Child Neurology: Functional Reorganization Mediating Supplementary Motor Area Syndrome Recovery in Agenesis of the Corpus Callosum

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Abstract

Supplementary motor area (SMA) syndrome is a typically transient condition resulting from damage to the medial premotor cortex. The exact mechanism of recovery remains unknown but is traditionally described as a process involving functional compensation by the contralateral SMA through corpus callosal fibers. The purpose of this case study is to highlight a distinct extra-callosal mechanism of functional recovery from SMA syndrome in a patient with agenesis of the corpus callosum (ACC). We present the clinical presentation and perioperative functional neuroimaging features of a 16-year-old patient with complete ACC who exhibited recovery from an SMA syndrome resulting from surgical resection of a right-sided low-grade glioma. Preoperative functional MRI (fMRI) revealed anatomically concordant activation areas during finger and toe tapping tasks bilaterally. Three months following surgery, the patient had fully recovered, and a repeat fMRI revealed shift of the majority of the left toe tapping area from the expected contralateral hemisphere to the ipsilateral left paracentral lobule and SMA. The fMRI signal remodeling observed in this acallosal patient suggests that within-hemisphere plasticity of the healthy hemisphere may constitute an alternative critical process in SMA syndrome resolution and challenges the traditional view that transcallosal fibers are necessary for functional recovery.
Pearls

- Supplementary motor area (SMA) syndrome is a condition resulting from unilateral injury to the medial aspect of the premotor cortex.

- The classical SMA syndrome is transient and is characterized by contralateral hemiparesis and hemiapraxia. Language deficits are commonly observed in dominant hemisphere SMA injuries.

- The most widely accepted theory attributes functional recovery to compensation by the intact contralateral SMA via commissural fibers of the corpus callosum (CC).

Oysters

- SMA syndrome should always be considered following medial premotor cortex injury. Even in patients exhibiting profound neurological deficits, significant recovery is expected.

- In patients with agenesis of the CC (ACC), recovery from SMA syndrome remains possible through extra-callosal compensatory mechanisms. Thus, ACC may not preclude surgical removal of lesions within the SMA

Case report
A 16-year-old right-handed girl with complete ACC was referred to the outpatient clinic for a 7-year history of refractory headaches. Initial neurological examination was normal. Brain MRI confirmed the complete ACC and revealed a non-enhancing lesion confined within the right SMA suggestive of a low-grade glioma (LGG) (Fig.1A). A task-based fMRI was performed (methodology described in eMethods in the Supplement) and revealed the location of finger and toe tapping activations within the expected regions of the contralateral sensorimotor cortex, but no SMA activity (Fig.1B,C). Language tasks disclosed a diffuse bilateral speech representation including the SMA on both sides. Considering the absence of CC fibers and the presumed lower likelihood of postoperative functional compensation, the risk of permanent deficits following resection of the SMA was deemed non-negligible. However, due to the poor outcome often associated with unresected LGG, a surgical treatment was favored. Cortical stimulation-guided gross total resection of the SMA tumor was performed.

Following surgery, the patient developed a left-sided tonus-sparing 3/5 hemiparesis and significant hemiapraxia, consistent with a motor SMA syndrome. At the three-month follow-up, she had fully recovered, and a repeat MRI showed no tumor recurrence (Fig.2A). Repeat task-based fMRI revealed expected finger tapping and right toe tapping areas, with the latter expanding to also encompass the left SMA (Fig.2B). Surprisingly, a considerable portion of the area activated by left toe tapping had shifted to the left paracentral lobule and the adjacent SMA (Fig.2C).

Discussion
The SMA is responsible for several key motor functions, including planning, initiation, and execution of voluntary movements as well as word production and articulation on the language-dominant hemisphere. Unilateral damage to the medial premotor cortex often results in the well-described SMA syndrome, a condition characterized by tonus-sparing contralateral motor weakness and hemiapraxia coupled with language impairments in dominant hemisphere injuries. A hallmark feature of SMA syndrome is the complete or near complete resolution of symptoms within weeks to months of onset. Although the transient nature of the observed deficits remains incompletely understood, cumulative evidence suggests that neurological recovery relies on the presence of an intact CC. Yet, our patient with ACC fully recovered, suggesting that extra-callosal mechanisms may be involved in SMA syndrome resolution.

Recovery from SMA syndrome has traditionally been explained by a process beginning after the cortical insult and involves a functional compensation enabled by fibers of the CC connecting the undamaged ipsilateral lateral premotor area to the contralateral SMA and premotor area of the healthy hemisphere. The exact compensatory mechanism of these commissural fibers remains incompletely understood but has been attributed to excitatory interhemispheric connections favoring functional activation of the homologous SMA and adjacent regions. While the aforementioned compensation is the most widely accepted mechanism of recovery, other processes have been proposed. Transcranial magnetic stimulation studies have shown that transcallosal inhibitory fibers may be present between homologous motor areas. Following unilateral injury, the presumed tonic inhibition is thought to be released, ultimately leading to functional hyperactivation of the undamaged contralateral region. Other reports have suggested that, in patients with slowly progressive unilateral SMA tumors, a CC-mediated gradual switch
of function to the contralateral healthy SMA may enable recovery following surgical resection of
the lesion. These theories postulate that the contralateral SMA acts as a functional substitute for
its injured counterpart and rely on CC-associated mechanisms.

The recovery observed in the current patient without a CC suggests that alternative
pathophysiological processes may be implicated in functional remodelling. Prior to surgery, our
patient did not exhibit SMA activation during motor tasks, a finding that is consistent with
previous studies. Following surgery, the left toe tapping area was mainly detected in the left
paracentral lobule and SMA, suggesting transfer of function to the contralateral side. The
unexpected left-sided SMA activation induced by left toe tapping suggests the presence of extra-
callosal within-hemisphere processes in functional reorganization which may have resulted from
a compensatory increase in activation from a previously undetected BOLD signal. This idea is
consistent with previous fMRI studies in patients with an intact CC which revealed a similar
pattern of SMA activation ipsilateral to limb movements following surgery. Indeed, few
studies have reported an increase in intra-hemispheric functional connectivity between
sensorimotor nodes of the healthy hemisphere during SMA recovery. Further, unilateral motor
movements have been shown to be represented bilaterally in the SMA but exhibit contralateral
predominance. Thus, unilateral SMA damage may uncover a functionally silent, albeit
present, network in the uninjured contralateral SMA, capable of supplanting function of the
injured cortex. This process may be facilitated by plastic functional changes within the
contralateral intact hemisphere.
The current study provides unique information regarding a distinct mechanism of recovery in SMA syndrome independent of the CC. It is worth mentioning that patients with ACC commonly develop strong extra-callosal interhemispheric connections that travel via the anterior commissure, the posterior commissure, or subcortical circuits (amygdalar, hippocampal and/or cerebellar circuits). These compensatory connections are potentially capable of taking over the function of the CC and may have played a role in the observed functional reorganization\textsuperscript{12,13}. However, their contribution does not preclude that intra-hemispheric plasticity of the healthy hemisphere was observed in our patient, and that similar within-hemisphere remodelling may be involved in SMA syndrome recovery in patients with an intact CC.

The favorable outcome seen in the current case suggests that resection of the SMA may be considered in patients with ACC. These findings may help address concerns regarding the safety of SMA resection in ACC and facilitate surgical decision-making and patient counselling. In addition, the functional restructuration observed despite the absence of CC suggests that unilateral within-hemisphere plasticity may constitute a previously overlooked critical process in SMA syndrome recovery and raises the question as to whether corpus callosal fibers are in fact requisite to overcome the functional deficits related to SMA injury.
Figure legends

Figure 1. Preoperative structural and motor task-based functional MRI. (A, upper item) Sagittal T2 weighting of FLAIR MRI sequences showing a 2.5 cm hyperintense infiltrative tumor confined within the right SMA (red arrow). (A, lower three items) Sagittal, axial and coronal T2 weighting of FLAIR MRI sequences highlighting the absence of CC (short cyan arrows). (B,C) Axial and coronal fMRI showing blood-oxygen-level-dependent (BOLD) activations of the middle portion of the contralateral primary sensorimotor cortex during finger tapping (B) and the superior aspect of the contralateral primary motor cortex during toe tapping (C). (D) T1 surface-based 3D reconstruction with superimposed regions activated during motor tasks revealed anatomically concordant functional areas.

Figure 2. Structural and motor task-based functional MRI three months following surgery. Clinically, the patient had completely recovered from the SMA syndrome. (A) Sagittal T2 weighting of FLAIR images revealing gross total resection of the tumor-infiltrated SMA with sparing of the paracentral lobule (red arrow). The absence of CC is notable above the frontal horn and body of the lateral ventricle (short cyan arrow). (B,C) Axial and coronal fMRI. (B) BOLD signals matched the location of the preoperative activations during finger tapping. (C) Activation maps revealed anterior expansion of the right toe tapping area (now incorporating most of the SMA) and contralateral transfer of a major part of the area activated by left toe
tapping to the left paracentral lobule and SMA. (D) T1 surface-based 3D reconstruction with overlaid task-activated regions highlighting the expansion of right toe tapping function and contralateral transfer of the left toe tapping area. The resection cavity is discernible at the medial aspect of the right premotor cortex.

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