INTRODUCTION

Neurologic symptomatology that develops unconsciously and is incompatible with known pathophysiologic mechanisms or anatomic pathways belong to Conversion Disorder (CD). CD diagnosis is based on the clinical history and the exclusion of physical disorders causing significant distress or social and occupational impairment. In a subgroup of CD, called functional weakness (FW), symptoms affecting limbs may be persistent, thus causing a permanent or transient loss of limb function. Physiotherapy, pharmacotherapy, hypnotherapy and repetitive transcranial magnetic stimulation (rTMS) have been proposed as treatment strategies for FW-CD. Herein, we report a 30 year-old male, presenting with lower limb functional paraparesis, having obtained positive, objectively, and stable effects from a prolonged r-TMS protocol associated to a multidisciplinary approach, including psychological and sexuological counseling, and monitored by gait analysis. We postulate that our rTMS protocol, combined with a multidisciplinary approach may be the proper treatment strategy to improve FW-CD.

CASE

The patient is a 30 year-old man, second child from non-consanguineous parents, born preterm (at 32 weeks) by Caesarean section. He was in incubator for two weeks. Family history was unremarkable. He presented normal psychomotor milestones. From 10 to 18 years-old, he presented with a growth hormone deficit, treated with a replacement therapy. At our observation (October 2016), he complained of low back pain and gait difficulties, worsened by physical exercise, for about...
10 years. At neurological examination, the patient presented with paraparesis so that gait was possible only with two canes; muscle strength assessment was difficult to evaluate since he complained of intense low back pain. Nonetheless, no objective signs of the central and peripheral nervous system impairment were detected. Psychological evaluation showed depressed mood, marked anxiety, severe phobic cues with hypochondria, and poor emotional control, according to the Minnesota Multiphasic Personality Inventory-2 score (MMPI-2) and Hamilton Rating Scale for Depression (HRS-D) (score: 18). The sexual counselling did not point out any sexual dysfunction. The patient was in a stable homosexual relationship, but his sexual orientation disappointed his relatives. Indeed, the first ever time he presented the ambulation deficit was somehow related to his coming-out, and he had the main symptom exacerbation following family's quarrels over his sexuality. Because of these symptoms, he underwent several investigations, including brain and spinal cord MRI with contrast medium, hips and pelvis X-ray, a complete neurophysiological evaluation (multi-modal evoked potentials, electromyography), blood tests (including inflammatory and autoimmune markers and muscle enzymes dosages), all within the normal range.

Therefore, the patient was diagnosed with FW-CD and thus recruited for an rTMS treatment, which consisted of 100 stimuli at 100% maximum stimulator output, randomly delivered to the right and left primary motor cortex of the arm-hand and leg motor areas, at 1 Hz, three times a week for three months. This protocol was adapted to the patient, employing the stimulation paradigms of previous studies (Table 1). The patient gave his written informed consent.

Psychological evaluation and gait-analysis were performed before (T0) and after the end (T1) of the rTMS protocol to evaluate rTMS after-effects. The gait analysis was performed by using the OptoGait system (Version 1.6.4.0, Microgate, Bolzano, Italy).

T0, we found abnormal values of each phase of gait and the temporal parameters of the gait, i.e., gait cycle (5,646 ± 2.553 sec), cadence (19 ± 13.8 step/min), and step time with a preservation of the step and stride length. The visual analogue scale (VAS) for low back pain yielded a score 7/10.

At T1, the subject reported an improvement in mood and

### Table 1. Comparison of the rTMS studies on FW-CD

| Study | FW patients | Clinical presentation | rTMS protocol | Outcome                  |
|-------|-------------|-----------------------|---------------|--------------------------|
| 14    | 3 (1 male)  | about 38 years of age | M1 15 Hz      | Marked improvement       |
|       |             |                       | 5 times/week  |                           |
|       |             |                       | for 2 weeks   |                           |
|       |             |                       | 110% RMT then |                           |
|       |             |                       | 90% RMT up to |                           |
|       |             |                       | 12 weeks      |                           |
| 15    | 70 (8–79)   | 55 Acute (since 4 days)| M1 iTBS       | Immediately or within hours in 89% |
|       | years of age| 15 chronic (since 240 days)| 1–2 session in one day|                           |
|       |             |                       | 100% MSO      |                           |
| 16    | 1 male, 24  | Hemiparesis that      | Vertex stimulation | patient able to walk again independently, immediately after |
|       | years of age| compromised walking   | Patterned rTMS*|                           |
| 17    | 1 male, 33  | Quadriplegia since 6 months | Right and left M1-HAND and M1-LEG | Initially progressive amelioration; then, further deterioration leading a new rTMS with amelioration |
|       | years of age|                       | 1 Hz          |                           |
|       |             |                       | 5 times/week  |                           |
|       |             |                       | for 8 weeks and, after, twice a week |                           |
| 18    | 11 (4 males), 34–64 years of age | Flaccid hand paralysis since 4 weeks to 25 years | Contralateral M1 stimulation | Improve in muscle strength |
|       |             |                       | 15 Hz         |                           |
|       |             |                       | 5 times/week  |                           |
|       |             |                       | for 2 weeks   |                           |
| Our  | 1 male, 30  | Flaccid paraparesis   | Right and left M1-HAND and M1-LEG | Marked improvement up to resolution |
| case  | years of age|                       | 1 Hz          |                           |
|       |             |                       | 3 times/week  |                           |
|       |             |                       | for 3 months  |                           |
|       |             |                       | 100% MSO      |                           |

*single rTMS session with 12 single pulses at initially 30% maximal stimulator output intensity and increasing I in 10% steps up to 80% of maximal stimulator output. MSO: maximal stimulator output, TBS: theta-burst stimulation, RMT: resting motor threshold.
anxiety (HRS-D: 7), hysteria and hypochondria items of the MMPI-2, and lower limb “weakness” with pain relief (VAS 3/10), being thus able to walk independently. We also found a significant improvement in the spatial, and temporal gait parameters (gait cycle: 1.707±1.2 sec; cadence 68.4±18.4 step/min).

**DISCUSSION**

FW-CD has a still not known underlying etiological mechanism. Although the former criterion contained in DSM-IV considered psychological factors as essential to perform FW-CD diagnosis,9 actually the DSM-V removed this aspect, considering that FW-CD are caused by a neurobiological component, even though stressful events may be possible causal concomitant factors influencing patients’ vulnerability.10

Treating FW-CD disorders using TMS was firstly postulated by Jellinek et al. in the nineties.11 Few years later, other authors showed that rTMS induces long-lasting clinical improvement by stimulating cortical areas and inducing changes in cortical excitability and the interconnected brain areas, even in FW-CD patients.12 The supporting available literature on the use of rTMS in FW-CD is very sparse, so any assumption of a beneficial effect needs to be seen with caution. Recently, a systematic review reported only 5 articles describing FW-CD treated by rTMS (Table 1),13 using different approaches and protocols.14-18 All of these FW-CD cases gained a short-term symptom improvement. Trying to understand the rTMS efficacy in FW-CD has been the objective of an increasing body of literature data, suggesting that focal functional abnormalities in central networks controlling motor cortex activity may play a role in the etiology of FW-CD,19 thus gaining positive effect by rTMS. The mechanisms of action by which rTMS seems to be really effective in these patients have been explained by the combined physiological, neurophysiological and neuro-modulatory induced effects.13 Considering the physiological aspects of the rTMS, the crucial effect of supra-threshold rTMS is related to the individual’s perception of the movements of their paralyzed limb induced by an external trigger, making them aware of the possibility of regaining the function. Furthermore, TMS exerts an additional placebo effect, especially if the information and the style used to inform the patients about the beneficial effects of this treatment strategy and purpose have been properly described.13

The neurophysiological mechanism of action of the rTMS has been supported by an increasing body of literature data, suggesting that focal functional abnormalities in central networks may be related to an unbalance between motor intention and motor execution or an overactive self-monitoring with enhanced limbic neural activity, which interferes with movement planning, beginning within the frontal regions and thereby disrupting motor execution.19 Moreover, functional-imaging methods demonstrated enhanced neural activity within the anterior cingulate area or orbito-frontal cortex and reduced neural activity within prefrontal motor areas during movement execution of the paralyzed limb in FW-CD patients.20 These abnormal activation patterns can be the cause of the unconscious inhibition of movement planning and execution.

Finally, it has also been reported that, considering the neuro-modulatory induced rTMS effects, a short-lasting rTMS protocols might not cause a durable change in cortical activity, whereas long-lasting changes in cortical neuro-plasticity might only be induced performing longer protocols (e.g., for one or more weeks), thus leading to long-term potentiation–using high-frequency (>1 Hz) or long-term depression-like changes using low-frequency (<1 Hz).14

Notably, in this case, we objectively documented the improvement using objective outcome measures (i.e. gait analysis) that lacks in the previous reported studies.

In our case, having obtained positive, objectively, and stable effects from r-TMS, we can postulate that our rTMS protocol, combined with a multidisciplinary approach (including a psychological and sexological support) may be beneficial for symptoms improvement.

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