Transcranial Low–Level Light Therapy: A New Hope for Preventing Cognitive Consequences of Traumatic Brain Injuries?

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In this issue of JAMA Network Open, Figueiro Longo et al1 describe the results of a randomized, sham-controlled trial that investigated the effects of transcranial low-level light therapy (LLLT) in inducing a neuroprotective response in the acute period after a traumatic brain injury (TBI) in humans. To my knowledge, this was the first clinical study using LLLT with the objective of helping patients with TBI to recover.

Traumatic brain injury can generate a wide range of physical, cognitive, and emotional disabilities, such as cranial nerve damage, neuroendocrine disorders, spasticity, permanent memory loss, posttraumatic sleep disturbances, emotional liability, augmented aggressive behavior, and even psychosis.2 The high frequency of physical trauma and the large variety of severe, trauma-related disorders make TBI a major cause of disability worldwide. The Global Burden of Diseases, Injuries, and Risk Factors Study of 2016 estimated that 759 persons of every 100 000 (age-standardized rate) currently live with disability after having experienced a TBI.3

So far, attempts to prevent the trauma have not contained the growing number of patients living with traumatic sequelae. Globally, between 1990 and 2016, the estimated TBI-related years lived with disability have increased by 8.4%. Mostly, this increase has been associated with the increasing rates of falls and road-associated injuries. Despite primary prevention efforts, those rates probably keep increasing as a consequence of the more frequent use of motor vehicles, unsafe road conditions, and higher alcohol consumption. In addition, in some conflict-affected countries of the Middle East, such as Syria, Iraq, and Yemen, or in countries with high rates of street violence, the incidence of TBI because of war, terrorism, and crime has not dropped significantly in recent years.3

If trauma cannot be prevented, secondary and tertiary prevention efforts might mitigate the development of disabilities after trauma and create better coping strategies regarding permanent functional impairments. Given the individual variability of trauma and the severity of its consequences, prevention and mitigation of TBI-related disabilities require long-term therapeutic programs that are individually tailored, intensive, and high cost. Multidisciplinary rehabilitation programs, including neuropsychological evaluation, cognitive retraining, physical and psychological therapy, and pharmacologic approaches to posttraumatic symptoms, have been the highest standard. Adjuvant treatments with potential neuroprotective effects, such as the use of amantadine or progesterone in the early phases of recovery, have yielded mixed results in randomized clinical trials including patients with severe TBI.4,5 Despite recent developments, the long-term follow-up of those who experienced a TBI suggests that there is still room for improvement.6,7

If proven safe and effective, LLLT could reduce disabilities produced by TBI and improve outcomes from such rehabilitation programs. According to Longo et al1, one of the mechanisms involved in TBI is axonal injury of white matter tracts leading to neuronal disconnection. Transcranial LLLT may induce recovery of myelin in axonal ramifications. Hypothetically, with the reinstauration of lost connections in the white matter tracts, some cognitive and emotional consequences of head trauma could be minimized.

To evaluate LLLT effectivity, however, is not an easy task. Given preclinical results, LLLT should be administered within 72 hours of injury. Very severe TBI or only mild TBI were not ideal grounds for testing cognitive improvement; therefore, Longo et al1 chose to recruit only patients with...
moderate-severity TBI. In a single emergency care unit, after two and a half years and the assessment of 4216 patients, researchers were able to allocate only 59 patients to LLLT or sham treatment.

In addition, owing to issues regarding acute-phase neuropsychological evaluation and short-term follow-up capacity, cognitive performance and assessment of emotional disturbances were not the main outcomes in Longo et al's study. Researchers have mainly relied on surrogate measures: magnetic resonance imaging diffusion parameters of the 18 major white matter tracts and scores on the Rivermead Post-Concussion Symptoms Questionnaire. At the end of the study, only 40 participants had 2 or more magnetic resonance imaging scans and produced main outcome data.

The main conclusion of the Longo et al study is that LLLT is safe when applied in the acute phase of TBI. However, given sample size restriction and the use of surrogate measures, it is too soon to reach a conclusion about LLLT efficacy. It is certainly justifiable to pursue further investigation. Larger multicenter trials with longer follow-up periods are the next step and should be pursued.

Notwithstanding, given the complexity and variability of TBI-related disabilities, it is unlikely that LLLT will assume an isolated role in the secondary prevention of physical, cognitive, and emotional repercussions of TBI. Individually tailored multidisciplinary rehabilitation programs will probably continue to be the standard of care after moderate and severe TBI. The adjuvant use of LLLT will be justifiable if proven cost-effective in reducing trauma sequelae or in shortening time to recovery from trauma. Moreover, pursuing gains in TBI treatment should accompany continuing investment in primary prevention strategies. Preventing trauma from falls, road accidents, terrorism, violence, and crime has the highest potential to achieve worldwide reduction of TBI-related disabilities.