CASE REPORT

Repetitive transcranial magnetic stimulation (rTMS) as a treatment for chronic dizziness following mild traumatic brain injury

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SUMMARY

A 61-year-old man sustained a mild traumatic brain injury (mTBI) following a pedestrian versus vehicle traffic accident. Post injury, he began to experience symptoms including light-headedness, spatial disorientation, nausea, fatigue and prominent dizziness brought on by postural change, physical activity or eye movements. Symptoms of dizziness persisted for over 5 years, despite numerous extensive and rigorous vestibular and vision therapy regimens. All investigations suggested normal peripheral and central vestibular functioning. The patient underwent 10 sessions of repetitive transcranial magnetic stimulation (rTMS) treatment, with stimulation of the left dorsolateral prefrontal cortex at 70% of resting motor threshold and a frequency of 10 Hz. Dizziness symptom severity and frequency were reduced by greater than 50% at 3 months post treatment, with a clinically significant reduction of dizziness disability from 40 to 21 points on the Dizziness Handicap Inventory. We propose rTMS as a safe, effective and cost-effective treatment option for patients who experience persistent post-traumatic dizziness secondary to mTBI.

BACKGROUND

It is currently estimated that up to 300 per 100 000 people seek medical attention for mild traumatic brain injury (mTBI) annually, worldwide.[1 2] Since many people with mTBI may not seek medical attention,[3] the true global population incidence is thought to be 45 million people annually, with most cases resulting from falls, sports and motor vehicle accidents.[2] It is estimated that 85%–90% of all mTBIs will have symptoms resolve within 1 month.[4] However, up to 10%–25% of patients with mTBI may develop persistent postconcussive symptoms (PPCS),[5 6] which can continue beyond 1 year post injury in more than 2% of patients.[5 7]

Ongoing vertigo, dizziness, imbalance and vision changes are common symptoms in the majority of patients following mTBI and are often associated with vestibular system impairments.[8 9] Up to 81% of these patients will have dizziness on initial examination,[10] which has been shown to prolong recovery when compared with other initial symptoms.[11] The aetiology of persistent post-traumatic dizziness may be peripheral or central in origin, affecting inner ear or central nervous system integration and output, respectively. Peripheral vestibular system may also affect eye movement through the vestibulo-ocular reflex (VOR). Thus, vestibular dysfunction can presents as balance impairments, dizziness, vertigo or VOR malfunctioning.[8] The most common cause of dizziness in patients with PPCS is benign paroxysmal positional vertigo,[12] which is commonly associated with dislodged otoconia in the posterior semicircular canal,[8] but other aetiologies such as VOR dysfunction, cervicogenic dizziness and post-traumatic vision syndrome may also occur.[13]

Treatment of post-traumatic dizziness in patients with PPCS can be difficult. Vestibular therapy, and to a lesser extent, vision therapy, have been shown to be of some value, but are not always successful. Further, medication and environmental modifications may mitigate symptoms but do not treat the cause. We currently lack a recommended and efficacious treatment for chronic dizziness in PPCS when symptoms persist beyond conventional therapies. This case highlights the use of repetitive transcranial magnetic stimulation (rTMS) as a novel treatment option for patients who suffer from PPCS and chronic dizziness secondary to mTBI.

CASE PRESENTATION

An otherwise healthy 61-year-old right-hand dominant man was struck by a vehicle in a crosswalk, causing him to be thrown a short distance before landing on his back and striking his head on pavement. He had a brief loss of consciousness and on waking, he experienced a transient paralysis of the extremities, lasting a few seconds. The patient was alert and oriented to person, place, time and situation, with a Glasgow Coma Scale of 15 when emergency medical services arrived. He was taken by ambulance in C-spine precautions to the local trauma centre where he had a chest ultrasound and was subsequently discharged home. The patient reported neck soreness, head pain (posterior) and left temporomandibular joint tenderness on the day of the injury. He required stitches in the posterior aspect of the head.

Initial symptoms in the days following the injury included dizziness (in which he described the world spinning), light-headedness, spatial disorientation, nausea and fatigue. These symptoms waxed and waned over time, but persisted and were present 5 years post injury despite seeing many specialists and engaging in a variety of interventions. In the mornings, on awakening, the patient tended to

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be symptom free. However, dizziness would worsen with any physical activity, prolonged mental activity, postural changes, converging eye movements and changes in depth and colour contrast. Symptoms improved with rest and immobility.

The patient had no family history of neurological conditions. He was on no medications at the time of the incident, with the exception of a daily multivitamin, vitamin C and vitamin D supplements. Venlafaxine (75 mg one time a day) was started 2 years post injury, which helped with mood but did not help with dizziness.

INVESTIGATIONS

The patient was seen by multiple specialists, including neurology, ear/nose/throat, physiatry, sports medicine, dentistry (for a temporomandibular joint night splint), orthopaedic surgery, neuropsychology and psychiatry. A diagnosis of post-traumatic dizziness of idiopathic origin was made. Imaging of the brain (MRI and MR angiogram) and cervical spine (MRI) was completed. There was no evidence of any significant vascular narrowing with the exception of possible minimal atherosclerotic changes at the left common carotid origin; otherwise, no vascular or post-traumatic pathology was identified. In particular, the vertebrobasilar system was patent throughout. There was no evidence of intracranial traumatic lesion or shear microhaemorrhage.

Further testing included neuropsychological assessment, vestibular evoked myogenic potential, computerised dynamic posturography and videonystagmography, which were all normal. A full physical examination was completed, which included postural heart rate and blood pressure, pulse oximetry, cardiology and respiratory examination, and a complete neurological examination, including cerebellar, cranial nerve, motor, sensory, reflexes, tone, frontal lobe release signs, Dix-Hallpike manoeuvre and vision assessment (visual acuity, eye tracking, visual fields and convergence). Only a mild length-dependent sensory polyneuropathy involving the distal 1/3 of the feet was found, which he stated was there prior to the injury. All blood tests, including complete blood count, electrolytes, fasting glucose, serum protein electrophoresis, vitamin B_{12}, thyroid stimulating hormonr, free thyroxine-4, morning cortisol, testosterone, insulin-like growth factor-1, vitamin D and inflammatory markers were within normal limits. A heavy metal screen found all trace elements to be within normal ranges.

The patient participated in extensive rehabilitation. A combination of vestibular therapy and physiotherapy of the cervical spine (including range of motion exercises, intermuscular stimulation, acupuncture, strengthening exercises and manual therapy) was unsuccessful and exacerbated symptoms. Extensive 15-week rehabilitative vision therapy with an optometrist was also unsuccessful. Binasal occlusion therapy (3 weeks) was tried with no benefit. Six months of craniosacral therapy was also completed with little to no benefit. Activator walking poles slightly improved stability and balance but did not reduce symptoms. The cost incurred for the aforementioned therapies was substantial, totalling approximately $C9550. This estimate included a vision therapy programme ($C5000), 11 physiotherapy sessions ($C1320), 25 craniosacral treatments ($C2345), 8 vestibular therapy sessions and several therapeutic massage treatments.

TREATMENT

The patient underwent 2 weeks of rTMS treatment (10 sessions), which was chosen based on the typical duration for chronic medication refractory depression and medication refractory migraine protocols.[14–18] Each session took approximately 45 min to complete and cost approximately $C300 based on current requirements for usage of the machine and labour. Brainsight TMS neuronavigation software (Rogue Research, Quebec, Canada) with the MRI of the patient was used for the localisation of the TMS stimulation site. The left dorsolateral prefrontal cortex (DLPFC) received rTMS stimulation at an intensity of 70% of resting motor threshold (RMT), with a frequency of 10 Hz. Ten trains of 60 pulses/train (total of 600 pulses) were administered at each session, with an intertrain interval of 45 s. RMT was identified using electromyography (EMG). EMG electrodes were attached to the *abductor digiti minimi* (ADM) muscle of the right hand during stimulation of the left primary motor cortex, allowing for the determination of optimal ADM muscle activation. The RMT was determined at each session and was defined as the minimal stimulation intensity required to elicit a motor-evoked response of 50 μV peak-to-peak amplitude in at least 5 out of 10 consecutive trials of motor cortex stimulation in the contralateral ADM muscle. The rTMS was well tolerated with no lasting side effects and only minor transient fatigue. TMS treatment is known to cause fatigue and minor irritation at the site, both of which resolve within hours.

OUTCOME AND FOLLOW-UP

Data were collected with multiple outcome measures, including dizziness symptom severity, dizziness symptom frequency, cognition, anxiety, depression, post-traumatic stress disorder and quality of life, at 2 weeks pretreatment, immediately following treatment, 1 month post treatment and 3 months post treatment. Pretreatment dizziness severity was reduced from 6.14 to 5.00 at 1 month post treatment and further reduced to 3.00 at 3 months on a 10-point Likert scale following rTMS completion. Symptom frequency (episodes of dizziness per week) was also reduced from 58.5 episodes/week prior to treatment, to 48 episodes/week at 1 month post treatment to 21 episodes/week at 3 months post treatment. The Dizziness Handicap Inventory (DHI) was used to assess the impact of dizziness on quality of life, with a disability cut-off point at 29/100 possible points.[19] The patient's DHI was 40/100 prior to rTMS treatment initiation and was reduced to 26/100 at 3 months post treatment. The minimally important change for the DHI has been identified by Tamber *et al*[19] to be 11 points, signifying this to be a significant reduction in dizziness disability. Quality of life improved slightly from 88/100 to 93/100 at 1 month post treatment, and to 95/100 at 3 months post treatment, using the Quality of Life after Brain Injury Questionnaire. All other outcome measures were nil at baseline or minimally changed.

DISCUSSION

Dizziness is a common problem following mTBI.[10] Post-traumatic dizziness as a symptom of acute mTBI has been noted to abate earlier than other symptoms such as fatigue and headache.[20] However, in those patients with persistent post-traumatic dizziness-targeted therapies such as vestibular and vision therapy can be particularly helpful, especially those that persist beyond the first couple of weeks post injury.[7 21] The patient described in the current case report, however, has relatively normal performances in all relevant vestibular assessments and has undergone numerous targeted vestibular and vision therapies with little-to-no effect.

Non-invasive brain stimulation techniques such as rTMS have become increasingly studied as tools for inducing short-term and long-term physiological effects in the brain.[22] While the

true mechanism is still currently unknown, theoretically, given the neurophysiological effects of TMS, this technique may: (1) decrease cortical hyperexcitability following acute mTBI; (2) modulate long-term synaptic plasticity and moderate maladaptive consequences of mTBI; and (3) facilitate cortical reorganisation and consolidation of learning in specific neural networks when combined with physical and behavioural therapy.[22] While single pulse TMS causes transient faciliatory or inhibitory effects lasting up to 10 min, repetitive stimulation is crucial for long-lasting therapeutic effects thought to be due to neuroplastic changes.[23] Since cortical projections of the vestibular system are widespread and interconnected with cognitive and affective networks, neuromodulation using rTMS could greatly influence motion perception and postural control.[24]

PPCS include somatic concerns such as headache, fatigue, anxiety, depressive symptoms, irritability, dizziness and cognitive deficits[25 26] and it has been suggested that these comorbidities are interrelated.[27] Thus, Koski *et al*[25] have hypothesised that rTMS over the DLPFC, which is an effective treatment for symptoms of major depressive disorder, may have utility in alleviating PPCS. In a study using a near-identical treatment protocol to the one described in this case, Koski *et al* showed a significant reduction in PPCS following 20 rTMS sessions in patients with mTBI with symptoms persisting for greater than 3 months.[25]

rTMS has been used as a treatment for other causes of dizziness. A double-blind sham-controlled study of eight right-handed women with a history of classic motion-triggered Mal de Debarquement Syndrome used 10 Hz rTMS stimulation of the left DLPFC and found a significant improvement in dizziness, mood and anxiety symptoms.[24] This study also used the DHI as a primary outcome measure for disability secondary to dizziness. Average baseline DHI scores were 45/100, and a reduction of approximately 10 points was seen in patients who received true rTMS, compared with sham, at 4 weeks post treatment similar to the results in this case report.

While rTMS has been studied more extensively in the treatment of depression,[28 29] stroke rehabilitation[30 31] and even tinnitus,[32 33] more work is needed to study the potential therapeutic effects in larger populations of patients who suffer from PPCS, particularly chronic post-traumatic dizziness. With a cost of $C300 per session, a protocol of 10 rTMS sessions has a relatively low-cost burden compared with many conventional therapies. Here, we propose that rTMS was a safe, effective and cost-effective treatment option for a patient who experience persistent debilitating dizziness secondary to mTBI.

Patient's perspective

I got to a point following my injury where I was looking for anything to help with my symptoms, and to a point where I felt that I had nothing to lose. I was willing to try anything. With regards to the treatment, there was some notable benefit. I would not consider it to be time-consuming and it was certainly not invasive. Generally, I would conclude that there were positive benefits, and I'm definitely less symptomatic now following the treatment compared to prior. It seems the symptomatic episodes are more noticeable now, only because they occur so infrequently. It's not even something I'm really thinking about anymore. Occasionally I'm reminded that I still have a brain injury, but for the most part (other than climbing ladders or participating in similar activities) I haven't imposed restrictions on anything that I do anymore. I've been thinking of riding my bike around the block for the first time in at least 4 years. In terms of normal day-to-day living, I no longer dwell on the symptoms. If you look at the timing, one would suspect that the result must be correlated to the treatment. I don't think anyone would object to this type of treatment, given how non-invasive it is. I'd certainly recommend the treatment to anyone.

Learning points

- Repetitive transcranial magnetic stimulation (rTMS) was safely administered to a patient with persistent postconcussion syndrome (PPCS) and treatment refractory idiopathic post-traumatic dizziness.
- This case report suggests that rTMS may improve post-traumatic dizziness symptoms burden at 1 and 3 months post treatment, but larger randomised control studies are necessary.
- A protocol of 10 rTMS sessions shares a similar if not lower cost burden than each of the conventional therapies previously tried by this patient.
- This case report suggests that rTMS may clinically improve the impact of dizziness on quality of life based on the Dizziness Handicap Inventory in a patient with PPCS and idiopathic post-traumatic dizziness at 1 and 3 months post treatment, but larger randomised controls trials are necessary.
- The mechanism of action and duration of symptom relief remains unknown; therefore, studies focusing on pathophysiology and long-term follow-up would be beneficial.

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