Journal of Neurology (2019) 266:631–635
https://doi.org/10.1007/s00415-018-09178-9

ORIGINAL COMMUNICATION

Long-lasting diagonistic dyspraxia suppressed by rTMS applied to the right motor cortex

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Received: 11 August 2018 / Revised: 23 December 2018 / Accepted: 27 December 2018 / Published online: 10 January 2019

Abstract

We describe the case of a 58-year-old patient with complete callosal agenesis, who developed after a stroke a long lasting and distressing diagonistic dyspraxia. We found two original treatments to relieve the patient from his left limb conflicting movements. Reinforcing left arm sensory input minimized dyspraxic movements but was difficult to apply daily and was found unsatisfactory by the patient. As left anarchic, unwished movements of diagonistic dyspraxia have been attributed to the lack of inhibition exerted by supplementary motor area on right motor cortex, we applied sham-controlled rTMS to the right motor cortex. This procedure provided a dramatic suppression of left-hand involuntary movements. To our knowledge, this is the first description of the successful treatment of diagonistic dyspraxia.

Keywords Diagnostic dyspraxia · Movement disorders · Corpus callosum · rTMS

Introduction

The concept of diagonistic dyspraxia (etymologically: a movement disorder due to the presence of two agonists) was introduced by Akelaitis and colleagues [1, 2] to describe a peculiar motor behaviour in two patients who received corpus callosotomy for intractable epilepsy. It represents a syndrome in which one of the patient's hands, usually the left hand in a right-handed patient, behaves in an antagonistic or, at least, uncooperative way. It is a synonym of intermanual conflict, a form of alien hand syndrome, and it is an active phenomenon, quite different from involuntary movement disorders such as grasping phenomena [3, 4].

Diagonistic dyspraxia is a rare movement disorder which has, until now, always been described in patients suffering from acute lesions of the corpus callosum, either after surgical callosotomy, or after a callosal infarction of hemorrhage. Since damage to the ventral part of the posterior end of the body of the corpus callosum has been proved to be crucial for the development of diagonistic dyspraxia, it is currently inferred that this syndrome reflects a disconnection of the right superior parietal lobule from the left, which is dominant for volitional control of movement in most right-handed subjects [4].

One of the characteristics of this fascinating and incapacitating phenomena is that it progressively disappears, a few weeks or months after corpus callosum injury [4]. This favorable clinical course has been interpreted as the consequence of a rewiring between the two hemispheres, either through adjacent callosal areas, or the anterior and posterior white commissures. In contrast, studies conducted in patients with callosal agenesis emphasized the absence of major disconnection symptoms, including diagnostic dyspraxia [5]. This paradox may be explained by the presence of

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00415-018-09178-9) contains supplementary material, which is available to authorized users.

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heterotopic interhemispheric fibers, which maintain a functional connectivity between the two hemispheres [6].

We describe the case of a patient with complete callosal agenesis, who developed after a stroke a long lasting and distressing diagonistic dyspraxia. We found two original treatments to relieve the patient from his left limb conflicting movements.

Case report

A 58-year-old right-handed man, GG, without any remarkable past medical history, developed suddenly a left hemiplegia with mild aphasia. Brain MRI revealed a right temporo-parietal hematoma attributed to the rupture of a cerebral arteriovenous fistula. Incidentally, it showed a complete callosal agenesis, which had been completely asymptomatic until this moment (Fig. 1). In the following months, left hemiplegia and aphasia rapidly resolved but, in the revalidation unit, the patient complained from a peculiar motor behaviour, dissociated from conscious volition, in his left hand. He noticed that his left hand frequently interfered with his right hand in an antagonistic way. For example, his left hand threw away a sock his right hand wanted to slip on. These conflicting, unvolitional movements of the left hand or leg occurred frequently in GG's daily life and dramatically limited his autonomy. For instance, once at home, he noticed that, when passing near the wash machine in his kitchen, he could not help from switching the machine on with his left hand, even if it was empty. As he tried to resist to the left hand will, the patient was stuck in front of the machine for more than one hour, until the left hand won and put the machine on. In a car, he was no longer able to drive and, as a passenger, had to bind his left hand to avoid any dangerous, conflicting movement.

The patient was admitted in our Neurology Department 4 years after his stroke, to assess his persistent, distressing diagonistic dyspraxia and to find a relief. Neurological examination was unchanged. On WAIS-III, IQ was 93 (verbal 96, performance 90). Language was fluent without word finding difficulty, but sometimes hesitant when GG had to speak about his left limbs, as if there was an interhemispheric conflict. Reading aloud and repetition were well performed. Auditory and reading comprehension were excellent. Writing with the left hand was clumsy but without aphasic error. There was a left-hand ideomotor apraxia, characterized by incomplete or perseverative movements on responding to a verbal command. Performance improved substantially with the use of an actual object. While elementary sensory perception was preserved on the left side, there was a 'pure astereognosia' of the left hand [7]. A left hemianopia was observed on visual field testing using a Goldmann perimeter. It was confirmed on a task of visual recognition with tachistoscopic presentation on both hemifields. Asked to give his responses in a time free, forced choice condition, the patient was unable to perceive any visual information presented on the left side.

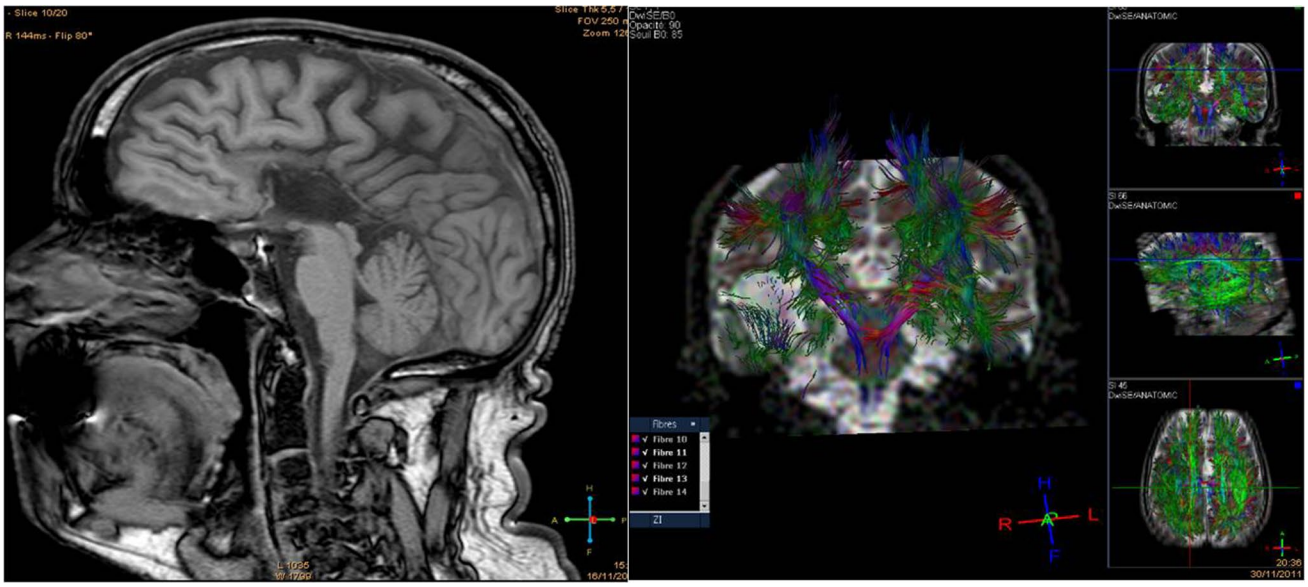

Fig. 1 Left: Brain MRI, sagittal slice. T1-weighted sequence. Complete corpus callosum agenesis, with absence of anterior and posterior white commissures. Right: Brain MRI, axial slice. DTI sequences. Red lines correspond to the interhemispheric fibers, green lines to the antero-posterior fibers, blue lines to the vertical fibers. Almost complete absence of connecting fibers between the two hemispheres

The left hand was animated by two sorts of abnormal movements: rare levitations, originating from the proximal part of the left arm, GG was almost able to suppress on request; antagonistic movements of the left hand, interfering with volitional movements of the right hand (see video, clip # 1). We tried two original therapeutical procedures.

Materials and methods

Controlling diagonistic dyspraxia by reinforcing the patient's left arm sensory input

We observed that GG was generally unaware of his left arm levitation, as if he was unable to integrate sensory information coming from this limb. Moreover antagonistic movements of the left hand seemed to be rather elicited by the manipulation of small, light objects, i.e. a wallet, the button of a machine or a cloth hanged on a hook. We supposed that reinforcing sensory input coming from the left arm might enhance the patient's awareness of his left arm and help him to control its movements.

In a baseline period, we asked GG to fill in two quality of life scales: (1) the EQ-5D1, which describes health-related quality of life states, consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression). For each dimension, the responses record three levels of severity (from 1 to 3: no problems/some or moderate problems/extreme problems). (2) the EQ-5D2, a standard vertical 20-cm visual analogue scale (similar to a thermometer) for recording an individual's rating for his current health-related quality of life state (EuroQol Group®). GG also recorded all the manual conflicts occurring during 1 week on a 3 point-severity scale (mild/moderate/severe). As his diagonistic movements were frequent, the patient selected those he considered as "severe" on the 3 point-scale. Then we asked the patient to bear at his left wrist a 1 kg lead bracelet for 3 weeks. The same scales and the 'movements agenda' were used to measure the patient's improvement after a 3-week experimental treatment.

Controlling diagonistic dyspraxia by inhibiting the contralateral motor cortex

We postulated that left antagonistic movements involved a selective activation of right motor cortex (M1), presumably released from conscious control by intentional planning systems [8]. Therefore, we proposed GG to assess the efficacy of inhibitory repetitive transcranial magnetic stimulation (rTMS) applied to right M1. Written informed consent was obtained from the patient before the study, which was approved by the local Ethics Committee. We used stimulation frequency of 1 Hz because low frequency rTMS (≤ 1 Hz) can decrease the excitability of the targeted cortical regions [9]. In our design rTMS (1 Hz, 70% of maximum stimulator output intensity, 2 sessions of 20 min in the morning, each 14 days, during 12 weeks) was performed using a commercially available figure-of-eight coil (outside diameter of each wing, 7 cm) and a MagVenture MagPro stimulator (Tonica Elektronik A/S, Denmark). Localization of M1 was performed with a neuronavigation system. The same assessment scales and 'abnormal movements agenda' were used at baseline and before each new rTMS session, during the 12 weeks experimental period. One blind sham session was randomly included in this experimental design. In this sham session, the coil was positioned tangentially to the scalp, with the handle pointing superiorly.

Results

Reinforcing sensory input

For the baseline period, GG's scores in the EQ-5D scale are given in Table 1. He noticed five severely disturbing movements of the left hand. Analysis of the experimental period was shortened to the first week: during this period, GG had persistent conflicting movements but he no longer recorded severe antagonistic movements of the left hand. However, he did not want to keep the lead bracelet on his wrist, because he was too disturbed in his fine movements, particularly for

Table 1 Influence of the two treatment procedures on GG's scoring in quality of life scales (EQ-5D1 and EQ-5D2)

Quality-of-life scales	Before left limb sensory stimulation (1 week)	After left limb sensory stimulation (1 week)	Before rTMS	After real rTMS (mean of 5 assessments)	After sham-session
EQ-5D1 "mobility"	2	1	2	1	2
EQ-D1 "self-care"	2	2	2	1	2
EQ-5D1 "usual activities"	2	2	2	1	1
EQ-5D1 "pain/discomfort"	2	2	2	1	2
EQ-5D1 "anxiety/depression"	1	1	1	1	2
EQ-5D2 VAS	28/100	40/100	29/100	90/100	70/100

eating or washing up. As a consequence, the estimated benefit of this treatment was relatively low on quality of life scales (Table 1) and the patient stopped his experimental treatment after 1 week.

Inhibiting the contralateral motor cortex

After the first day of rTMS, GG described a dramatic improvement of his left limb control. While he experienced four 'severe' movements in the week preceding rTMS, he no longer had conflicting movements, even of mild intensity, thereafter. This effect maintained over the different active rTMS sessions in the three following months (Table 1). He acknowledged he was again able to put himself rapidly his clothes, use correctly his cutlery, pay at the baker's, etc. for the first time since he left the revalidation center. After the sham stimulation, the patient noticed a worsening and the recurrence of involuntary left movements (Table 1).In a 12-month follow-up of treatment without blinded procedure, the positive effect maintained (see video, clip # 2). However, we had the opportunity to observe that diagonistic dyspraxia reappeared twice, when the rTMS sessions were twice postponed 1 week later, for technical reasons.

Discussion

Our patient had a complete callosal agenesis, a condition which does not produce the classical signs of disconnection between both hemispheres or, at the most, subtle deficits on tasks involving transfer of motor and visuo-spatial skills [5, 10]. This paradox is explained either by the presence of alternate interhemispheric pathways such as the anterior commissure or by the development of 'Probst bundle', an aberrant intrahemispheric white matter tract which increases the use of ipsilateral pathways [6, 10]. MRI exploration showed the bilateral presence of Probst bundles in GG's brain (Fig. 2). We may hypothesize that the parietal damage disrupted compensatory mechanisms permitted by ipsilateral alternate pathways. Therefore, signs of callosal disconnection occurred some weeks after the stroke, as it has been previously observed in patients presenting a corpus callosum damage [1, 2, 4, 11].

Movement intention and awareness in response to environmental stimuli is driven by a parietal–premotor network [12]. Alien hand movements have been shown to emerge following lesions of the posterior parietal cortex, which brings motor intentions to consciousness [8]. GG interpreted his unwished movements from the left limb as driven by visual stimuli from his environment. As no visual information was processed in the right hemisphere, we may hypothesize that, in a given context, some grasping of handling movements were elicited by a mirror neuron system from both

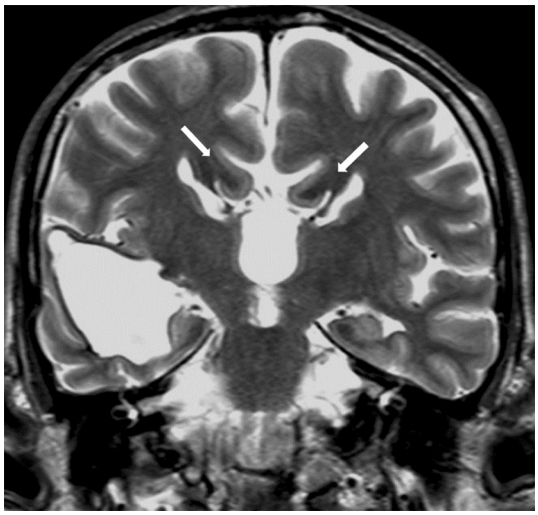

Fig. 2 Brain MRI. Coronal slice. T2-weighted sequence. Presence of bilateral Probst bundle(arrows). Right temporal ischemic stroke

parietal lobes [13]. As right parietal sensory integration was disturbed by the stroke sequels, we tried to enhance somatosensory input from the left limb with a lead-bracelet. It produced a mild but unsatisfactory control of left limb antagonistic movements.

Anarchic, unwished or apparently purposeful movements have been attributed to damage to the medial frontal regions (supplementary motor area, SMA), or disconnection of this area, which is able to exert an inhibitory output on M1 [14]. Patients lacking the entire corpus callosum have been proved to display abnormal intrahemispheric excitability of M1 [15]. Therefore, we inferred that GG's right SMA was unable to suppress unwished motor commands. Considering the easiness to target motor cortex by rTMS, we proposed to inhibit the efferent part of the right parietal–premotor movement network. The results were strikingly positive since diagonistic dyspraxia disappeared and the patient's life regained to normal. The visual assessment scale of EQ-5D1 of the sham treatment scored at an intermediate value between baseline and the optimum obtained by real rTMS. It might be interpreted as the consequence of an after effect of the real stimulation, since a mild improvement of involuntary movements remain present when rTMS were postponed.

Sham-controlled rTMS proved the benefit of the procedure. A source of concern might be the difficulty to perfectly apply sham sessions in the context of rTMS procedure. A systematic review of blinding success in trials of rTMS applied to the dorsolateral prefrontal cortex found that people in real rTMS groups were significantly more likely to think they had received real rTMS compared with those in sham rTMS groups [16, 17]. In our case, we cannot rule out that GG perceived a slight difference between active and

sham sessions. The fact that he observed a recurrence of its symptoms when rTMS were postponed might be interpreted as a simple *nocebo* effect. However, it is striking to observe that neurologists and medical physiotherapists failed to find any relief for GG diagnostic dyspraxia in the past 4 years, until rTMS was applied. Moreover, by contrast with *placebo* effect, the dramatic benefit of rTMS remained constant over the 12-month follow-up, during which diagonistic dyspraxia regularly reappeared when the 2 weeks interval between rTMS procedures was not respected.

Compliance with ethical standards

Conflicts of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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