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rTMS can improve post-stroke apraxia of speech. A case study

To the editor

Apraxia of Speech (AoS) is a rare disorder of motor speech planning distinct from both aphasia and dysarthria. It is characterized by inconsistent articulatory errors imposing a trial-and-error approximation to a target word, slow speech rate, segmentation of syllables, sound distortions and substitutions [1]. At difference with aphasia, in fact, in AoS errors are non-linguistic in nature (i.e. they are neither lexical nor morphological) and other language-related abilities (i.e. reading and auditory comprehension and writing) are usually preserved. Compared with dysarthria, AoS is not caused by muscle weakness or incoordination, and the errors are inconsistent and unpredictable [2].

AoS can characterize the onset of neurodegenerative diseases or, it can follow brain strokes that often result in aphasia. A favourable effect on AoS patients suffering from both aphasia and AoS has been shown for transcranial direct current stimulation [3]. So far, however, no studies investigated the effects of repetitive transcranial magnetic stimulation (rTMS), which may be effective in aphasia, in patients with a pure form of AoS.

Case report

In this study, a 53 years old man, right handed, with pure AoS was prospectively studied seven months after stroke. Stroke was due to the left internal carotid artery occlusion ultimately leading to focal cerebral ischemia in the left fronto-parietal cortex. After initial right hemiplegia, intravenous thrombolytic therapy led to a fast neurologic recovery, except for the persistence of language deficits. These were only partially responsive to standard speech treatment administered twice a week for about five months. Then, isolated AoS was diagnosed. For example, when the patient was asked to repeat the word *"calcolatrice:/kalkola'tritse/"* (calculator, in Italian) three times, the patient produced the following:/*Kak:ol'-tritse/-/kaltola'tritse/-/Kartola'titse/*(see video S1, supplemental online contents).

Supplementary video related to this article can be found at https://doi.org/10.1016/j.brs.2018.12.006.

Seven months after stroke a magnetic resonance imaging examination (MRI) of the brain showed that the ischemic damage principally involved the pre-central gyrus, the inferior frontal gyrus (IFG, Broca's area) and the rolandic operculum, in accordance with previous reports about AoS [4] (Fig. 1).

The core of the diagnostic process was the detection of 1) effortful trial-and-error groping with repeated self-corrections; 2) dysprosody; 3) articulatory inconsistencies on repeated productions of the same utterance and/or 4) obvious difficulty initiating utterances [2].

As a primary endpoint index, three subtests of the Apraxia Battery for Adults-2 (ABA-2, heretofore ABA-2_{sf} - short from) [5] were administered: *increasing word length part A*; *increasing word length part B*; and *repeated trials subtest.* Each subtest involved 30 sequences of three words of increasing length. Score 1 was assigned to correct and intelligible repetitions, score 0 otherwise (total cumulative possible score = 90). In the validated Italian translation of the test [6], available on request, care was taken in reproducing the number of syllables and the co-articulatory complexities, regardless of semantic differences. For instance, "*thick-thicken-thickening*" was substituted by "*re-regio-regale*". A battery of 10 more standardized tests in their Italian versions was also administered, namely: Robertson's diadochokinesis; neuropsychological examination for aphasia (ENPA): repetitions of words/nonwords/sentences; denomination of nouns and verbs; semantic and phonemic fluency; Aachener Aphasia Test "scene" (AATs); Token test. The tests were administered 1 month before rTMS treatment (T-1), immediately before treatment (T0), immediately following the last session (T1), one month (T2) and three months (T3) after rTMS. The Token and the AATs tests were normal at T-1 and they were no longer administered.

Inferential statistics on this single case was attempted a) by applying a repeated ANOVA with Tukey's post-hoc tests to the ABA-2_{sf}, by considering its three subtests as repeated manifestations of the same latent trait across time points, and b) by considering the Minimal Real Difference [7], available from the literature or from internal databases as a threshold for significance of individual changes in the other tests. The p-level was set at 0.05. No multiplicity corrections were applied. All numeric data are available on request.

After the T0 assessment, excitatory 10Hz rTMS was delivered to the Broca's area in 10 subsequent working days. An oil-cooled angulated figure-of-eight coil was adopted (Neuro-MS/D Therapeutic Variant biphasic magnetic stimulator, external diameter of each coil 100mm, model AFEC-02-100-C, Neurosoft Ltd., Ivanovo, Russia). The Broca's area was identified through optoelectronic neuronavigation (Polaris Vicra -NDI International, Waterloo, Ontario, Canada, and Softaxic software, E.M.S.,Bologna-Italy) on brain images coming from MRI (3.0T Siemens Avanto, Siemens AG, Erlangen, Germany). Twenty trains of 10Hz rTMS at 90% of rMT were delivered for 5s with 5s of inter-train interval. Overall, a total of 1000 pulses were applied in a session lasting 3′13" [8]. The guidelines for safe use of rTMS [9] were followed. The study addressed the principles of the Helsinki declaration for medical research involving human participants (World Medical Association, 2013). Oral informed consent was obtained, formally documented, and witnessed.

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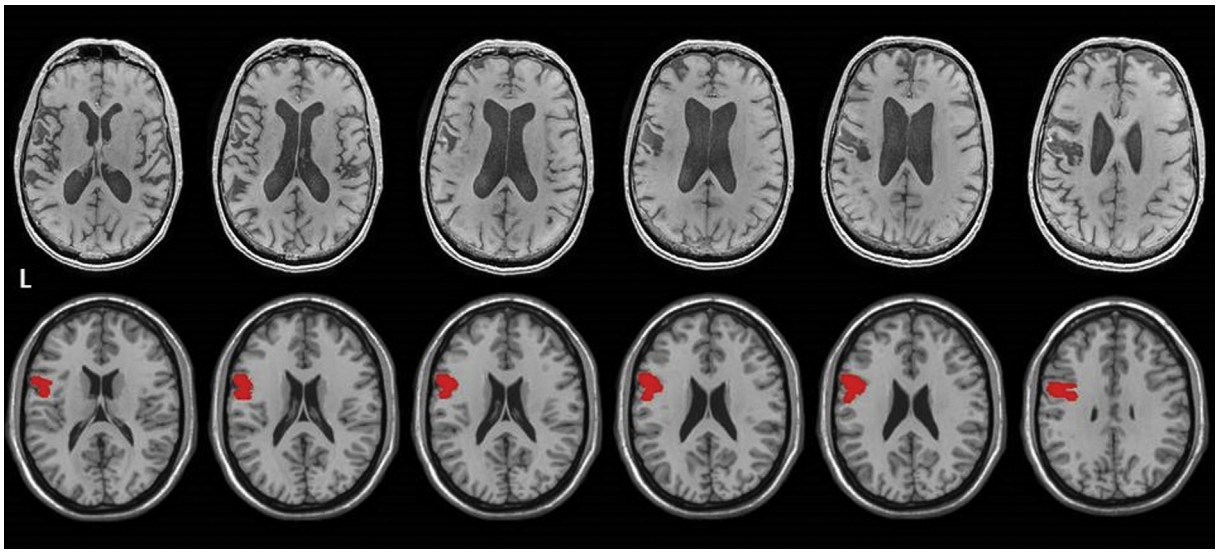

Fig. 1. The upper row shows patient's T1-weighted magnetic resonance imaging (1 mm-thick slices acquired on a 3T MRI). Images have been mirrored. The second line shows the reconstruction of the brain MRI scans on MRIcro version 1.4 (MRIcro program). Slices at the approximate levels of the original MRI scans are represented. The ischemic areas are marked in red. Cortical lesions can be seen on the pre-central gyrus (about 47% of the volume of the entire ischemic lesion), the inferior frontal gyrus (Broca's area, about 20%), the rolandic operculum (about 10%), the post-central gyrus (about 7%). Of note, less than 1% of the damage affects the temporal lobe (superior temporal gyrus - Wernicke's area). The ipsilateral subcortical nuclei and the insula are spared. Subcortical lesions can be seen within the cerebral white matter (about 15% of the total lesion volume). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

No adverse events were recorded. All scores were stable in the month before treatment. The ABA-2_{sf} scores, cumulated across its three items, changed after rTMS treatment from 32/90 (T0) to 64/90 (T1,T2) and 56/90 (T3). Changes were significant between T0 and T1 for all of the three subtests. The ENPA nonwords repetition increased from 0 to 4 from T0 to T1 (a significant change) and declined to 2 at T2 and T3. No other significant changes were detected.

Discussion

Results suggest that rTMS can be effective on AoS symptoms, affecting neural circuits that are at least partially distinct from other language circuits. The improvement observed for nonwords repetition suggests that results also reflect a better phonological analysis. This is consistent with recent evidences that the Broca's area belongs to a cortical network that supports phonological working memory [10]. We remark that a relevant practice effect cannot be ruled out completely in this work; yet, such effect appears to be unlikely for two main reasons. First, the practice effect would have biased also some of the 8 otherwise not responsive tests. Second, the MRD threshold for individual change adopted here is in itself partly “detrended” and thus robust with respect to a practice effect. All considered, it seems reasonable to hypothesize that rTMS may be a promising approach to rehabilitation in AoS.

Declarations of interest

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