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Transcranial magnetic stimulation and bladder function: A systematic review

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HIGHLIGHT

- Motor evoked potentials can be recorded from pelvic floor muscles but poor reproducibility has been observed.
- Some studies have used therapeutic repetitive TMS in patients with lower urinary tract dysfunctions.
- The promising results should be replicated in controlled studies with larger sample size.

ABSTRACT

Objective: We aimed at assessing the usefulness of motor evoked potentials (MEPs) for exploring the integrity of striated sphincters and pelvic floor motor innervation in normal subjects and of repetitive transcranial magnetic stimulation TMS (rTMS) in patients with neurogenic bladder dysfunction.
Methods: A systematic literature search was conducted using PubMed and Embase.
Results: We identified, reviewed and discussed 11 articles matching the inclusion criteria.
Conclusions: The assessment of MEPs could represent a useful tool in the investigation of patients with urologic disorders. High frequency rTMS can improve detrusor contraction and/or urethral sphincter relaxation in patients with multiple sclerosis and bladder dysfunction. Low frequency (LF) rTMS seems to be an effective treatment of neurogenic lower urinary tract dysfunctions in subjects with Parkinson's disease and possibly other neurodegenerative disorders. Furthermore, rTMS might have the potential to restore bladder and bowel sphincter function after incomplete spinal cord injury. LF rTMS could also relieve some symptoms of bladder pain syndrome and chronic pelvic pain.
Significance: The clinical applicability of MEPs appears to be questionable, since a poor reproducibility was detected for all pelvic floor muscles. The use of rTMS in this field is emerging and the results of a few preliminary studies should be replicated in controlled, randomized studies with larger sample sizes.

1. Introduction

The transcutaneous electrical stimulation applied over the primary motor cortex (M1) has for the first time enabled the functional assessment of the corticospinal pathways serving the

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striated sphincters and the pelvic floor muscles (Snooks and Swash, 1984). However, its clinical use is hampered by the poor tolerance to the scalp sensations caused by the transcranially applied electrical stimulus (Thiry and Deltenre, 1989). The transcranial magnetic stimulation (TMS) is a noninvasive approach that has become an established routine method in the neurophysiological evaluation of motor corticospinal pathways (Rossini et al., 2015). TMS is mostly used to study the central and peripheral motor pathways to the skeletal muscles, but it can also be employed to examine the integrity of the motor efferents of striated sphincters. The use of motor evoked potentials (MEPs) elicited by TMS to explore the integrity of pelvic floor motor innervation has rarely been reported in the literature.

On the other hand, repetitive TMS (rTMS) can modulate cortical excitability and induce long-lasting neuroplastic changes also when it is applied over the cortical areas corresponding to the pelvic region. rTMS can be delivered as continuous trains of low frequency (LF, 1 Hz) or bursts of higher frequency (HF, $\geq$5 Hz) rTMS. Overall, LF rTMS is thought to decrease, while HF rTMS usually increases cortical excitability in the targeted region (Fitzgerald et al., 2006; Rossi et al., 2009; Lefaucheur et al., 2014).

We aimed at providing here a systematic review of: (1) the studies that employed TMS to examine pelvic floor muscle function and the integrity of pelvic floor motor innervation; (2) the studies using rTMS techniques for the treatment of neurogenic bladder dysfunction.

2. Methods

A literature review was conducted using MEDLINE, accessed by Pubmed (1966 – February 2019) and EMBASE (1980 – February 2019) electronic databases. The following medical subject headings (MeSH) and free terms were searched: "transcranial magnetic stimulation", "repetitive transcranial magnetic stimulation", "motor evoked potentials", "bladder", "striated sphincter/s", "urethral sphincter/s, "pelvic floor", "micturition", "urinary tract dysfunction".

Only original articles written in English were considered eligible for inclusion. Review articles were excluded. For the selected titles full-text articles were retrieved, and reference lists of them were searched for additional publications. The principal investigators of included studied were contacted when necessary to require additional information. Two review authors independently screened the titles and abstracts of the initially identified studies, and then assessed the methodological quality of each study and risk of bias, including blinding. This search strategy yielded 12 results; one of them was excluded after reading the full paper because suitable TMS data were lacking, thus leaving 11 studies which were included this review. A flow-chart (Fig. 1) illustrates the selection/inclusion process.

3. Motor evoked potentials

In 1990 Eardley and colleagues first described a technique for recording the electromyographic (EMG) response from the striated urethral sphincter to TMS and transcutaneous magnetic stimulation of the spinal cord. In the first study eleven control subjects and three patients with neurological disease have been examined (Eardley et al., 1990). The most reliable response to TMS applied over the primary motor cortex (M1) were obtained after voluntary tonic muscle contraction (facilitation); the mean latency of the MEP facilitated responses in the striated sphincter was 26.4 ms (±2.21). The authors thus concluded that the assessment of MEPs latency recorded from the striated urethral sphincter may represent a useful tool in the investigation of subjects with micturition disorders.

Urodynamic and neurophysiological examinations were performed by the same research group in 24 patients suffering from multiple sclerosis (MS) with urinary disturbances (Eardley et al., 1991). Urethral sphincter EMG revealed only slight abnormalities, while central conduction studies showed abnormal sensory conduction in 88% and abnormal motor conduction in 80% of the patients, respectively.

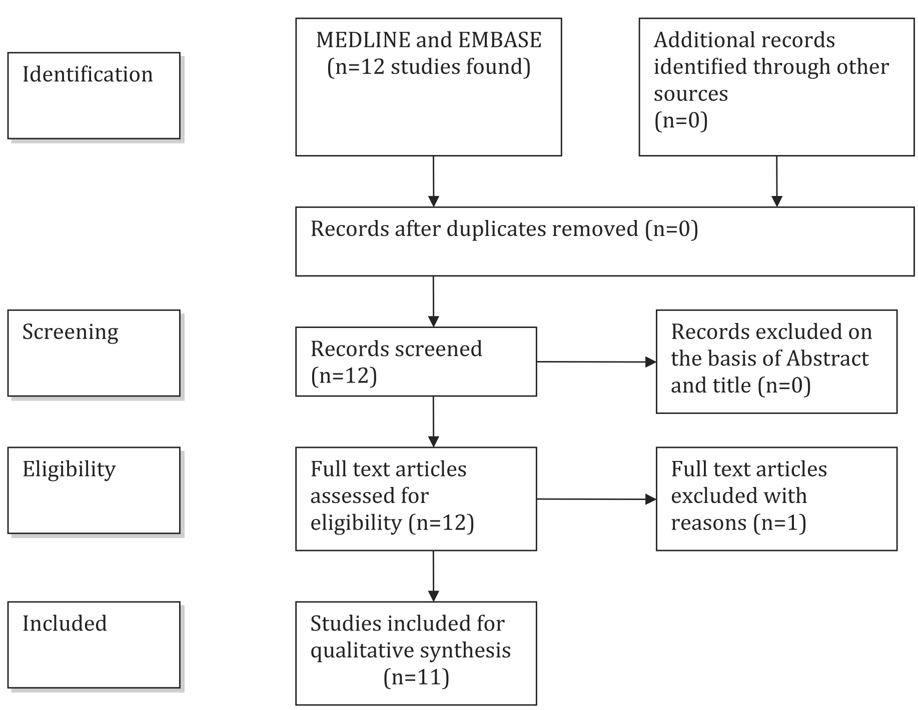

Fig. 1. Flow-chart showing the selection/inclusion process.

Brostrom and colleagues assessed the long-term test-retest reproducibility of pelvic floor MEPs by recording from the external urethral sphincter (EUS) and the puborectal muscles (PR). MEPs were recorded with the pelvic floor relaxed and with moderate to maximum contraction (facilitation). The audio output of the EMG-signal was used during testing to ensure a sustained contraction. The means vs. differences plots showed a large scatter of intra-individual test-retest values, and a poor reproducibility was detected in all examined pelvic floor muscles (Brostrom et al., 2003a) (Fig. 2). In another study the same authors aimed to provide normative data for the motor innervation of the EUS and the PR (Brostrom et al., 2003b). It was only possible to detect reproducible latencies after cortical stimulation with muscle facilitation in some subjects, and technical difficulties were also encountered with spinal stimulations. The authors concluded that the clinical applicability of TMS techniques in the study of pelvic floor muscles innervation appears to be problematic.

In a more recent study, EMG responses from the Urethral Compressive Musculature (UCM) were recorded after cortical TMS and lumbosacral single pulse magnetic stimulation (Schmid et al., 2005). Also the mechanical UCM pressure responses (=EPC) were evaluated simultaneously with EMG recordings by means of a microtip pressure transducer catheter with integrated bipolar surface electrodes. MEP and EPC recordings from the UCM were found to represent useful and well tolerated diagnostic tools in patients with neurogenic incontinence, and may help in differentiating between central and peripheral lesions of the motor efferent neurons innervating the UCM.

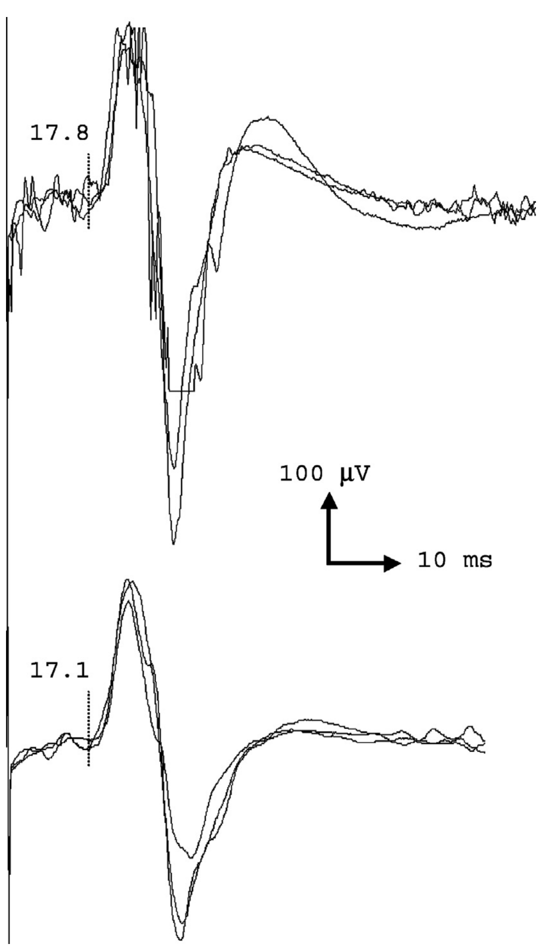

Fig. 2. Motor evoked potentials (MEPs) after cortical transcranial magnetic stimulation (TMS) recorded from the puborectal muscle in a 50-year-old woman. First test (upper traces) and second test (lower traces) of serial measurements with an interval of 39 weeks. Note the great variability in amplitudes, and the importance of replicated amplification settings for serial measurements, even if one could be tempted to decrease the gain in the first test (upper traces). Reproduced with permission from Brostrom et al. (2003a, 2003b).

4. Therapeutic interventions

4.1. Multiple sclerosis

The effects of HF (5-Hz) rTMS over the M1 were assessed in ten patients with multiple sclerosis (MS) complaining of lower urinary tract (LUT) symptoms either in the filling or voiding phase (Centonze et al., 2007). Twenty trains of 50 stimuli at 100% RMT (train duration: 10 s) separated by a 40-s pause were delivered for a total of 1000 pulses (total duration: 16 min) once a day for five consecutive days over two consecutive weeks. The results showed that TMS applied over the motor cortex ameliorated the voiding phase of the micturition cycle, thus indicating that the enhancement of corticospinal tract excitability might be useful to increase detrusor contraction and/or facilitate urethral sphincter relaxation in MS patients with neurogenic bladder dysfunction.

These results in MS patients with detrusor hypocontractility demonstrated that HF rTMS, a techniques aimed at enhancing cortical excitability, was able to improve the voiding phase, without producing effects on the filling phase. It has been hypothesized that the increase of corticospinal tract excitability after excitatory rTMS especially ameliorates detrusor contraction.

4.2. Parkinson's disease

In eight patients with Parkinson's disease (PD) 1 Hz rTMS over M1 was found to be able to improve temporarily LUT dysfunction, enhancing bladder capacity and the first sensation of filling phase (Brusa et al., 2009). Nine hundred stimuli were delivered at 65% of maximal stimulator output once a day for five consecutive days over two consecutive weeks. Urodynamic evaluation was constituted by a medium filling (50 mL/min) water cystometry, followed by pressure/flow study with surface striated pelvic floor EMG. Furthermore, a significant decrease of International Prostate Symptoms Score (a widely used questionnaire for quantitative evaluation of subjective LUT), was detected, which is related to an improvement of the filling phase symptoms. These beneficial effects lasted for up to 2 weeks after the end of the rTMS application. rTMS may thus be an effective, non-invasive alternative therapeutic option for PD patients with urinary disturbances.

It has been postulated that, while in MS patients HF rTMS may strengthen descending projections between the motor cortex and the spinal interneuronal circuits, thus improving the voiding phase, in PD LUT are mainly related to an opposite pattern of involuntary detrusor overactivity, which is evident during the storage phase. LF rTMS decreases activity in the descending projections and is therefore able to reverse LUT disturbances in PD patients, enhancing bladder capacity and the first sensation of bladder filling.

4.3. Spinal cord injury

The relationship between corticospinal activation and the pudendal reflex in the anal sphincter muscle, as a physiological marker for the urethral sphincter, has been evaluated in twenty-six males with incomplete, chronic grade C or D [American Spinal Injuries Association (ASIA) Impairment Scale (AIS)] neurologically graded supra-sacral traumatic spinal cord injury (SCI) (Vasquez et al., 2015) (Fig. 3). TMS applied over the vertex, using a double-cone coil at its the optimal position for eliciting an anal sphincter MEP, was effective in facilitating the pudendo-anal reflex (PAR)

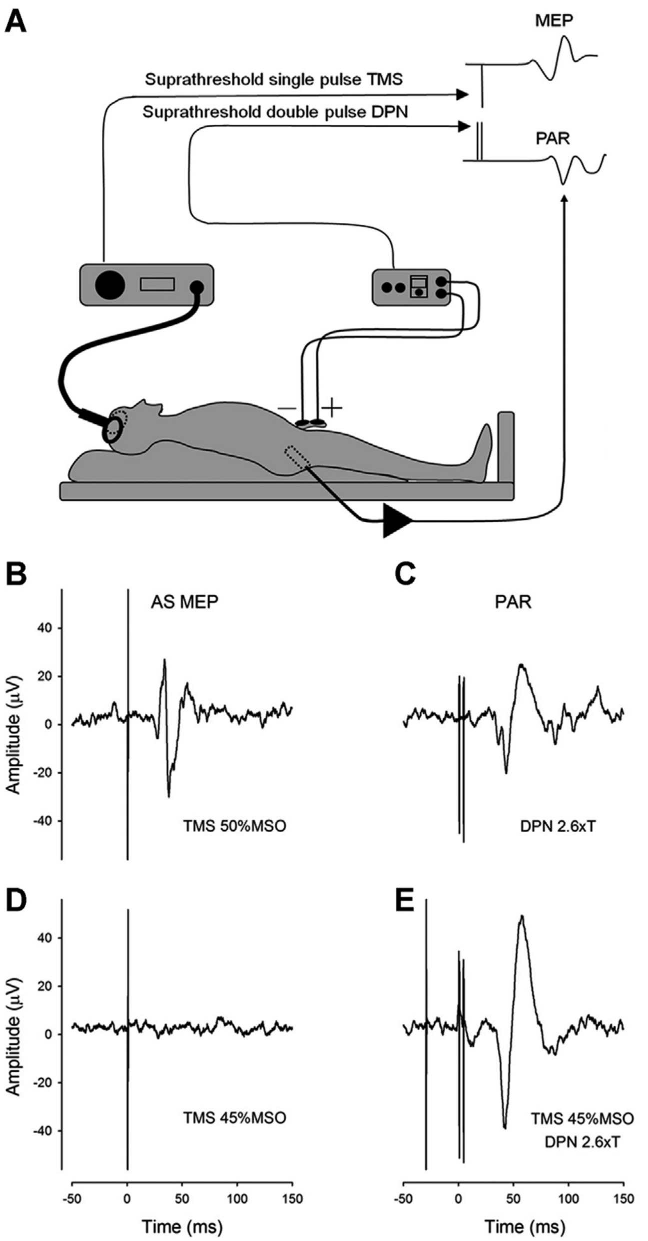

Fig. 3. (A) Experimental set-up showing position of dorsal penile nerve (DPN) stimulating electrodes, anal sphincter electromyographic (EMG) recording electrode and the TMS double- cone coil. Insets: idealized pudendo-anal reflex (PAR) and anal sphincter motor evoked potential (MEP). (B–E) Anal sphincter EMG averaged (n = 10) evoked responses in a control subject. (B) MEP to cortical TMS at 50% maximum stimulator output (MSO). (C) PAR response to stimulation of the DPN at 2.6 times sensory threshold (18 mA). (D) Lack of response to TMS at 45%MSO. (E) TMS at 45% of the MSO preceding DPN at 2.6 times sensory threshold by 30 ms. The DPN stimulus in D now elicits an enhanced PAR that is approximately double the peak-to-peak size of the unconditioned PAR. Reproduced with permission from Vasquez et al. (2015).

when the TMS pulse occurred 20 ms before the dorsal penile nerve stimulus in 12 out of 23 subjects with incomplete SCI. The facilitation of the PAR after cortical stimulation was not related with the scores on the International Consultation on Incontinence Modular Questionnaire, which assesses the amount, frequency and timing of urine leakage. These findings indicate that cortical conditioning of the PAR may help in evaluating the degree of corticospinal control remaining after iSCI.

4.4. Bladder pain syndromes

The usefulness of LF rTMS of the dorsolateral prefrontal cortex (DLPFC) has been explored in a 68-year-old woman with bladder pain syndrome (BPS), a pathologic condition that is characterized by suprapubic pain, urgency and increased micturition frequency (Nizard et al., 2018). Sixteen sessions of high intensity (110% of RMT) LF (1 Hz) rTMS (1,200 pulses per session) applied over the DLPFC, first on the right hemisphere (one daily session for 5 days, followed by one weekly session for 5 weeks), and then on the left hemisphere (one monthly session for 6 months) were able to relieve the most important symptoms of BPS, such as pain, urinary symptoms and interference with physical functioning. Several neural mechanisms may be responsible for the analgesic effects of the DLPFC stimulation. Descending pain modulatory projections from the rostral ventromedial medulla (RVM) could be blocked by inhibitory stimulation applied to certain cortical regions (readily accessible to rTMS) connected to the RVM, such as the DLPFC (Burgess et al., 2002; Staud, 2013). On the other hand, the DLPFC has been demonstrated to be involved in cognitive and attention-related regulation of pain as well as in expectation-related placebo analgesia (Mayberg et al., 2002; Benedetti et al., 2005; Geuter et al., 2017). In a sham controlled double-blind study, rTMS (30 consecutive trains of 50 stimuli delivered at 20 Hz at 110% of the RMT separated by intertrain intervals lasting 30 s) were delivered for five consecutive days in 20-min sessions with an H-coil over the M1 area corresponding to the pelvic region in fifteen subjects with Bladder Pain Syndrome/Interstitial Cystitis (BPS/IC) (Cervigni et al., 2018). Active rTMS treatment was found to improve chronic pelvic pain (as assessed by means of the Visual analogue scale, Functional Neuropathic Pelvic Pain, Neuropathic Pain Symptom Inventory, McGill questionnaire, and the Central Sensitization Inventory), and associated urinary disorders (as assessed by the Overactive Bladder Questionnaire score, bladder emptying, and daily urinary frequency) (Fig. 4). The authors also assessed the safety and tolerability of the rTMS associated with standard drug therapies in these patients with neuropathic pain that does not respond to pharmacological treatment alone. No serious adverse events were reported during the study.

In a recent study, the modulation of the pelvic floor muscles after rTMS applied to the supplementary motor area (SMA) has been investigated in six patients with urologic chronic pelvic pain syndrome (Yani et al., 2019). Each patient received two rTMS pro-

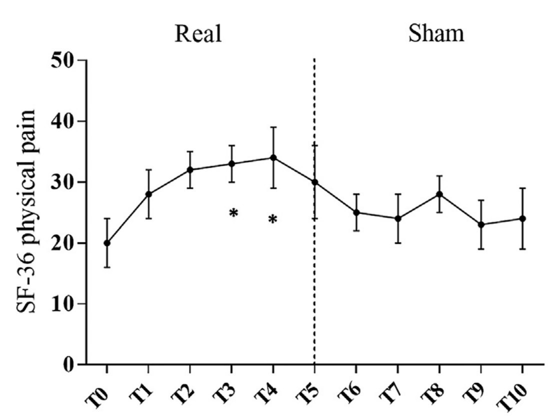

Fig. 4. Mean changes induced by deep H-coil repetitive TMS (rTMS) on the SF-36 (range 0–100) subscore related to physical pain over time in patients with Bladder Pain Syndrome/Interstitial Cystitis. Larger values indicate improvement. Repeated measures analysis of variance (ANOVA) disclosed a significant within-subject effect at T3 and T4 compared with T0. Reproduced with permission from Cervigni et al. (2018).

tocols (HF TMS and LF TMS) with a 1 week washout period; both rTMS protocols were applied to the pelvic floor representation in SMA, as previously defined (Asavasopon et al., 2014; Yani et al., 2018). HF-rTMS reduced and LF-rTMS increased resting pelvic floor activity. HF-rTMS enhanced and LF-rTMS reduced SMA activity, as assessed by means of functional magnetic resonance imaging (fMRI). These findings suggest an important inhibitory effect of SMA activity on pelvic floor tone after voiding.

5. Discussion

The clinical applicability of MEPs to explore the integrity of the central and peripheral motor pathways to pelvic floor muscles is thought to be questionable. In some subjects, it was possible to record reproducible latencies of MEPs after cortical TMS only with muscle activation. Notably, some women lack this ability to contract the pelvic floor muscles (Bump et al., 1991), and this could represent a confounding factor due to lack of facilitation or aberrant function of the corticospinal pathways. Therefore, the poor reliability and long-term reproducibility of pelvic floor muscles MEPs renders their serial measurement unreliable for clinical purposes, in particular with regard to monitoring of a disease progression or the effects of causative factors and possible interventions/therapies. Similarly, due to this poor reliability, single measurements are unsuitable for diagnosing sub-clinical neuropathy, since only gross deviations can be considered of clinical significance.

However, it cannot be excluded that pelvic floor muscles MEP testing can be useful in research setting, i.e. in comparative studies of potential neurogenic causes of LUT diseases. Adaptations of more advanced TMS techniques (i.e. grid-oriented coil positioning, double-pulse stimulation) could improve MEPs reproducibility. This variability could also be exploited to explore the mechanisms of control and modulation of the non-direct corticospinal projections to the striated sphincters.

The specific methodological problems with the methods of measurement are related to both, stimulus and recording sites for pelvic floor muscles MEPs. The cortical representation of the pelvic floor muscles in the inferomedial precentral gyrus lies deeper from the site of stimulation and occupies a smaller volume of neural tissue compared to hand and foot cortical motor representation areas. Furthermore, direct EMG recording of the urethral sphincter and other pelvic floor muscles is usually used only in a limited number of carefully selected cases, due to the remarkable technical difficulties, such as the small dimension with difficult access (especially in older and parous women) and the constant motor unit activity (in particular of the sphincters).

Nevertheless, in some studies MEP and EPC from the UCM were found to be useful and well tolerated diagnostic tools in patients with neurogenic incontinence, that allow distinguishing between central and peripheral lesions of the motor efferent pathways to the UCM (Schmid et al., 2005). On the other hand, for paraplegic patients improvements in bladder and bowel function represent clear priorities over any other impairment to ameliorate the quality of life, and even for tetraplegics subjects rank second only to the recovery of hand function. However, attempts aiming at restoration of bladder and/or bowel function after incomplete SCI (iSCI) have received less attention than that for either upper or lower limb function (Grill et al., 2001; De Groat and Yoshimura, 2006; Craggs et al., 2007).

The development of novel strategies targeting these specific visceral functions would benefit from a more accurate knowledge of the extent to which subjects with iSCI have preserved voluntary control of sphincter muscles. Moreover, due to the remarkable variability in the impact of SCI on pelvic floor control, the neurophysiological assessment of the residual function of the corticospinal pathways that innervate the pelvic floor muscles as well as of the functional status of pudendal reflexes (detrusor hyperreflexia and areflexia, detrusor-external sphincter dyssynergia) could help in the implementation of specific and individual protocols.

The control of bladder function, in particular of sphincters and pelvic floor muscles, depends on the integrity of descending pathways that originate in both the brainstem pontine areas and the cerebral cortex (Craggs et al., 2007; Vasquez et al., 2015; Ellaway et al., 2014). SCI above the sacral spinal cord leads to pathological conditions such as neurogenic detrusor over-activity and detrusor sphincter dyssynergia. Due to the interaction between corticospinal drive and reflex control of pelvic sphincter musculature, rTMS techniques might thus be useful also in the functional recovery of these bladder and bowel sphincter/reflexes disturbances. Interestingly, it has been demonstrated using fMRI that specific motor cortical areas, which have different connectivity to distinct brain networks, are involved in different pelvic floor muscles synergies (Rana et al., 2015).

The important LUT dysfunctions in patients with PD are mostly related to an opposite pattern of involuntary detrusor overactivity that becomes evident during the storage phase (Pavlakis et al., 1983). Therefore, in the study of Brusa and co-workers inhibitory rTMS may have produced an inverse modulation of the descending corticospinal tract projecting to the detrusor muscle, resulting in a restoration of the bladder overactivity (Brusa et al., 2009). These mechanisms should be better defined in future studies directly assessing EMG activity of pelvic floor and sphincter muscles before and after rTMS intervention.

Moreover, rTMS might also exert remote effects on subcortical regions such as the Pontin Micturition Center, the site of descending excitatory projections to parasympathetic sacral centres, and the periaqueductal grey, which plays a crucial role in the brain control of micturition (Nour et al., 2000).

In conclusion, rTMS, together with other electrophysiological investigations, deep-brain stimulation, or sacral anterior root stimulation, which may be applied in combination with a non-invasive and highly specific deafferentation of posterior roots, may pave new ways for the management of neurogenic LUT dysfunction in PD and perhaps other neurodegenerative disorders. Furthermore, rTMS may have the potential to restore bladder sphincter function in subjects with iSCI, to improve detrusor contraction and/or urethral sphincter relaxation in patients with MS and bladder dysfunction, and to relieve symptoms of BPS or chronic pelvic pain.

It should be noted that, according to the evidence-based guidelines of the International Federation of Clinical Neurophysiology (Lefaucheur et al., 2014), only a Class II study (randomized-placebo controlled trial with at least 10 patients receiving real treatment) has been performed, while the others were Class IV studies (uncontrolled studies or case report). Therefore, to date no recommendation other than that a level C evidence ("possible efficacy") of HF rTMS over M1 using H-coil in patients with BPS/IC can be made.

However, these preliminary studies with heterogeneous protocols in small cohorts of patients provide the basis for designing future studies to determine if TMS modulation of different cortical areas (including M1, DLPFC, SMA) may offer a potential treatment option to ameliorate chronic neurologic and urologic conditions. The initial promising findings should be replicated in future controlled, randomized studies with larger sample sizes.

Declaration of Competing Interest

All authors disclose potential conflicts of interest.

References

Asavasopon S, Rana M, Kirages DJ, Yani MS, Fisher BE, Hwang DH, et al. Cortical activation associated with muscle synergies of the human male pelvic floor. J Neurosci 2014;34:13811–8.

Benedetti F, Mayberg HS, Wager TD, Stohler CS, Zubieta JK. Neurobiological mechanisms of the placebo effect. J Neurosci 2005;25:10390–402.

Brostrom S, Jennum P, Lose G. Motor evoked potentials from the striated urethral sphincter and puborectal muscle: reproducibility of latencies. Clin Neurophysiol 2003a;114:1891–5.

Brostrom S, Jennum P, Lose G. Motor evoked potentials from the striated urethral sphincter and puborectal muscle: normative values. Neurourol Urodyn 2003b;22:306–13.

Brusa L, Finazzi Agrò E, Petta F, Sciobica F, Torriero S, Lo Gerfo E, et al. Effects of inhibitory rTMS on bladder function in Parkinson's disease patients. Mov Disord 2009;24:445–8.

Bump RC, HurtWG Fantl JA, Wyman JF. Assessment of Kegel pelvic muscle exercise performance after brief verbal instruction. Am J Obstet Gynecol 1991;165:322–7.

Burgess SE, Gardell LR, Ossipov MH, Malan Jr TP, Vanderah TW, Lai J, et al. Time-dependent descending facilitation from the rostral ventromedial medulla maintains, but does not initiate, neuropathic pain. J Neurosci 2002;22:5129–36.

Centonze D, Petta F, Versace V, Rossi S, Torelli F, Prosperetti C, et al. Effects of motor cortex rTMS on lower urinary tract dysfunction in multiple sclerosis. Mult Scler 2007;13:269–71.

Cervigni M, Onesti E, Ceccanti M, Gori MC, Tartaglia G, Campagna G, et al. Repetitive transcranial magnetic stimulation for chronic neuropathic pain in patients with bladder pain syndrome/interstitial cystitis. Neurourol Urodyn 2018;37:2678–87.

Craggs M, Balasubramaniam V, Kuppuswamy A, Maksimovic R, Ellaway P. The interaction of brain pathways and sacral reflexes following spinal cord lesions in man. Neurourol Urodyn 2007;26:614–5.

De Groat WC, Yoshimura N. Mechanisms underlying the recovery of lower urinary tract function following spinal cord injury. Prog Brain Res 2006;152:59–84.

Eardley I, Nagendran K, Kirby RS, Fowler CJ. A new technique for assessing the efferent innervation of the human striated urethral sphincter. J Urol 1990;144:948–51.

Eardley I, Nagendran K, Lecky B, Chapple CR, Kirby RS, Fowler CJ. Neurophysiology of the striated urethral sphincter in multiple sclerosis. Br J Urol 1991;68:81–8.

Ellaway PH, Vásquez N, Craggs M. Induction of central nervous system plasticity by repetitive transcranial magnetic stimulation to promote sensorimotor recovery in incomplete spinal cord injury. Front Integr Neurosci 2014;8:42.

Fitzgerald PB, Fountain S, Daskalakis ZJ. A comprehensive review of the effects of rTMS on motor cortical excitability and inhibition. Clin Neurophysiol 2006;117:2584–96.

Geuter S, Koban L, Wager TD. The cognitive neuroscience of placebo effects: concepts. predictions, and physiology. Annu Rev Neurosci 2017;40:167–88.

Grill WM, Craggs MD, Foreman RD, Ludlow CL, Buller JL. Emerging clinical applications of electrical stimulation: opportunities for restoration of function. J Rehabil Res Dev 2001;38:641–53.

Lefaucheur JP, Andre-Obadia N, Antal A, Ayache SS, Baeken C, Benninger DH, et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). Clin Neurophysiol 2014;125:2150–206.

Mayberg HS, Silva JA, Brannan SK, Tekell JL, Mahurin RK, McGinnis S, et al. The functional neuroanatomy of the placebo effect. Am J Psychiatry 2002;159:728–37.

Nizard J, Esnault J, Bouche B, Suarez Moreno A, Lefaucheur JP, Nguyen JP. Long-term relief of painful bladder syndrome by high-intensity, low-frequency repetitive transcranial magnetic stimulation of the right and left dorsolateral prefrontal cortices. Front Neurosci 2018;12:925.

Nour S, Svarer C, Kristensen JK, Paulson OB, Law I. Cerebral activation during micturition in normal men. Brain 2000;123:781–9.

Pavlakis AJ, Siroky MB, Goldstein I, Kranne RJ. Neurourological findings in Parkinson's disease. J Urol 1983;129:80–3.

Rana M, Yani MS, Asavasopon S, Fisher BE, Kutch JJ. Brain connectivity associated with muscle synergies in humans. J Neurosci 2015;35:14708–16.

Rossi S, Hallett M, Rossini PM. Pascual-Leone A; Safety of TMS Consensus Group. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin Neurophysiol 2009;120:2008–39.

Rossini PM, Burke D, Chen R, Cohen LG, Daskalakis Z, Di Iorio R, et al. Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N Committee. Clin Neurophysiol 2015;126:1071–107.

Schmid DM, Curt A, Hauri D, Schurch B. Motor evoked potentials (MEP) and evoked pressure curves (EPC) from the urethral compressive musculature (UCM) by functional magnetic stimulation in healthy volunteers and patients with neurogenic incontinence. Neurourol Urodyn 2005;24:117–27.

Snooks SJ, Swash M. Perineal nerve and transcutaneous spinal stimulation: new methods for investigation of the urethral striated sphincter musculature. Br J Urol 1984;56:406–9.

Staud R. The important role of CNS facilitation and inhibition for chronic pain. Int J Clin Rheumatol 2013;8:639–46.

Thiry AJ, Deltenre PF. Neurophysiological assessment of the central motor pathway to the external urethral sphincter in man. Br J Urol 1989;63:515–9.

Vasquez N, Balasubramaniam V, Kuppuswamy A, Knight S, Susser J, Gall A, et al. The interaction of cortico-spinal pathways and sacral sphincter reflexes in subjects with incomplete spinal cord injury: a pilot study. Neurourol Urodyn 2015;34:349–55.

Yani MS, Fenske SJ, Rodriguez LV, Kutch JJ. Motor cortical neuromodulation of pelvic floor muscle tone: potential implications for the treatment of urologic conditions. Neurourol Urodyn 2019;38:1517–23.

Yani MS, Wondolowski JH, Eckel SP, Kulig K, Fisher BE, Gordon JE, et al. Distributed representation of pelvic floor muscles in human motor cortex. Sci Rep 2018;8:7213.