unsurprisingly negatively affect their quality of life as well.^{11,12} Surgical
31 resection of the epileptogenic focus is an alternative option if medical treatment fails
32 to offer a satisfactory control of seizure attacks.^{13,14} However, resective surgery of the
33 cortex does carry the risk of postoperative deficits, particularly if the focus lies in
34 proximity to the eloquent cortex. Thus, a thorough understanding of the pattern of
35 corticospinal projections before resection of the epileptogenic focus is mandatory to
36 maximally reduce any possible postoperative deficits.

37 A congenital or early-acquired insult of the brain might result in reorganization
38 of the corticospinal projections because of the greater neuroplasticity in

1 childhood.^{10,15} Therefore, there is the possibility that the eloquent cortex shifts to the
2 unaffected hemisphere or to another part of the affected hemisphere, which will
3 certainly influence the surgeon's decision-making when performing resective epilepsy
4 surgery. This is because the possibility and severity of postoperative deficits will
5 differ according to the kind of functional reorganization of the brain. In a previous
6 study, three out of 10 epileptic children possessed ipsilateral corticospinal projections
7 from the contralesional hemisphere, three patients presented with corticospinal
8 projections from both hemispheres, and four patients had preserved corticospinal
9 projections from the affected hemisphere.¹⁶

10 Currently, neuroimaging and brain stimulation either intraoperatively or
11 extraoperatively as well as intraoperative neuromonitoring all could be utilized solely
12 or collaboratively to determine the pattern of corticospinal projections, the extent of
13 the lesion, and the relationship with its contiguous tissue. These are crucial for
14 surgical decision-making and the prediction of functional outcomes.^{10,17} Hooi et al.
15 even proposed that when combining quantitative diffusion tensor imaging fibre
16 tracking and fractional anisotropy values, one can predict the post-operative high
17 cognitive and neuropsychological outcomes such as in language, memory, and
18 attention.¹⁸ However, some of these procedures require active patient participation
19 and cooperation, which is frequently very challenging in patients with congenital
20 hemiparesis due to their younger age and/or associated mental deficits. This case
21 report shows how intraoperative brain mapping helps to define the pattern of
22 corticospinal projections and how it can contribute to surgical decision-making during
23 resective epilepsy surgery and in turn lessen the possibility of new postoperative
24 motor functional deficits. However, this technique cannot replace the role of
25 pre-operative functional MRI and awake surgery regarding mapping of the linguistic
26 centres.

27 Chandra et al. published a retrospective study in 2008, reviewing 462 cases aged
28 between 4 to 23, undergoing hemispherotomy for intractable seizures. Of all cases,
29 four experienced immediate post-operative weakness, which improved to preoperative
30 level in 5 to 8 weeks. The study illustrated that even though hemispherotomy is
31 considered safe for functional maintenance, worsening motor function is still likely to
32 occur.¹⁹ We exerted every effort to preserve this young man's functionality because
33 although he had borderline intellectual disability, he was holding a full-time sheltered
34 job and was financially independent. Thus, when the intraoperative brain mapping
35 revealed bilateral corticospinal projections, given his high functionality and personal
36 expectation, the surgeon decided to perform frontal corticectomy and under guidance
37 of DCS, spared the eloquent cortical region (underneath disc 16) to avoid causing any,

1 albeit trivial according to previous research, but possible new deficit, which may have
2 impeded his current daily performance.

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4 TCS over the bilateral hemispheres (using either C3/Cz or C4/Cz montages) is
5 applied before craniotomy and DCS over the lesioned hemisphere is applied after
6 craniotomy. Conventional C3/C4 montage is not recommended during TCS in order
7 to avoid deeper penetration of the stimulus current with simultaneous activation of the
8 bilateral corticospinal tracts, which certainly will confound the results. Based on the
9 information gathered from the aforementioned approaches, we could first identify the
10 pattern of corticospinal projections before craniotomy and then accurately define the
11 non-eloquent area using DCS, which in turn guided surgical resection and
12 successfully accomplished the surgical goal. In this patient, corticospinal projections
13 from both hemispheres to target muscles in the paretic limb rendered the resection
14 less risky. Furthermore, the technique is simple because no cooperation or
15 participation is required from the patient, who remained under anaesthesia. This
16 patient sustained no new functional deficits after operation and had stayed seizure free
17 six months after the operation.

18 The main difference of this approach, unlike previous routine applications, is that
19 we recorded CMAPs over the bilateral limb muscles simultaneously instead of only
20 over the contralateral muscles to determine the corticospinal projection pattern. We
21 believe that it has the potential to replace preoperative fMRI and TMS in resective
22 epilepsy surgery, particularly for young patients. Not only can it improve the safety of
23 surgical procedures, it helps to predict the functional outcome as well.

24

25 **Disclosure**

26 The authors report no conflict of interest concerning the materials or methods used in
27 this study or the findings specified in this paper.

28

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31 commercial, or not-for-profit sectors.

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1 Figure 1. Brain magnetic resonance imaging showing tissue loss and cystic
2 encephalomalacia in the left parietal and temporal lobes and insular regions (left, axial
3 view on T1-weighted imaging; right, frontal view on T2-weighted imaging).

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1 Figure 2a. While stimulating with C3/Cz montage, we obtained a motor response
2 from only the right hand muscle (left). However, when stimulating with C4/Cz
3 montage, there were compound muscle action potentials in the hand muscles and the
4 abductor hallucis bilaterally (right).

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1 Figure 2b. Corticospinal projections from both hemispheres to target muscles in the
2 right paretic limbs made the resection of the left epileptogenic focus less risky in this
3 patient.

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1 Figure 3. Disc 16 (left, yellow arrow) was the only area with a motor response from
2 the hand muscle when performing direct cortical mapping with multipulse train
3 stimulation (middle) and was preserved after resection (right).

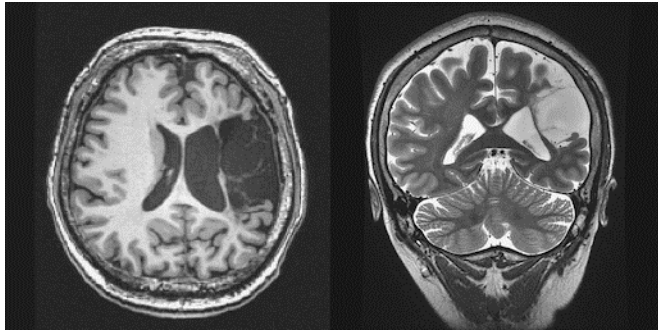
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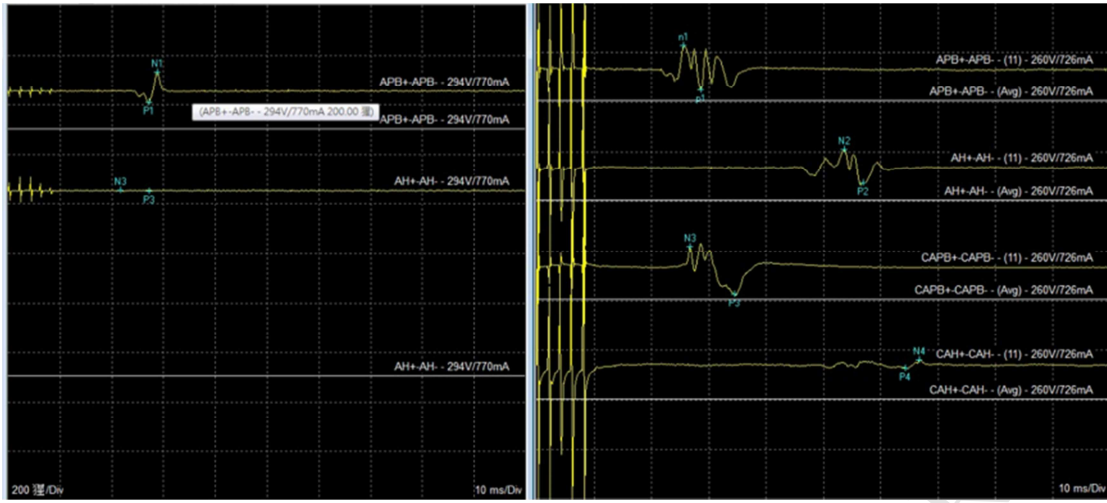
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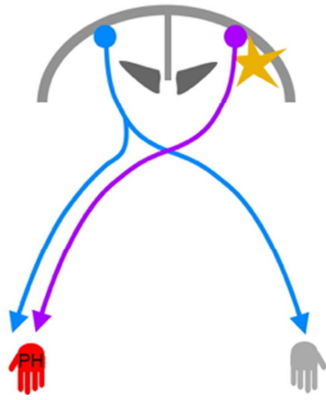
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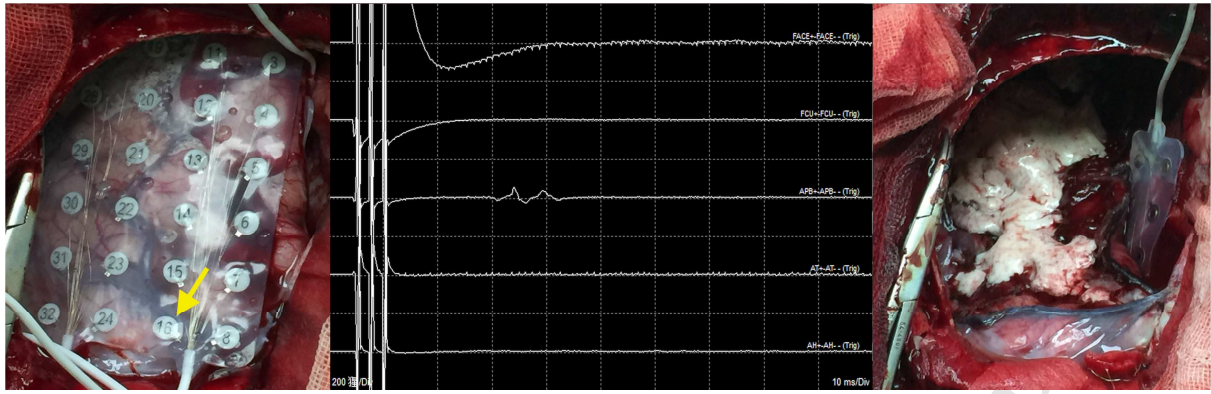


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Highlights

- CMAPs were simultaneously recorded over the bilateral limbs muscles
- TCS was applied bilaterally before craniotomy and DCS over the lesioned side after
- The non-eloquent area was successfully defined and functionality was preserved