# Stroke improvement with magnetic stimulation recapitulates ontogeny

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## Abstract

A patient with chronic brainstem CVA sequelae received one cycle of magnetic stimulation to treat her dysphagia and serendipitously obtained a minimal improvement in her axial movement. Two additional cycles gave her improved postural control and then distal movement, preceded by a display of ipsilateral and contralateral motor evoked potentials, respectively. Magnetic stimulation at 10 Hertz produces cortical disinhibition and reopens the critical neurodevelopment periods. The ontogenic pattern of hemiplegia recovery in this patient may be explained by an increased and rejuvenated brain plasticity due to critical period reopening through cortical disinhibition. **(Acta Med Colomb 2022; 47. DOI: https://doi.org/10.36104/amc.2022.2253).**

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## Introduction

Spontaneous recovery from hemiplegia following a cerebrovascular accident (CVA) has an ontogenic pattern (1) that is accompanied by increased critical neurodevelopmental period proteins (1). Reopening of the critical periods has been proposed as a CVA treatment (2, 3). It has been suggested that rTMS at 10 Hertz can reopen the critical periods in adult patients with amblyopia, (4). In patients with post-CVA hemiplegia, rTMS at 10 Hertz may reopen the critical periods and produce movement recovery with an ontogenic pattern.

## Clinical case

This was a 38-year-old patient with a severe neurological deficit 17 months after experiencing a brainstem hemorrhage secondary to the rupture of an arteriovenous malformation, which did not require surgical treatment (Figure 1). The neurological exam showed an alert patient with normal language comprehension, severe dysarthria, minimal movement of the uvula and soft palate, a very reduced gag reflex, right hemiplegia, left hemiparesis, a permanently flexed head, severe trunk instability and inability to stand. The patient communicated through an alphabet board used by her caregiver in response to blinking. A neurorehabilitation expert recommended the use of noninvasive brain stimulation as an adjuvant to rehabilitation. She underwent rTMS for her CVA in an off-label treatment modality (5-7). This manuscript was approved by the ethics committees of Fundación Universitaria Sanitas (CEIFUS 1382-20), and Hospital Infantil de San José (113/2020).

### First cycle

We adapted a bilateral 10 Hertz rTMS protocol for dysphagia (10), as the patient's severe motor deficit contraindicated the use of inhibitory stimulation (8, 9) and the patient could attend a maximum of three sessions per week. We administered 20 rTMS sessions using a MagPro R30 machine, a figure-eight coil (MCF-B65), and a frequency of two or three sessions per week. Each session began by locating the "hot spot" and determining the resting motor threshold (rMT). The rMT was based on observing a minimal muscle contraction. Due to the severe oropharyngeal motor deficit and constant head flexion, we used the upper extremity as the "hot spot." The "hot spot" was able to be located over the right primary motor cortex (M1) and the rMT was obtained from the left abductor pollicis brevis muscle. The magnetic pulse over the left hemisphere did not cause muscle contraction, and therefore we located the left "hot spot" in a homotopic M1 site and used the right rMT. The rTMS was applied over the right M1 in five-second trains at 10 Hertz frequency and an intensity of 90% rMT, with a 55-second interval between trains, for 15 minutes and a

total of 750 pulses. This was followed by the same protocol on the left M1. After this cycle, the patient had improved swallowing and, unexpectedly, voluntary contraction of the right rhomboid muscles.

**Second cycle**

No further improvement was seen after two months of rehabilitation, and a second cycle was applied. A cone-shaped coil (D-B80) was added to stimulate the motor cortex of the lower limbs. This coil was placed on the medial sagittal plane, wherever the greatest contraction of the left anterior tibialis muscle was seen. Ten-second rTMS trains were applied at 10 Hertz and 90% rMT, with a 50-second interval between trains, for 20 minutes and a total of 2,000 pulses (11). The frequency of the sessions was the same as in the first cycle, and the sessions alternated between the first cycle protocol and the lower limb protocol. At the beginning of this cycle, the routine search for the right hemisphere "hot spot" caused muscle contraction of the right paralyzed arm; that is, the ipsilateral motor evoked potential (iMEP) was seen. A few days later the patient began to have voluntary proximal movement of the right upper and lower limbs. After 14 sessions, proximal movement recovery was significant and magnetic stimulation was discontinued. One month later, the patient was able to hold up her head, maintain a sitting position and stand on her own (Figure 2).

**Third cycle**

Four months after the second cycle, the patient continued to have a paralyzed right hand, did not have dynamic equilibrium while standing, and a third cycle of 20 sessions was conducted using the same parameters as the second cycle. In this cycle, the routine search for the left M1 "hot spot" caused right hand contraction; that is, the motor evoked potential (MEP) appeared. At the end of this cycle, the patient had slight voluntary movement of the right abductor pollicis brevis muscle.

## Discussion

An adult patient with a chronic brainstem CVA improved her hemiplegia after receiving three rTMS cycles, which were initially aimed at treating dysphagia.

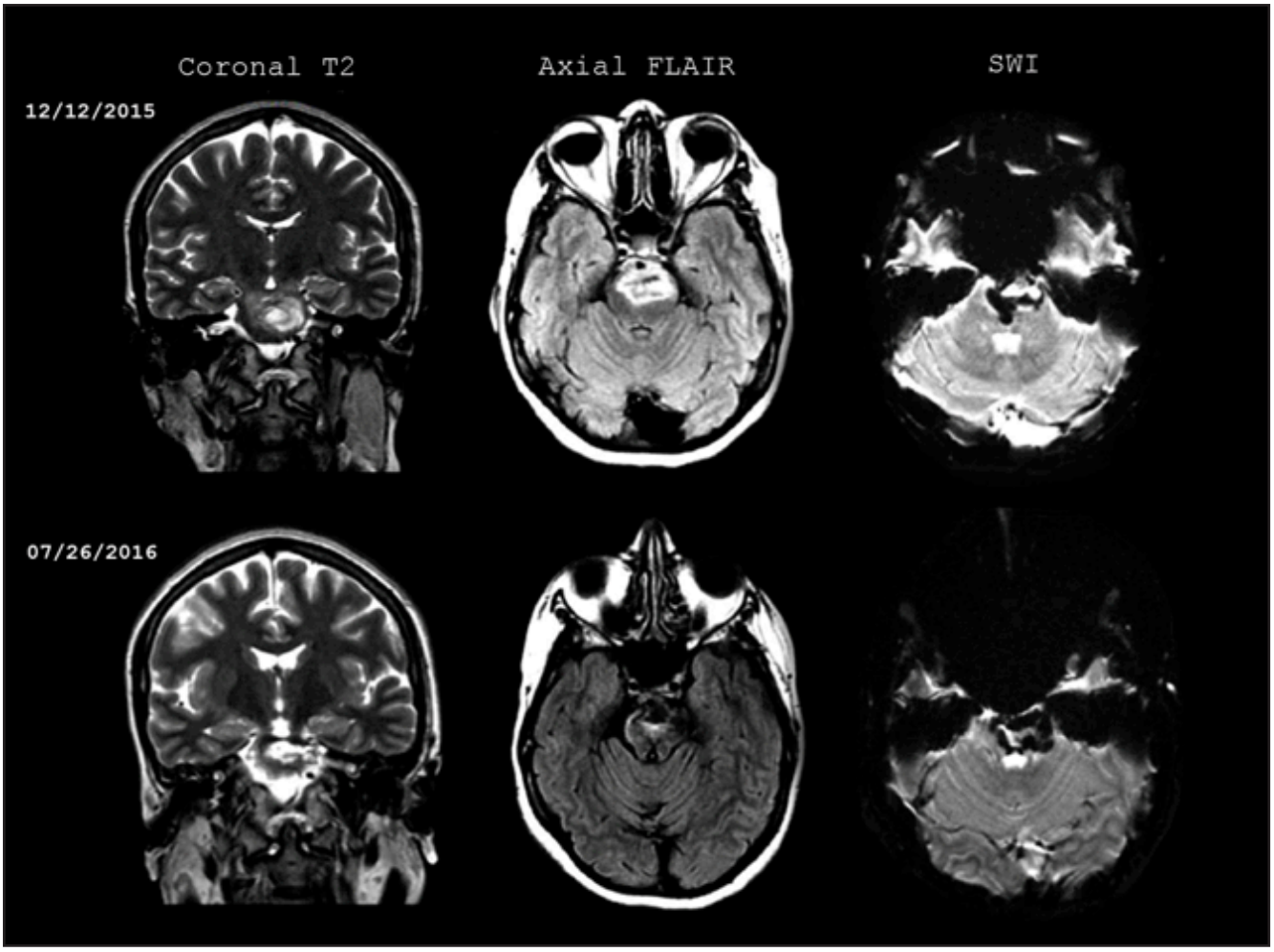


**Figure 1.** *Initial brain magnetic resonance and follow up seven months after the CVA. Brainstem hemorrhage extending form the mesencephalon to the protuberance, with a heterogenous signal on T2, and perilesional edema on FLAIR. On SWI, the blood remains in different stages of progression, with no changes in size compared to the initial images.*

At the end of the first cycle, swallowing improved and voluntary movement unexpectedly appeared in the right rhomboid muscles. Swallowing is the model for studying the reorganization of axial muscle motor control following a CVA (12). Axial muscles are innervated by the corticoreticulospinal tract (CRST) (13). We applied bilateral rTMS over M1, the site from which part of the CRST originates (13). Thus, we suspect that the appearance of voluntary axial movement was caused by CRST activation (14).

With the second cycle, the iMEP was visualized in the paralyzed arm, followed by recovery of proximal movement and postural control. This confirmed our suspicion of CRST activation (14), since this tract is responsible for iMEP (15, 16) and innervates the axial-proximal muscles responsible for postural control (13). In adults, iMEP is subject to cortical inhibition (16). Cortical disinhibition allows latent pathways to be unmasked (17). We speculated that cortical disinhibition produced by rTMS at 10 Hertz (18) was responsible for unmasking the CRST ipsilateral to the hemiplegia. This supports the proposed therapeutic effect of the ipsilateral CRST for proximal movement rehabilitation (19) and the contraindication for applying inhibitory ipsilateral stimulation in patients with severe CVA (8, 9), as it inhibits the CRST (9).

Ontogenically, the iMEP disappears at age 10 due to inhibitory processes (20). In adult patients with severe motor deficits following a CVA, CRST disinhibition causes the iMEP to reappear (21), but this is associated with a poor prognosis (21). The opposite occurs in hemiplegic adolescents, in whom the appearance of the iMEP marks the beginning of recovery (22). Children recover better than adults after a CVA, due in part to brain plasticity (23). Young brains have greater plasticity because they have less cortical inhibition than adults (24). Cortical disinhibition increases and rejuvenates brain plasticity by reopening the critical periods (25). The rTMS at 10 Hertz causes cortical disinhibition (18). It has been suggested that rTMS at 10 Hertz causes a reopening of the critical periods (3,4), as it improves adult patients with amblyopia (4). In addition, rTMS at 10 Hertz over M1 increases the expression of c-fos and zif268 proteins (26), whose genes participate in the critical periods (27). We speculate that, in our patient, the rTMS at 10 Hertz over M1 reopened the critical periods and increased brain plasticity at a level which allowed the iMEP to appear and recovery to commence, as occurs in adolescents (22). This would support critical period reopening as CVA treatment (2, 3), and leads us to suggest that the poor prognosis of iMEP in adult patients with severe CVA (21) could be related to insufficient brain plasticity, and that cortical disinhibition with rTMS at 10 Herz could help resolve it.

**Figure 2.** *Postural control. The patient sitting and standing while supervised. Note the head support and trunk control.*

The MEP of the paralyzed hand appeared during the third cycle, followed by the onset of minimal distal voluntary movement, events related to the corticospinal tract (CST) (15). Corticospinal tract activation using high-frequency rTMS has a PLP-like effect (5-7). We have speculated that our patient's recovery began with an axial-proximal movement due to ipsilateral CRST unmasking and continued with distal movement due to CST PLP. Unmasking and PLP are two brain plasticity mechanisms which require cortical disinhibition (17, 28). Thus, we support the idea that cortical disinhibition maximizes the efficiency of the corticospinal tracts of patients with CVAs (5, 29), allowing effective cerebral reorganization (5, 29). We also support the idea that cortical disinhibition is a novel treatment strategy for CVAs (30), and suggest that it can be achieved by applying rTMS at 10 Hz.

Ontogenically, distal movement is produced only after there is an adequate proximal movement (31). This ontogenic pattern also occurs during spontaneous recovery from post-CVA hemiplegia (1) and was the pattern we obtained in our patient. In 2008, the London group proposed that recovery from a major CVA requires phased recruitment of the ipsilesional M1 and the contralesional premotor area (29), and that the latter is not required for recovery from a minor CVA (29). Our patient had a severe axial-proximal motor deficit and therefore required CRST recruitment. Most of the CRST fibers originate from the premotor area (13). We speculate that recruitment of the premotor area depends on whether there is adequate axial-proximal movement, and thus the London group's proposal would be the neurophysiological correlate of the ontogenic post-CVA recovery model (29).

This study has several limitations. First, since only one case is reported, spontaneous recovery cannot be ruled out, nor can the placebo effect be ruled out in the absence of

blinding. In addition, we did not conduct neurophysiological or tractography studies, nor did we systematically obtain the iMEP. Future studies are needed with a detailed evaluation in a larger sample size to confirm these findings.

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