Article published online: 2022-02-03

Neuropsychiatric Treatment for Mild Traumatic Brain Injury: Nonpharmacological Approaches

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Semin Neurol 2022;42:168–181.

Abstract

Postconcussive symptoms following mild traumatic brain injury (mTBI)/concussion are common, disabling, and challenging to manage. Patients can experience a range of symptoms (e.g., mood disturbance, headaches, insomnia, vestibular symptoms, and cognitive dysfunction), and neuropsychiatric management relies heavily on nonpharmacological and multidisciplinary approaches. This article presents an overview of current nonpharmacological strategies for postconcussive symptoms including psychoeducation; psychotherapy; vestibular, visual, and physical therapies; cognitive rehabilitation; as well as more novel approaches, such as neuromodulation. Ultimately, treatment and management of mTBI should begin early with appropriate psychoeducation/counseling, and be tailored based on core symptoms and individual goals.

Keywords
- ► concussion
- ► mild traumatic brain injury
- ► neuropsychiatry
- ► nonpharmacological treatment

Concussion, or mild traumatic brain injury (mTBI; used here interchangeably), comprises approximately 75 to 85% of all TBIs.[1] The majority of mTBIs tend to resolve within weeks; however, approximately 10 to 30% of patients report prolonged or chronic postconcussive symptoms (PCSs).[2] While the high degree of heterogeneity in diagnostic criteria for PCS makes it difficult to specify a prevalence estimate, the most common symptoms include cognitive impairment, fatigue, posttraumatic headaches, insomnia, and mood disturbance.[3,4] Risk factors for chronic PCS are poorly understood. Research to date generally offers mixed results and varies depending on the specific subpopulation studied, but several factors appear to be fairly well established, including female sex, non-white ethnic groups, substance use, comorbid physical and mental health conditions, premorbid pain disorder, and history of somatization.[4–8] Moreover, there is evidence that certain factors are less prognostic of chronic PCS or long-term functional outcomes than originally believed, such as a prior history of concussion.[6,8–10] In addition, there appears to be a negative bidirectional effect of depression on the recovery process, with mTBI symptoms being more persistent when accompanied by depression.[11]

The treatment of PCS is complex, and decision-making relies on a limited evidence base.[12,13] Clinical practice guidelines for mTBI recommend hierarchical symptom-based management that gives priority to the treatment of depression and anxiety, sleep problems, and posttraumatic headache (►**Fig. 1**).[14] This is important because mental health complications, sleep problems, and pain may contribute to and perpetuate other nonspecific mTBI symptoms (e.g., cognitive

published online February 3, 2022

Issue Theme Neuropsychiatry; Guest Editors: Aneeta Saxena, MD, and David L. Perez, MD, MMSc, FAAN, FANPA

Thieme Medical Publishers, Inc., 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA

DOI https://doi.org/10.1055/s-0041-1742143.
ISSN 0271-8235.

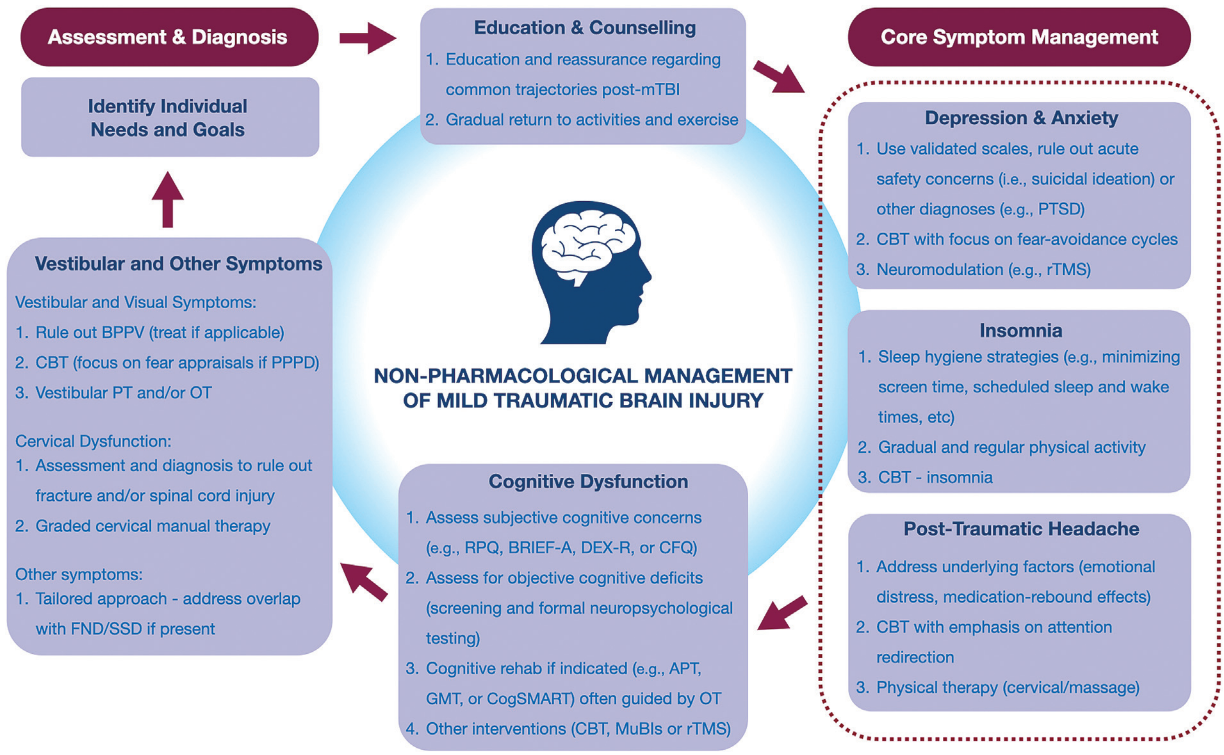

Fig. 1 Non-pharmacological approaches for the management mild traumatic brain injury. APT, attention process training; BPPV, benign paroxysmal positional vertigo; BRIEF-A, Behavior Rating Inventory of Executive Functions for Adults; CBT, cognitive behavioural therapy; CFQ, cognitive failures questionnaire; DEX-R, dysexecutive questionnaire revised; dlPFC, dorsolateral pre-frontal cortex; FND, functional neurological disorder; GMT, goal management training; MuBIs, music-based interventions; OT, occupational therapy; PPPD, persistent postural perceptual dizziness; PTSD, post-traumatic stress disorder; PT, physiotherapy; RPQ, Rivermead Post Concussion Questionnaire; rTMS, repetitive transcranial magnetic stimulation; SSD, somatic symptom disorder.

impairment, fatigue).[6,11] Thus, addressing these symptoms first can lead to improvement in other domains.[15,16] Nonpharmacological approaches are a mainstay of managing PCS from mTBI, and optimal care should involve individualized symptom-specific treatments.[13] In this article, we review current nonpharmacological approaches for PCS including psychoeducation; psychotherapy; vestibular, visual, and physical therapies; and cognitive rehabilitation (see ►**Table 1**). We also highlight emerging treatment strategies such as neuromodulation and music-based interventions (MuBIs). Lastly, we comment on many unregulated alternative treatments, supplements, and devices available with limited evidence for concussion, and discuss the role of placebo effects in this complex neuropsychiatric patient population.

Psychoeducation and Counseling

Psychoeducation and counseling involve provision of information and support for patients with mTBI. Some key components include guidance on symptom self-management, reassurance that most symptoms improve within several weeks, and advice that after a brief period of rest during the acute phase after injury (24–48 hours), patients can become progressively more active as tolerated.[14,17]

Short-term psychoeducation sessions (e.g., a brief web-based intervention, or one to two sessions providing information on the management of concussion symptoms) have been evaluated following mTBI with mixed results.[18–21] Matuseviciene et al[20] found significant reductions in self-reported PCS 3 months after a single counseling session with a neurorehabilitation specialist that involved encouragement of gradual return to activities and written information on mTBI. However, the same group did not find significant improvement in another cohort.[19]

More intensive and multicomponent psychoeducational and counseling interventions have also been explored for PCS. A recent systematic review and meta-analysis evaluated 11 studies that used psychoeducation and counseling interventions for PCS following mTBI in comparison to treatment-as-usual (e.g., single session of verbal education on concussion symptoms, reassurance, or provision of written materials with suggestion to follow-up with a general practitioner) and reported mixed results.[22] Interventions were heterogenous and included either extended follow-up with a neurorehabilitation specialist and multidisciplinary team, or personalized phone calls in addition to provision of an educational brochure or booklet. Several studies reported benefits in PCS following extended multidisciplinary psychoeducational and counseling interventions,[19,20,23–26] while others found that such interventions performed comparably to treatment-as-usual.[18,21,27–29] Moreover, most postinterventional benefits did not appear to be sustained at long-term follow-up (e.g., 6 or 12 months).[19,24,25]

Table 1 Overview of select studies incorporating nonpharmacological approaches for the treatment of mild traumatic brain injury

Study	Design	Participants (*n*)	Intervention	Primary outcome	Main results
Psychoeducation and counseling					
Teo et al[22]	Systematic review (17 studies total, most were RCTs)	3,081	Psychoeducation (8 studies, typically involved extended follow-up with a specialist, or provision of brochures or booklets), or telephone-based problem-solving (4 studies)	PCS	No intervention was found to be effective in reducing PCS at 3–6 mo follow-up; however, an overall small effect size was found in pooled functional outcomes at 6 mo
Thastum et al[31]	Open-label, parallel-group RCT	112	Interdisciplinary, individually tailored intervention of 8-wk duration based on gradual return to activities and principles from CBT compared with usual treatment	PCS via change in RPQ score from baseline to 3-mo follow-up	Significant reduction in PCS at 3-mo follow-up in the intervention group
Psychotherapy					
Tomfohr-Madsen et al[48]	Parallel-group RCT	24 (adolescents aged 12–18)	CBT-insomnia compared with usual treatment for 6 wk	Sleep quality via ISI score 1-mo posttreatment	Significant improvements in sleep
Silverberg[52]	Case series	4	Behavioral therapy involving graded exposure to triggers that are prone to sensitization (e.g., stress, light flicker, loud noise) for 8 sessions	Headache frequency/intensity via changes in headache diary	Variable improvement in headache frequency/intensity and headache trigger avoidance
Potter et al[56]	RCT	46[a]	CBT, 12 sessions, wait-list control group	PCS (RPQ) and quality of life (BICRO and QOLAS), average of 6-mo follow-up	Mild improvements in quality of life and PCS at 6-mo follow-up
Physical therapies					
Alsalaheen et al[71]	RCR	114	Customized vestibular rehabilitation (e.g., gaze fixation and balance exercises)	Vestibular and gait symptoms (via self-report and physical exam)	Reductions in dizziness with improved gait and balance function
Cheever et al[75]	Systematic review (5 studies, most RCR)	171	Active rehabilitation	Pain (NPS) and medical clearance via physical exam	Graded cervical manual therapy was shown to reduce time to symptom resolution and medical clearance
McIntyre et al[77]	Systematic review (12 studies, most PC, case series, or RCR, with 3 RCTs)	482	Subsymptom threshold aerobic exercise (e.g., 20 min of exercise that provoked symptoms, 5–6 d per week)	PCS	Improved PCS overall
Cognitive rehabilitation					
Mahncke et al[114]	RCT	83	Computer-based cognitive training program (games tailored for specific cognitive domains with increasing difficulty) vs. standard games for 13 wk	Cognition (composite score of neuropsychological tests)	Significant improvements in cognitive function that was sustained at 3-mo follow-up

Table 1 (*Continued*)

Study	Design	Partici-pants (*n*)	Intervention	Primary outcome	Main results
Neuromodulation					
Mollica et al[130]	Systematic review (11 studies total, most were RCTs)	197	rTMS (depression—2 right dlPFC, 2 bilateral dlPFC; headache and pain—3 left dlPFC, 2 PMC; general PCS—2 left dlPFC)	Depression (HDRS, 1 study; MADRS, 3 studies) Headache (NPS and diary, 5 studies) General PCS (RPQ, 2 studies)	Improved depression in 2 of 4 studies, improved headache in 4 studies, improved central pain (1 study), mixed results for general PCS (1 of 2 studies)
Music-based interventions					
Vik et al[147]	Prospective cohort	7	Piano exercises with increasing difficulty with at-home practice for 8 wk	Cognitive function (neuropsychological testing), pre–post fMRI	Improvements in CVLT-2 scores, improved overall functioning (6 of 7 participants returned to work), and corresponding functional connectivity changes in the OFC

Abbreviations: BICRO, Brain Injury Community Rehabilitation Outcome Scale; CBT, cognitive behavioral therapy; CVLT-2, California Verbal Learning Test; dlPFC, dorsolateral prefrontal cortex; fMRI, functional magnetic resonance imaging; HDRS, Hamilton Depression Rating Scale; ISI, insomnia severity index; MADRS, Montgomery-Asberg Depression Rating Scale; NPS, numeric pain scale; OFC, orbitofrontal cortex; PCS, postconcussive symptoms; QOLAS, Quality of Life Assessment Schedule; RCR, retrospective chart review; RCT, randomized control trial; RPQ, Rivermead Post-Concussive Questionnaire; rTMS, repetitive transcranial magnetic stimulation.

[a]Included patients with mild and moderate TBI.

Recent trials not included in the above systematic review that incorporate an interdisciplinary approach also reveal mixed results. A pilot study of 25 patients randomized to either treatment-as-usual or a psychoeducational and counseling intervention targeting sleep, attention, anxiety, and memory ("SAAM") symptoms once weekly for 4 weeks did not result in improved PCS.[30] However, a trial involving 112 patients with mTBI randomized to receive either enhanced treatment-as-usual versus an interdisciplinary, individually tailored intervention of 8 weeks of duration based on gradual return to activities and cognitive–behavioral therapy (CBT) principles resulted in significant reductions in PCS that were maintained at 3-month follow-up.[31] This study highlights the importance of integrating multidisciplinary approaches in the management of mTBI.

Additionally, patients at high risk of developing chronic PCS may benefit from extra support. In a study that included 221 patients with mTBI who were at high risk for chronic PCS, psychoeducation, and cognitive rehabilitation decreased the frequency of PCS at 6 months compared with treatment-as-usual (6 vs. 52%, $p < 0.001$).[32]

Lastly, more novel educational approaches for mTBI include integration of app-based resources. A recent review of app-based resources for concussion concluded that of 13 concussion psychoeducation apps, 5 were well-suited to provide evidence-based information (as determined by scores on the Mobile Application Rating Scale [MARS]) on mTBI management (Concussion Coach, World Rugby Concussion, CDC Heads Up!, Concussion Ed, and LifeArmor), and that Concussion Coach and LifeArmor contained information specific to military populations and addressed mental health information and coping strategies as well.[33] Patients can also be directed to www.headinjurysymptoms.org or www.neurosymptoms.org (specifically, the section under "post-concussive syndrome") for additional psychoeducation for ongoing symptoms post-mTBI.

Psychotherapy

Psychological factors, such as preinjury mental health problems and postinjury emotional distress, can strongly influence recovery from mTBI.[10,34] Certain maladaptive (unhelpful) illness beliefs (e.g., catastrophizing)[35] and behavioral coping styles (e.g., avoidance)[36–38] also predict higher symptom burden and disability. These psychosocial risk factors are modifiable and can be targeted with psychologically informed interventions to mitigate poor outcomes.[39]

To date, psychological interventions for mTBI are most commonly informed by the cognitive–behavioral model.[39,40] The cognitive–behavioral model proposes that beliefs influence emotional, physiological, and behavioral responses. Accordingly, CBT aims to alter unhelpful beliefs and coping behaviors to improve health outcomes. Other models have also been applied to mTBI, such as acceptance and mindfulness-based therapies.[41,42] Rather than attempting to modify or alter unhelpful beliefs, mindfulness, acceptance, and experiential strategies are used alongside behavioral principles to help individuals return to valued activities. The rationale for psychotherapy is strong given the influence of psychosocial factors, such as illness beliefs and coping styles, on recovery from mTBI.

Symptom-Based Management

Psychologically informed interventions, such as CBT, have potential to treat many symptoms of mTBI, such as anxiety, depression, sleep impairment, and posttraumatic headache.[43] Despite this, few psychologically informed interventions have been evaluated in mTBI samples, and as such, evidence for this symptom-based approach is largely extrapolated from other clinical populations (e.g., primary headache disorder).

Mood and Anxiety

CBT and other psychotherapeutic treatment modalities are well-established in treating mood, anxiety, and stress-related disorders.[43,44] A recent systematic review of psychotherapy for depression and/or anxiety for individuals with persistent postconcussion symptoms found that seven of eight studies reported reductions in psychological distress.[22] Psychotherapy modalities included CBT, problem-solving therapy, mind–body interventions, and acceptance and commitment therapy (ACT).[22]

Sleep Problems

Insomnia is one of the most common sleep disturbances in the post-acute stages of mTBI.[14] CBT is the nonpharmacological treatment of choice for either primary insomnia or insomnia associated with a medical or psychiatric condition,[45] including mTBI.[14] CBT for insomnia (CBT-I) is effective at improving sleep outcomes and treatment gains are maintained up to a year compared with nonactive controls (e.g., nontreatment control, waitlist control, usual care, or education about sleep hygiene).[46] In mTBI, an online CBT program was feasible and demonstrated larger reductions in sleep disturbance compared with an education control.[47] Results from a pilot randomized controlled trial (RCT) support CBT for insomnia treatment in adolescents post-mTBI compared with a treatment as usual waitlist control group.[48]

Posttraumatic Headache

Posttraumatic headache (PTH) can be caused and/or perpetuated by sleep problems, emotional distress, medication-rebound effects, and environmental triggers (e.g., bright lights).[14,49,50] Psychologically informed treatment can be implemented to manage PTH, as well as its perpetuating factors. Much of this work has been conducted in individuals with primary headache disorder.[50]

A review of randomized clinical trials assessing the efficacy of psychological treatment for primary headache disorders included relaxation training, progressive muscle relaxation, behavior training in migraine self-management, mindfulness-based therapy, autogenic training, CBT, and biofeedback.[51] The pooled effects in meta-analysis demonstrated that those receiving any kind of psychological treatment reported fewer headache days per month than those in control groups,[51] and CBT appears to be a safe and well-tolerated intervention with no adverse effects reported in a recent case series.[52]

Persistent Postural Perceptual Dizziness and Vertigo

Some patients report vestibular impairment, such as persistent postural perceptual dizziness (PPPD) and vertigo. Chronic disability associated with PPPD can be maintained by certain illness belief and anxiety patterns.[53] As such, clinical practice guidelines suggest vestibular treatments, as well as psychological treatment to address anxiety.[14]

Psychological treatment, such as CBT and ACT, has been used to treat patients with PPPD. Cognitive–behavioral models of PPPD examine the cognitive and emotional responses to symptoms of dizziness, such as fear appraisals (e.g., fear of falling), catastrophic beliefs, and anxiety in an attempt to help patients respond to dizziness in a more adaptive way.[53] Sixty percent of patients reported improvement in chronic subjective dizziness, or PPPD, following a course of CBT.[54] In a feasibility pre–post study, the majority of participants with PPPD (74%) reported remission and/or good treatment response following 6 months of ACT with vestibular rehabilitation.[55]

Psychotherapy for Overall Postconcussion Symptoms and Functional Outcomes

The previously described studies were designed to measure the efficacy of psychotherapy for a particular problem (e.g., insomnia). Some psychological interventions have instead targeted an overall reduction in PCS. A recent systematic review identified eight RCTs assessing psychotherapy for persistent PCS and several functional outcomes.[22] Psychotherapy modalities included CBT, problem-solving therapy, mind–body interventions, and ACT. Civilians with mTBI who received CBT[39,56] or telephone counseling that included psychoeducation, reassurance, and specific symptom management[23] reported a reduction in PCS. In a trial of CBT versus telephone counseling (i.e., reassurance and education), participants who received telephone counseling reported fewer postconcussion symptoms.[57] However, reductions in PCS were not found for military veterans who received telephone problem-solving therapy.[24] Another systematic review and meta-analysis examined the effects of CBT on several primary outcomes, including postconcussion symptom severity, depression, anxiety, and social integration. CBT did not lead to improvement in PCS severity compared with controls (e.g., waitlist, usual care, psychoeducation, telephone counseling). Small effects were found for depression, anxiety, and social integration.[58]

Several trials have evaluated multicomponent rehabilitation that includes psychotherapeutic components. They include cognitive rehabilitation[59,60] and gradual return to activities with CBT principles for adults,[31] and collaborative care combined with CBT for adolescents.[61] They show promise for improving emotional distress and functional outcomes.

There is growing interest in using clinical phenotyping to provide tailored and individualized treatment to patients based on symptom presentation or modifiable risk factors.[62–64] One such promising avenue is providing rehabilitation that targets specific modifiable behavioral coping styles, such as fear avoidance.[36,37,65] Fear avoidance behavior is a coping style in which people avoid or escape from activities or situations that might exacerbate their symptoms. Fear avoidance behavior predicts disability and higher symptom burden in post-acute mTBI.[36] The fear avoidance construct also plays a role in symptom maintenance and disability in chronic pain,[66] which can be targeted with graded exposure therapy, a treatment based on CBT principles.[67] Providing more targeted treatment via clinical subtyping, such as graded exposure therapy to mTBI patients with high fear avoidance, may help improve outcomes.

Physical Therapies

Vestibular and Visual Symptoms

Dizziness and balance dysfunction are associated with threefold increase in unemployment among TBI survivors.[68] Unfortunately, their management can pose a major challenge given a variety of factors, including few effective pharmacological agents, unclear etiology (with 25% of vestibular diagnoses being cryptogenic in chronic TBI cases),[69] and the fact that brain injury can impact both peripheral and central components of the balance system.[68]

Mechanisms of vestibular dysfunction in mTBI are poorly understood and likely multifactorial in many cases. Dysfunction of the vestibulo-ocular reflex (VOR) can result in symptoms such as movement-related dizziness and difficulty maintaining balance with head movements because the VOR coordinates eye movement with head movement to provide clear vision during motion.[70] While VOR function generally recovers spontaneously over time without intervention, for those who do not recover, vestibular rehabilitation is a commonly prescribed evidence-based intervention for both adults and children.[71,72] It is, however, important that vestibular physical therapy be customized for the patient's level of function (i.e., taking into account comorbidities) and expected level of recovery.[73] Notably, other contributors to early persistent dizziness should also be considered and addressed including posttraumatic migraine, visual–perceptual disturbances, and cervical spine dysfunction.[72] The presence of benign paroxysmal positional vertigo (BPPV) should also always be ruled out prior to initiating any other exercises, as it is a common cause of dizziness and imbalance and can be treated through repositioning techniques.[74]

One of the major areas of treatment in vestibular rehabilitation is restoration of dynamic gaze stability—the ability to maintain focus while the head is in motion.[72] This should be done in a way that optimizes performance while minimizing symptom exacerbation (i.e., gradual progression of task complexity). For a more detailed review of dynamic gaze stability following TBI, see the article by Wallace and Lifshitz.[70] Another major component of vestibular rehabilitation is restoration of postural control as patients may have difficulty maintaining balance when walking across different environments, especially under conditions of divided attention.[72] Overall, a comprehensive balance assessment is needed to assess visual dependency, postural responses, and use of vestibular cues. The therapist may then work with the patient to reduce visual resilience through closed eye activities before proceeding to oculomotor rehabilitation. Finally, as mentioned earlier, PPPD (a functional neurological disorder) and other psychological factors may have complex bidirectional interactions with vestibular dysfunction post-mTBI.

Cervical Dysfunction

Cervicogenic symptoms (such as neck pain or immobility) following mTBI are common and increase the risk of developing persistent PCS by 2.5 to 6 times.[75] Graded cervical manual therapy is the treatment of choice with evidence for reduced time to symptom resolution and medical clearance.[75] More detail on treatment approaches for cervical symptoms can be found in a recent systematic review.[75]

Overall Postconcussion Symptoms

Based on limited available data, aerobic activity appears to assist with mood, energy, and overall functioning in mTBI, but has more muted effects on cognition and balance and coordination.[76] The role of aerobic exercise in concussion recovery has been evaluated with reported benefits after as little as 20 minutes of exercise 5 to 6 days per week at 80% of the heart rate that provokes symptoms.[77,78] Graded exertional exercise should be incorporated along with pacing to limit the degree of fatigue in the early stages of recovery in those who have symptoms that are tolerable at rest.[76]

Cognitive Rehabilitation

Persistent self-reported cognitive deficits following mTBI are common.[79] Cognitive domains commonly affected include attention, memory, processing speed, and executive function—with some studies revealing associated changes in brain microarchitecture[80] and/or functional changes in brain subnetworks.[81] Sometimes deficits in those with mTBI are subtle and cannot be readily detected by standard clinical screening tools such as the MoCA.[82] Persistent objective cognitive deficits following mTBI with such tests are relatively uncommon.[83] It can be helpful to supplement PCS scales, which include only a small number of items querying general cognitive problems,[84–86] with other self-reported scales designed to characterize cognitive difficulties, such as the Behavior Rating Inventory of Executive Functions for Adults (BRIEF-A),[87,88] Dysexecutive Questionnaire Revised (DEX-R),[89] or the Cognitive Failures Questionnaire (CFQ)[90,91] which are well-validated scales originally developed for the moderate brain injury population but have also been used in the mTBI population. Issues flagged by such self-assessment tools can then be further investigated through formal neurocognitive testing or validated computerized test batteries.[92] Cognitive rehabilitation should be considered as a treatment option when clinically significant objective cognitive deficits have been found following valid testing.[18] Three examples of evidence-based interventions that have been manualized for cognitive rehabilitation include Attention Process Training,[93] Goal Management Training,[94] and CogSMART compensatory cognitive training.[95]

Attention Process Training is based on a clinical model of attention that was derived from observations from the assessment and rehabilitation of individuals with the full spectrum of traumatic brain injury.[93,96] The Attention Process Training program is a direct training approach aimed at improving underlying attention deficits found in patients with acquired brain injury through structured drills targeting specific attention areas in conjunction with metacognitive strategies (e.g., feedback, self-monitoring, strategy training).[97] Attention Process Training uses computer-based tasks to address attention in hierarchical manner across the different dimensions of attention and executive control (e.g., sustained attention, working memory, selective attention, suppression, and alternating attention). Attention Process Training has shown some efficacy for both adults[98,99] and pediatric populations with acquired brain injuries[100]; however, there are concerns regarding limited generalization beyond the actual tasks performed during the treatment.[101]

Building on a similar framework as Attention Process Training, Goal Management Training is an effective therapist-led metacognitive training program that has been used to improve executive functioning in a wide range of acquired brain injury populations[102] including mTBI,[103] the greatest effect being improvement on performance of instrumental activities of daily living that are sustained on follow-up. Unlike Attention Process Training, patients report that Goal Management Training strategies are readily applied and consolidated in everyday life well after the end of training.[104] It has been extensively reviewed[102,105] and draws upon theories concerning goal processing and sustained attention[106] which posit that executive deficits emerge from disruption of the sustained attention system which is responsible for maintaining higher order goals in mind while inhibiting automatic process—resulting in distracted behavior.[92] The aim of Goal Management Training is to train individuals to periodically stop ongoing behaviors to reevaluate and define goal hierarchies and monitor performance. This is achieved through a combination of psychoeducation, interactive tasks that help patients identify their own personal goals, in-class discussion of real-life examples of goal attaining failures, and homework assignments aimed at promoting greater self-awareness spread over approximately 20 hours of training (generally over the course of several weeks). Goal Management Training also incorporates mindfulness meditation to train one's ability to bring attention to the present moment to monitor the relationship between current circumstances and higher order goals.[102] Notably, Goal Management Training has not been extensively tested specifically within the mTBI population and this represents an avenue for future research. This patient population may be particularly well positioned to benefit from Goal Management Training, given its high metacognitive demand is not suitable for patients with severely compromised insight or memory impairments—skills that are generally well preserved in mTBI. In addition to studies utilizing classical Goal Management Training, there have also been several studies that have combined it with other training approaches such as errorless learning,[107] emotional regulation,[104] and problem-solving therapy.[108] Proprietary Goal Management Training kits are available through GoalManagementTraining.com.

Cognitive Symptom Management and Rehabilitation Therapy (CogSMART) training program aims to improve cognition (both subjective and objective neuropsychological performance) following mTBI.[95,109] It is a 12-week therapist-led intervention that involves psychoeducation about TBI, strategies to improve postconcussion symptoms such as insomnia, fatigue and headaches, and training of compensatory strategies in domains of prospective memory, attention, learning, memory, and executive functioning. The CogSMART program centers around teaching compensatory strategies to help clients work around cognitive deficits (e.g., using external reminders such as calendars and lists, or learning new encoding strategies to improve recall). In a randomized control trial involving veterans with mild to moderate TBI, those who completed the CogSMART program, compared with an active control group, reported significantly greater improvements in PCSs, prospective memory, and greater attainment of competitive work with small to medium range effect sizes at 12-month follow-up.[95,109] Notably, however, there is limited research using the CogSMART system for mTBI patients outside the veteran population. The CogSMART manual is available to the public free of charge at www.cogsmart.com.

While cognitive rehabilitation programs are generally facilitated through in-person programming, there have also been successful trials of tele-rehabilitation[110] as well as online self-directed cognitive training across TBI severity.[111] Indeed, there is growing evidence for the use of computer-based cognitive interventions that can be completed from home.[112,113] In a recent meta-analysis of such interventions applied toward a general acquired brain injury population,[113] these programs generally ranged from 10 to 20 hours of instruction spread over 20 to 30 sessions of 30- to 45-minute duration. However, compared with the manualized cognitive programs described previously,[93–95] the meta-analysis revealed less robust effects with significant improvements only in visual and verbal working memory, which also did not generalize to other aspects of cognition or daily living. This contrasts with equivocal improvements in cognitive symptoms observed in military service members with mTBI who received manualized rehabilitation versus computer-based rehabilitation. This suggests that the mTBI population may be more amenable to computer-based training compared with the general ABI population.[59] This has been highlighted by a recent randomized-control trial involving a plasticity-based cognitive training program (computer games tailored for specific cognitive domains with increasing difficulty) for veterans with mTBI. Following 13 weeks of 1-hour daily training 5 days per week, the intervention group had significantly improved composite scores of cognitive function in comparison to an active control group (standard computer games), with results sustained at 3-month follow-up.[114] Across these studies, improved cognitive test performance rarely translates into improved daily functioning, suggesting that combining self-directed cognitive training with other therapist-led interventions may be important.

Beyond cognitive training programs, other nonpharmacological methods for facilitating cognitive recovery following mTBI include optimizing management of other symptoms that may intimately interwoven with cognition. Most notably, this includes insomnia, pain/headaches, and mood dysregulation. Mindfulness-based stress reduction for reducing mental fatigue[115] and exercise programs are also important complementary considerations.[116] Interestingly, some have argued that CBT approaches to postconcussion symptom management may be more potent in reducing symptoms than traditional cognitive rehabilitation.[15]

Patients with mTBI often present with cognitive symptoms that do not coincide with objective evidence of cognitive impairment (e.g., on neuropsychological testing), particularly those with psychological distress.[117–119] In this case, treatment should be directed at psychological distress and/or negative beliefs about cognition (as discussed in the previous section) rather than at remediating or compensating for cognitive impairment. Indeed, improved postconcussion symptoms following cognitive rehabilitation may be mediated by reductions in psychological distress.[120] That said, we are not aware of any intervention studies to date specifically targeting cognitive symptoms in the absence of objective cognitive impairment after mTBI. Given the overlap with functional cognitive disorder presenting in other clinical contexts,[121,122] applying clinical management strategies for functional cognitive disorder may be helpful.[123,124] Lastly on the horizon, there is growing interest in the use of brain stimulation techniques such as repetitive transcranial magnetic stimulation (TMS) for improving cognition; however, results thus far have been mixed.[125,126]

Other Emerging Treatments

Neuromodulation

Accumulating neuroimaging research demonstrates evidence that concussion and PCS are disorders of brain network dysfunction,[127] and neuromodulation interventions targeting implicated brain regions and networks could offer an optimal new treatment strategy.[128] Technologies such as TMS, a safe, well-tolerated and noninvasive device with FDA approval for the treatment of depression, obsessive–compulsive disorder, and migraine, offer the potential for focal cortical stimulation.[129] Repetitive TMS (rTMS) has the most data to date for the management of concussion/mTBI compared with other neuromodulation technologies (e.g., transcranial direct current stimulation).

A recent systematic review on rTMS for concussion evaluated 11 studies ($n = 197$), the majority of which were sham-controlled with RCT designs, but all were small pilot samples ($n < 30$).[130] Postconcussive depression (seven studies) and headache (four studies) were the most commonly investigated symptoms. Positive results were found in two out of four studies with depression as a primary outcome, and all three studies that assessed depression as a secondary outcome. All four rTMS studies for postconcussive headache reported positive results. All seven of these studies targeted the dorsolateral prefrontal cortex (dlPFC), a well-recognized target from large trials of non-TBI depression,[131] that has been implicated in concussion pathogenesis.[132] The depression literature proposes therapeutic mechanism(s) based on the dlPFC's anticorrelation to the subgenual cingulate cortex and modulation of relevant default mode and central executive network dynamics.[133] The dlPFC may have also been selected in some of these reviewed trials for practical purposes, as there are established methods for stimulating this region without the need for MRI guidance (e.g., 5–6 cm anterior to the motor hot spot).[129] However, as highlighted in a case report by Siddiqi et al,[134] advanced targeting techniques such as individualized resting-state network mapping for treatment-resistant postconcussive depression could be an important new strategy moving forward. They identified left-right dlPFC rTMS targets that were spatially distinct from those identified by conventional methods, and rTMS applied to those targets resulted in dramatic improvement in depression scores.

Four trials included in the aforementioned review reported consistent benefits from high-frequency TMS targeting the left dlPFC on frequency and severity of posttraumatic headaches.[130] However, only one study found sustained improvements in posttraumatic headache at 1-month follow-up posttreatment,[135] and another study reported improved rates of return to work despite no significant group differences in headache pain or frequency.[136] Notably, posttraumatic headache severity/chronicity can be highly associated with mood and other psychological factors,[137] and thus it is possible that the benefits from this rTMS protocol on headache were due to improvement in mood. Moreover, there did not appear to be a mechanistic rationale specific to posttraumatic headache. Burke et al[138] recently showed that regions of gray matter volume loss in migraine patients localize to a common brain network defined by connectivity to the visual cortex. In addition, the direction of this connectivity implicated visual cortex hyperactivity and thus these findings may offer a mechanistic rationale for existing TMS migraine protocols (inhibitory to visual cortex).[138] Despite similarities in clinical phenotypes and potential shared underlying mechanisms of posttraumatic headaches and migraine, no posttraumatic headache rTMS treatment studies have investigated a visual cortex target to date.

Only one study in the aforementioned review specifically focused on postconcussive cognition as a primary outcome (alongside depression).[139] Compared with a sham stimulation group, 10 sessions of 2,000 pulses at 1 Hz over the right dlPFC was associated with significant improvements in working memory and executive function. However, they did not conduct any follow-up, and thus the results are limited. Moreover, post-TBI cognitive difficulties may partially be a direct result of the brain injury itself, but contributing postconcussive factors such as depression, headache/pain, and insomnia often perpetuate these deficits and disentangling etiological origins is challenging.[137]

Elucidating the efficacy of neuromodulation for PCS will rely on larger sham-controlled randomized trials, longer and more consistent follow-up periods, and incorporation of pre–post functional neuroimaging/neurophysiological measures to better understand relevant neurobiology and mechanisms of therapeutic response.

Music-Based Interventions

Music-based interventions are emerging as a new potential treatment strategy for neurologic[140] and psychiatric[141] patient populations, including TBI,[142] as they are safe, economic, and can be creatively tailored to meet specific functional goals. MuBIs are typically selected and delivered by a credentialed music therapist based on empirically supported models, and can involve active (improvisation, singing, clapping, or dancing) and/or receptive (purposeful music listening to identify emotional content emerging from music) techniques.[140] Mechanistically, MuBIs appear to engage both cortical and subcortical areas governing attention, working memory, planning, and flexibility and can modulate these areas over time.[140,143] In more recent years, a growing understanding of neuroscientific underpinnings of music processing has allowed more precise targeting of specific cognitive domains.[144,145] This has led to growing calls for the integration of MuBIs in the care pathway of TBI, particularly to target postconcussive cognitive impairment, and for more research to be done in this area.[142,146]

Only one study of MuBIs has focused on PCS after mTBI. Vik et al[147] evaluated the effects of an 8-week biweekly 30-minute piano instruction program for seven patients following mTBI compared with two healthy control groups (11 musicians, and 12 nonmusicians). Piano exercises gradually progressed in difficulty and patients were additionally required to practice at home for 15 minutes per day. All seven mTBI patients had received traditional cognitive rehabilitation during their outpatient care without improvement and were all on leave from work, despite being an average of 2 years postinjury. Patients with mTBI experienced significant improvements in California Verbal Learning Test-2 performance, and six of seven patients returned to work in their full premorbid capacity. Furthermore, these clinical changes were coupled with functional reorganization in the orbitofrontal cortex (OFC), specifically with increased connectivity between left anterior and posterior OFC compared with healthy controls, as well as increased connectivity between right middle prefrontal cortex, right anterior insular cortex, left rostral anterior cingulate cortex, and the right supplementary motor cortex,[147,148] which are important nodes in the salience and frontal-executive neural networks.[149] MuBIs may exert their procognitive effects in TBI by enhancing connectivity between the salience and frontal-executive networks, as well as reduced connectivity between salience network and default mode network.[143,150]

Given that TBI-related cognitive impairment has limited treatment options and MuBIs have no major risk of harm, MuBIs could be offered where resources are available. Ideally, delivery of MuBIs would be performed by a trained music therapist in collaboration with either an occupational or physical therapist following a validated protocol.[145,147,150] There is potential to deliver MuBIs by a credentialed music therapist virtually as well. However, many communities may not have access to therapists or specialized resources. This barrier can be overcome using modified self-directed protocols (e.g., learning an instrument via internet or phone-based applications, memorizing lyrics and singing along to favorite songs, or tapping along to the beat while listening to their favorite pieces of music, for at least 15 minutes daily), although collaboration among local university-based music therapy departments (if applicable) would be recommended. Additional resources and information on university-based music therapy programs and credentialed therapists can be found at nmtacademy.co, or www.musictherapy.org.

Placebo Effects

Placebo effects can be defined as beneficial therapeutic effects derived from contextual variables surrounding administration of a treatment rather than the treatment itself. There has been growing research demonstrating that placebo effects meaningfully modulate brain regions and neurotransmitter systems.[151] This includes activation of prefrontal circuits involved in expectation and assigning meaning/emotion (e.g., dlPFC, OFC, ACC) and reward centers (e.g., ventral striatum), as well as inhibition of anxiety and stress-response circuits (e.g., amygdala).[151,152] PCSs have been proposed to have high placebo responsiveness, and this makes sense as there is overlap between brain areas functionally altered in mTBI and those implicated in placebo neurobiology.[153] While empiric research on the topic of placebo effects and mTBI/concussion treatment is limited, the booming concussion "industry" of unregulated and/or alternative treatments might provide real-world evidence of the placebo responsiveness. Patients often anecdotally report major clinical improvement from such therapies (despite little or no evidence that they have a specific effect) and thus could be benefiting via mechanisms related to placebo effects. Furthermore, there are many device-based treatments whose elaborate and intensive therapeutic context could offer particularly large placebo effects.[154] This remains a very controversial topic with many scientific and ethical issues needing further study, most notably if/how placebo effects could be harnessed in concussion recovery.

Conclusion

A significant subset of patients may experience prolonged symptoms following concussion/mTBI that result in functional impairment. Core components of PCS management include psychoeducation and counseling on return to activities and exercise. Patients with an especially problematic symptom or two (e.g., headache or sleep problems) may benefit from specialized interventions targeted at those particular symptoms. Patients with a myriad of prolonged symptoms should be considered for multidisciplinary treatment. It is clear from the available literature that there is no one-size-fits-all approach for PCS. Thoughtful coordination of available resources tailored to the patient's needs should be the standard of care, especially for chronic and severe cases.[27] While there are no current "disease-modifying" treatments for concussion/mTBI, many promising new treatments are emerging, including neuromodulatory devices that could target specific brain circuits disrupted in concussion/mTBI.

Authors' Contributions

Concept and design: M.J.B., A.M. Drafting of the manuscript: A.M., A.D., M.C., N.S., M.J.B. Critical revision of the manuscript: A.M., A.D., M.C., N.S., M.J.B.

Funding

Investigators were supported by funding from the Liu Fu Yu Charity Foundation (M.J.B.).

Conflict of Interest

None declared.

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