Use of Complementary and Alternative Medicine in Treating Individuals with Traumatic Brain Injury

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Abstract This article presents an overview of the clinical trials literature on complementary and alternative medicine for traumatic brain injury. In searches of PubMed and the Allied and Complementary Medicine Database, trials of acupuncture, acupressure, creatine, homeopathy, hyperbaric oxygen therapy, mindfulness-based practices, music therapy, neurotherapy, Tai Chi, and yoga were identified. Because of the high risk of bias in most of the studies reviewed, the evidence base is inadequate to recommend any specific complementary and alternative medicine treatments for traumatic brain injury, although promising findings were identified for a number of treatments. Safety data on many of the interventions were lacking.

Keywords Complementary and alternative medicine · Traumatic brain injury · Clinical trials

Introduction

This article presents an overview of the research literature on complementary and alternative medicine (CAM) for individuals with traumatic brain injury (TBI), with a focus on clinical trials. It is not, however, a systematic review and we have not made attempts to formally grade the evidence. Rather, it is designed to educate the reader about

CAM and its relevance to persons with TBI and provide a synopsis of the “state of the science.”

What Is CAM?

The National Center for Complementary and Alternative Medicine (NCCAM) describes defining CAM as “difficult” for two reasons: first, because CAM covers a very wide range of interventions and, second, because what is considered CAM is in constant flux [1•]. CAM is therefore typically defined chiefly by what it is not. CAM encompasses all health interventions that are not part of “conventional” biomedical Western medicine as practiced by physicians with MD or DO degrees and allied health professionals (physical therapists, psychologists, registered nurses, etc.) [1•, 2]. This can include “natural products” (e.g., herbal remedies, vitamins), mind and body medicine (e.g., meditation, yoga), manipulative and body-based practices (e.g., massage, chiropractic manipulation), movement therapies (e.g., Feldenkrais method, Alexander technique), and energy therapies (e.g., Qigong, Reiki) [1•]. CAM also includes whole medical systems such as homeopathy and ayurvedic medicine and traditional Chinese medicine (TCM), and some CAM interventions cut across multiple categories [1•]. For example, acupuncture can be classified in four different ways (mind and body, energy, manipulative and body-based, TCM) [1•]. Some interventions may even overlap with each other (e.g., mindfulness practices and yoga). CAM interventions are said to be complementary when used in tandem with standard biomedical approaches and alternative when used instead of such approaches.

The boundaries between CAM and conventional medicine can be fluid, and some CAM interventions have crossed over to a greater or lesser extent into conventional medicine (e.g., use of omega-3 fatty acids [3], relaxation

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training [4]). Patterns of use also differ from country to country, with widespread use of CAM approaches in the developing world (e.g., 40 % of medical care in China, 80 % of care in Africa [5, 6]) and regional variations in developed countries (e.g., greater use of homeopathy and acupuncture in German-speaking countries [7•]).

Why Is CAM Important?

CAM is important for several reasons. First, it is widely used and popular, even in countries where most people have access to Western biomedical interventions [7•]. Frass et al. [7•] conducted a systematic review of studies of CAM use in Asia, Australia, Europe, and North America involving more than 275,000 respondents. Although there was considerable variability in self-reported use of CAM (5–75 %), on average, about a third of respondents reported using CAM treatments. Chiropractic, herbal medicine, massage, and homeopathy were the most widely used interventions. The findings also indicated a clear increase in the proportion of people using CAM over time. In the USA, use of CAM in adults increased from 36 % in 2002 to 38.3 % in 2007, with pain being the most frequent treatment target [8•]. Reflecting this popularity, CAM interventions are increasingly covered by health insurance and made available through public health services [9–11]. Unfortunately, research on CAM lags behind biomedical research and is inadequate both in quantity and in quality [12, 13]. This is of grave concern, as it limits the ability of patients and health care practitioners to make informed decisions regarding the risks and benefits of CAM interventions. The value of the CAM industry is estimated at \$60 billion a year [14], including \$34 billion a year in the USA [8•, 9], a significant cost to patients, payers, and tax payers for interventions with limited evidence to support their safety and efficacy.

A second important issue related to CAM use is that CAM treatments are often perceived as safe because they are “natural” [15] despite the fact that they can be harmful on their own [1•, 16, 17] or in combination with other treatments [1•, 18, 19, 20]. Their use as alternatives to biomedical care (as opposed to as complementary treatments) may also result in unnecessary morbidity [21]. The fact that CAM treatments are often loosely regulated or unregulated by government agencies is also cause for concern. This lack of oversight makes CAM users more vulnerable to charlatans and exploiters of the credulous [22].

A third reason that CAM is important is that it is a potentially valuable resource in the armamentarium of patients and clinicians. CAM approaches may provide relief for patients who cannot be helped adequately by other methods. Many patients have positive perceptions of CAM and believe it to be helpful [23•, 24] but are

concerned by their traditional health care providers’ ignorance about or resistance to CAM [25]. Physicians’ attitudes to CAM appear to differ depending on the type of therapy under consideration, highlighting another problem with lumping so many treatment approaches under the CAM rubric [10]. Indeed, there is considerable controversy over CAM, with seemingly entrenched opinions on either side as to whether its benefits are merely placebo effects [22]. Whereas some arguments center around whether or not CAM treatments can be fairly tested at all using existing methods [26, 27•], others focus on the theoretical underpinnings of CAM approaches [28], and around the quality of the evidence for and against them [29, 30].

Relevance of CAM for TBI

Increasingly, TBI is coming to be seen as a chronic health condition resulting in fluctuating cognitive, physical, emotional, and behavioral symptoms as well as comorbidities and functional difficulties [31]. Because of the diversity of TBI-related challenges, treatment typically needs to be multimodal [32], and some medications or pharmacological combinations may exacerbate or create symptoms. Furthermore, the evidence base for pharmacological and behavioral treatment of chronic TBI is still quite limited [33]. For these reasons and because of initial indications of interest in CAM in TBI populations [23•] and the population at large [8•], better understanding of the evidence for CAM is warranted among rehabilitation professionals. The purpose of this review is therefore to summarize the research on CAM in individuals with TBI.

Method

We conducted a search of the PubMed database and the Allied and Complementary Medicine Database (AMED) using a variety of search terms from the NCCAM website listing of CAM therapies and from reviews of the CAM literature. Search terms were “traumatic brain injury” and those listed in Table 1. Only controlled clinical trials and meta-analyses published in English, French, or Hindi in peer-reviewed journals were considered. This search yielded 141 articles (83 from PubMed and 58 from AMED), of which 16 were included. All were in English. Five systematic review articles yielded an additional ten studies (four in English, five in Chinese, one in German) for a total of 26 articles reporting on 23 clinical trials and one meta-analysis. Where available, Cochrane review conclusions were given preference over those from individual articles. Articles on aerobic exercise, inpatient parenteral and enteral nutrition techniques, therapeutic hypothermia, psychotherapy, and oculomotor rehabilitation were not

included because they are not normally considered to be CAM. Studies without TBI controls or with mixed brain injury samples (e.g., stroke and TBI) where TBI results were not reported separately were also excluded.

Results

Relevant articles were identified in the CAM domains described below.

Natural Products

Creatine

Creatine is an amino acid that is produced in the liver, kidney, and pancreas [34]. Creatine is thought to offer therapeutic benefits by stimulating protein synthesis or reducing protein degradation, stabilizing biological

membranes, and preventing adenosine triphosphate depletion, which occurs in patients with TBI [35].

Sakellaris et al. [35, 36] conducted a randomized controlled trial (RCT) in which 39 children aged 1–18 years with severe TBI were randomized to receive a daily dose of 0.4 g/kg creatine in an oral suspension of water or apple juice ($n = 20$) or no treatment ($n = 19$) for 6 months. It appears that treatment began on the inpatient unit and continued at home after discharge. The groups were not significantly different at the baseline, and outcomes were assessed by a blinded physician 3 and 6 months after injury. Two children in each group died within 3 months of injury. No other adverse events were reported. The duration of intubation, stay in the ICU, hospital stay, and posttraumatic amnesia were all shorter in the creatine group, but only the duration of post-traumatic amnesia was statistically significantly shorter ($p = 0.019$). Three-month outcomes were significantly better in the treatment group on the extended Glasgow Outcome Scale (GOS) ($p = 0.004$) and differential outcome scale ($p < 0.001$ – 0.006), but not on the assessment of functional

Table 1 Search terms and articles found by complementary and alternative medicine category

Category	Search term	Articles included
General terms	Alternative medicine, complementary	NA
Art therapies	Art, dance, music	None
Natural products	Creatine	Sakellaris et al. [35, 36]
	Antioxidants, cannabis, chelation, dietary supplements, Echinacea, ginkgo, ginseng, herbal, naturopathy, nutrition, saw palmetto, valerian, vitamin, wort	None
Mind and body medicine/ manipulative and body-based practices/energy therapies	Acupressure	McFadden et al. [38]
	Acupuncture	Wong et al. [39•], Ding et al. [40], Song et al. [41], Cao et al. [42], Chang and Liu [43], Zollman et al. [44]
	Mindfulness	McMillan et al. [48]
	Tai Chi	Gemmell and Leathem [50], Blake and Batson [51]
	Yoga	Silverthorne et al. [52]
	Breathing, chiropractic, hypnosis, imagery, massage, meditation, osteopathy, Qigong, Reiki, relaxation, touch	None
Movement therapies	Alexander technique, Feldenkrais, Rolfing	None
Medical systems	Homeopathy	Chapman et al. [54•]
	Ayurvedic, Chinese medicine, naturopathy	None
Other approaches	Hyperbaric oxygen therapy	Bennett et al. [57•], Rockswold [59], Xie et al. [60], Rockswold et al. [61, 66], Ren et al. [62], Artru et al. [63], Mao et al. [64], Holbach et al. [65], Wolf et al. [69•]
	Biofeedback, neurofeedback	Tinius and Tinius [71] Schoenberger et al. [72]

Categories have been collapsed where search terms fit into multiple categories. All search terms are listed in only one category, even if they fit into more than one.

NA Not applicable

outcome in children with head injury (FOC). At 6 months, 89 % of the creatine group had “good recovery,” compared with 6 % of the control group ($p < 0.001$), and had significantly better FOC cognitive ($p < 0.001$) and personality/behavior ($p < 0.001$) scores and FOC self-care ($p = 0.029$) and communication ($p = 0.018$) scores. Although these results suggest significant potential benefits of creatine, the sample was small, reporting of the method was incomplete, and the absence of a control treatment is a significant source of bias.

Mind and Body Medicine/Manipulative and Body-Based Practices/Energy Therapies

Acupressure

Acupressure is a form of TCM and is thought to act by affecting the flow of a vital force known as Qi and relieving imbalances that may be present by either stimulating or easing the flow of Qi [37]. Acupressure involves the application of pressure to specific points on the skin (acupoints or meridian points) using hands, fingers, or thumbs to affect the flow of Qi [37, 38]. It is distinct from acupuncture in that it is noninvasive and does not involve penetration of the skin with a needle [39•]. The exact mechanism through which acupressure works remains unclear, although theories postulate various mechanisms, such as its impact on the release of neuropeptides, activation of the opioid system [37], and modulation of the autonomic nervous system to reduce respiration, heart rate, and blood pressure [38].

McFadden et al. [38] conducted a single-blind RCT to investigate the effects of eight 40-min acupressure treatment sessions on cognitive sequelae of TBI. In their study, 42 community-based adults aged 18–44-years with mild-to-moderate TBI were randomized using a random number generator to receive either active acupressure treatment or sham acupressure treatment. Cognitive function (working memory, attention, motor speed, and spatial problem solving) was assessed using a battery of neuropsychological tests. To assess neurophysiological changes, event-related potentials were recorded while participants were engaged in the Stroop task. Compared with those in the placebo group, those in the active acupressure group demonstrated a reduction in P300 latency (increased speed with which memory operations occur) ($p = 0.011$) and amplitude (the degree of memory engagement) ($p = 0.010$). The active-treatment group also demonstrated improvements in attention as compared with the placebo group on the Stroop task and Digit Span task ($p < 0.05$). There were no significant between-group differences on other measures of neuropsychological function or measures of anxiety, depression, or loneliness. The study only assessed immediate effects of

acupuncture. Adverse effects were not reported. No power analysis or measures to control for multiple comparisons were reported, and thus the study has increased risk of both type I and type II error.

Acupuncture

Acupuncture is one of the best known and most medically accepted forms of CAM [10] and has been practiced in China and other Asian countries for thousands of years. Acupuncture most commonly involves penetrating acupoints (see the definition of acupressure) with thin, solid, metallic needles either by hand or through electrical stimulation [39•].

A Cochrane review of the empirical literature assessed the safety and efficacy of acupuncture in the acute management or rehabilitation (or both) of patients with a TBI [39•]. This review is particularly valuable to non-Chinese-speaking audiences because it surveyed the Chinese language medical literature. The authors of the review identified 37 articles (three in English and 34 in Chinese), of which 33 were excluded owing to low methodological or reporting quality. All four studies that were included were RCTs but were deemed to carry a high risk of bias (e.g., failure to report randomization sequence generation and allocation concealment, failure to blind, failure to use a placebo or sham control group). The trials included a total of 294 participants and compared needle acupuncture or electroacupuncture plus another therapy with the other therapy alone. No adverse effects were reported. The studies found improvements relative to control treatment acutely in the Glasgow Coma Scale scores ($p = 0.02$) [40], GOS scores ($p < 0.00001$ [40], $p = 0.04$ [41]), and motor and speech functions ($p = 0.0002$) [40]. After rehabilitation, participants receiving acupuncture had improvements compared with controls in overall functional outcome on the Barthel index ($p = 0.006$) [42] and modified Barthel index ($p < 0.00001$) [43], in motor function measured using the Fugl–Meyer assessment ($p < 0.00001$) [43], and in muscle strength grading ($p = 0.001$ – 0.0001) [42].

In a pilot RCT of the effect of acupuncture on insomnia, cognition, and mood after TBI, 20 participants were randomized to receive treatment as usual plus acupuncture or treatment as usual alone [44]. Sleep time and insomnia severity did not differ significantly between the groups after treatment, although there were significant within-group improvements in the acupuncture group insomnia severity ($p < 0.01$). The acupuncture group also showed improvements on measures of cognition ($p < 0.01$, $p = 0.01$) and depression ($p < 0.01$) not seen in the control group. Unfortunately, this study had a risk of bias comparable to the studies identified in the Cochrane review [39•]. Clinical trials with lower risk of bias are necessary to

determine if acupuncture is safe and effective in individuals with TBI.

Mindfulness-Based Practices

Mindfulness-based practices (MBPs) are based on training in the Eastern contemplative practice of mindfulness and aim to create greater awareness and acceptance of the here and now [45, 46]. Research suggests that MBPs improve psychological difficulties such as anxiety, stress eating and affective disorders, and psychological and physical function in medical conditions such as cancer, multiple sclerosis, and chronic pain [47].

In a single-blind RCT of 145 individuals with TBI of varying severity, McMillan et al. [48] used attentional control training (ACT), a breathing-based procedure modeled on mindfulness techniques. Forty-four subjects with differing degrees of TBI severity were randomized to receive five 45-min sessions of practice using an ACT audiotape with limited therapist contact. When compared with participants receiving physical exercise treatment ($n = 38$) or no treatment ($n = 48$), the group receiving ACT treatment did not differ significantly on measures of cognitive function, mood, or symptom reporting following therapy [48]. It is not clear from the study if adverse effects were assessed, and randomization procedures were not described. The existing evidence thus does not support the use of MBPs in TBI, at least, as delivered on audiotape.

Tai Chi

Tai Chi is a martial art form developed in China around the seventeenth century. Rooted in the Chinese philosophical tradition of Taoism, Tai Chi entails practicing diaphragmatic breathing with soft, low-impact and low-speed movement [49]. Tai Chi has been shown to improve functioning in various psychological and physiological conditions, such as cardiovascular, orthopedic, and neurological diseases [49].

Gemmell and Leathem [50] used a wait-list controlled RCT design to study the effects of a 6-week Tai Chi course where 18 participants with TBI received two 45-min sessions per week. The study found significant within-group improvements in mood states (as assessed by the visual analogue scale), such as anger, confusion, sadness, being afraid, tension, energy levels, and happiness after Tai Chi. However, there were no between-group differences in the various mood states. Further, the investigators did not find significant differences between the intervention group and the wait-list control group in self-esteem or in physical, social interactions, or mental well-being [50]. Activities were significantly less impaired because of emotional problems (emotional role) in the Tai Chi group than in the

wait-list group ($p = 0.007$). Sources of potential bias in the study included failure to control for multiple comparisons, failure to report between-group differences at baseline and after the intervention, and small sample size.

In a pilot unblinded RCT, Blake and Batson [51] examined the effects of an 8-week Tai Chi Qigong intervention; Tai Chi Qigong is a form of Tai Chi that has fewer physical and cognitive demands than ordinary Tai Chi. Participants with TBI at a day center were randomly assigned using a computer-generated random number table to receive the intervention ($n = 10$) or to a control group ($n = 10$). No adverse events were reported by any of the participants, and small but significant improvements in mood scores ($p = 0.026$) were noted in the Qigong group as compared with the control group as well as significant within-group changes for the Qigong group in mood and physical self-esteem. ($p = 0.042$; $p = 0.017$). There were no significant between-group differences in self-reported and family-reported measures of physical functioning, flexibility, self-esteem, and social support for exercise habits. The study only reported on the immediate effect of the intervention and did not assess long-term effects [51]. Larger, more rigorous clinical trials are needed to fully explore the potential benefits of Tai Chi in individuals with TBI.

Yoga

Yoga is an ancient mind–body practice of Indian origin that typically involves use of physical postures, breathing techniques, and meditation or relaxation [1•]. In a nonrandomized study of the benefits of breath-focused yoga on respiratory, physical, and psychological functioning in individuals with severe TBI, ten individuals who attended 40 weeks of weekly yoga classes were compared with four controls who received no treatment [52]. The yoga group experienced significant improvements on measures of respiratory functioning and self-reported physical and psychological well-being, but controls showed only marginal improvement. However, the groups were not compared statistically. Owing to the very high risk of bias in this study, no conclusions can be drawn about the efficacy of yoga for individuals with TBI.

Medical Systems

Homeopathy

Developed in Germany by Samuel Hahnemann at the end of the eighteenth century, homeopathy uses remedies that are derived from plants, minerals, or animals. The main principle underlying homeopathy is that of *similia similibus curentur* (“like is cured by like”), which holds that a disease can be cured by a dilute version of a substance that produces similar symptoms in healthy people [53]. Homeopathic remedies are

diluted many times until they contain little or none of the supposedly curative substance. The healing properties of the substance are thought to be “remembered” by the water in which it is diluted and intensified with each dilution. Homeopathy is highly controversial as its tenets violate basic principles of physics and chemistry [28].

Chapman et al. [54•] conducted a well-designed, adequately powered, double-blinded RCT of homeopathic treatment versus placebo in 60 individuals with chronic mild TBI whose injury had occurred at least 3 months prior to study enrollment (mean 2.93 years). Homeopathic treatment was customized on the basis of individual symptoms as is standard practice in homeopathy. Each subject in the active-treatment group received only a single medicine selected by consensus of two study physicians from a list of 18 possible remedies (e.g., silver nitrate, water hemlock, Indian cockle, bushmaster snake venom, nutmeg, silica). The efficacy of homeopathy in improving self-reported symptoms, functional disability, and participation in daily activities was examined. A multivariate analysis combining the three primary outcomes showed a significant benefit of homeopathy over placebo ($p = 0.046$). Further analyses indicated that the effects on the measures of self-reported symptoms and participation were not significant, although the effect on functional disability was significant ($p = 0.009$) and the effect size was in Cohen’s “medium” range. When the ten most frequent TBI symptoms were examined, there was a significant effect for homeopathy compared with placebo ($p = 0.027$). Adverse events were infrequent. They included increased depression (one in each group) and, in the homeopathy group, nausea, vomiting, dizziness, slight fever, and fluctuation in cognitive symptoms. Despite the promising results of this study, no further trials of homeopathy in individuals with TBI have been published. Given that systematic reviews suggest that homeopathy does not have effects beyond placebo for many conditions [55], further trials of homeopathy in TBI are indicated to determine if the results of Chapman et al. can be replicated.

Other Approaches

Hyperbaric Oxygen Therapy

In the acute phase after TBI, ischemia and anaerobic metabolism can lead to a chemical chain reaction at the cellular and mitochondrial level which may result in secondary brain injury and death [56]. Hyperbaric oxygen therapy (HBOT) involves exposing the injured individual to 100 % oxygen in an airtight vessel at greater than normal atmospheric pressure in order to increase oxygen supply to the brain, reduce swelling, and limit damage [57•]. HBOT is a good example of a therapy which straddles the boundary

between conventional medicine and CAM with some medically accepted clinical applications (e.g., for carbon monoxide poisoning) and others that are considered CAM (e.g., for cerebral palsy) [58].

A Cochrane review and meta-analysis [57•] to assess the adjunctive effects of HBOT in individuals with TBI identified seven trials that met the inclusion criteria [59–65]. The trials included data on 571 participants (285 HBOT and 286 control) and dosing was highly variable (three to 40 sessions). The risk of bias was high. No trial sham treatments were administered, blinding was generally not used, and adequate randomization procedures were not described. In two of the studies, unfavorable outcome scores on the GOS 1 month after treatment were significantly lower than in the those treated with HBOT [relative risk for unfavorable outcome with HBOT 0.74, 95 % confidence interval (CI) 0.61–0.88, $p = 0.001$]. There was also evidence of a significant reduction in the risk of death for those receiving HBOT (relative risk 0.69, 95 % CI 0.54–0.88, $p = 0.003$). There were also suggestions of benefits for intracranial pressure in individuals with myringotomy and improvement in Glasgow Coma Scale score (MD 2.68 points, 95 % CI 1.84–3.52, $p < 0.0001$). There was evidence of some increased risk of significant pulmonary impairment in those receiving HBOT ($p = 0.007$). Overall, there was no evidence of improvement in long-term functional outcome or performance of activities of daily living in those receiving HBOT.

In an RCT of combined HBOT and normobaric hyperoxia compared with standard treatment in 42 individuals with severe TBI, Rockswold et al. [66] found an absolute reduction of 26 % in mortality for the combined-treatment group ($p = 0.048$) as well as an absolute 36 % improvement in 6-month GOS favorable outcome ($p = 0.024$) using a blinded assessor. This suggests that HBOT, in combination with normobaric hyperoxia, may have beneficial effects on outcomes.

There is also some interest in HBOT as a postacute treatment for milder forms of TBI, particularly in the military [67, 68]. In a double-blind RCT at the US Air Force School of Aerospace Medicine, 30 sessions of HBOT or sham HBOT over 8 weeks were used to treat postconcussion symptoms in 50 military service members with one or more mild TBIs. Symptoms were measured before treatment and 6 weeks after completion of treatment. The symptoms of both groups improved, and there were no differences in outcomes for the two groups [69•].

The literature on the benefits of HBOT is mixed, although there are indications that it may reduce the risk of death and improve some clinical parameters when administered acutely. The evidence gathered to date suggests that it does not lead to improved long-term outcomes when administered in isolation nor to improvements in

postconcussion symptoms. Well-designed, blinded, controlled trials are necessary to assess its benefits.

Neurotherapy

Neurotherapy or EEG biofeedback uses operant conditioning of brainwave patterns to restore normative electrophysiological functioning in the brain, and there are several methods for doing so [70].

Keller used standard EEG neurofeedback to treat attentional impairments in 12 individuals with TBI of moderate severity still in the phase of spontaneous recovery. They were compared with a matched control group of nine individuals who received computerized attention training [71]. Group assignment alternated and no blinding was described. Both groups showed improvements on attention tasks, but the neurofeedback group showed significantly greater improvement on two attention measures ($p = 0.032$ and 0.006).

The Flexyx neurotherapy system combines EEG biofeedback and photic stimulation using glasses with light-emitting diodes that translate EEG signals into subthreshold LED pulses [72]. A small wait-list-controlled RCT ($n = 12$) found significant improvements in the treatment group compared with the control group in primary symptoms ($p < 0.01$), depression ($p < 0.02$), general fatigue ($p < 0.02$), mental fatigue ($p < 0.02$), and neuropsychological measures of attention ($p < 0.05$), verbal learning ($p < 0.03$ – 0.05), and complex attention ($p < 0.03$) [72].

The limitations of these studies include small sample sizes, lack of blinding, inadequate randomization procedures, failure to correct for multiple comparisons, and the lack of an active control (Flexyx). Although the study results were promising, these limitations introduce significant risk of bias.

Excluded Articles

A number of articles showing therapeutic benefits were excluded on methodological grounds (e.g., use of mixed samples and absence of adequate control groups) in the areas of outpatient HBOT [68], MBPs [73–75], music therapy [76–79], neurotherapy [39, 70, 71, 80, 81], and osteopathic manipulative therapy [82].

Conclusion

There is insufficient evidence regarding the efficacy and safety of CAM treatments in individuals with TBI to make practice recommendations. Further research with low risk of bias in the areas of acupuncture, creatine, HBOT, homeopathy, and neurotherapy is necessary to replicate and build on initial promising findings. Studies should include appropriate

control interventions and groups, adequate blinding, adequate randomization procedures, specification of primary outcomes, and sample sizes based on power analyses, and should control for multiple comparisons. Other areas of CAM hold promise for TBI, but research is sparse and of low methodological quality. For example, art therapies [76, 83] and yoga [84] should, in theory at least, hold a host of potential benefits for individuals with TBI, such as improving attention and other cognitive functions, improving balance and coordination, reducing stress and distress, facilitating communication, and facilitating adjustment to disability. Further research in these areas is needed to supplant the largely anecdotal reports of benefit [85]. Future CAM trials should systematically measure and report adverse effects.

Given the popularity and widespread use of CAM interventions and their potential for benefit and harm, rigorous study of CAM interventions should be a funding priority. In the meantime, clinicians considering referring individuals with TBI to CAM and individuals with TBI considering using CAM should educate themselves by seeking out the extensive research literature on CAM and using resources such as the NCCAM website. It is recommended that they exercise appropriate openness, caution, and skepticism in considering CAM approaches and the claims for their safety and efficacy.

This study was not a systematic review and did not use exhaustive search techniques and formal evidence grading. Nor was evidence with the highest risk of bias included (case studies, uncontrolled trials). Thus, it does not present a complete picture of the CAM literature in TBI.

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Compliance with Ethical Requirements This article does not contain any studies with human or animal subjects performed by any of the authors.

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