

# FAQs Related to Mild Traumatic Brain Injury Study

## **What makes this newsworthy?**

Mild Traumatic Brain Injury (mTBI) is the signature injury of recent military conflicts (diagnosed in more than 300,000 members of the US armed forces). Many service members and Veterans suffer physical, psychological, emotional, and cognitive problems for years after their injury. To date, there has been no effective intervention for persistent cognitive deficits from mTBI that can be broadly applied across the diverse mTBI population. With today's publication of results in *Brain: A Neurology Journal* (of a four-year, DoD-funded study, conducted at five military and Veterans' medical centers), that has changed. A plasticity-based, computerized, brain-training program (BrainHQ) became the first such intervention shown effective in improving overall cognitive performance. In addition, the study showed that the intervention could be applied remotely (in patients' homes, under remote supervision from a coach) and broadly across the study's mTBI population.

## **What issue did the study focus on?**

More than 413,000 members of the US military have been diagnosed with a Traumatic Brain Injury (TBI). Of these, more than 82% are classified as mild TBI (mTBI), commonly following concussion or blast exposure. In many cases, servicemembers can experience a full recovery from a "mild" TBI – but for those who do not, cognitive consequences can persist for years with life-altering results. This risk is notably higher for servicemembers returning from the Iraq and Afghan conflicts than for civilians – and as a result, this injury has been called the "signature injury" of those conflicts.

Current best practices for treatment of persistent cognitive deficits in people with a history of mTBI focus on in-person, customized cognitive rehabilitation, which can be helpful, but is costly, time-consuming, requires travel for treatment, and relies on the craft and expertise of the healthcare provider.

No computerized cognitive training has previously been shown effective in a gold-standard study. This study focused on whether a plasticity-based, computerized brain training intervention could be broadly and remotely applied and could produce significant improvements in persistent cognitive deficits across a diverse population.

## **What was the design of the study?**

This was a multi-year, multi-site, prospective, parallel-armed, double-blinded, randomized controlled trial, with an active control group. The DoD funded the BRAVE study with a research

grant from the Congressionally Directed Medical Research Program (CDMRP) to examine the use of a brain-plasticity-based cognitive training program (BrainHQ) as an intervention for service members and Veterans suffering from cognitive impairment following mTBI. The study was conducted through a nationwide network of five military and Veterans' medical centers (NICoE/Walter Reed National Military Medical Center in Bethesda; Schofield Barracks/Tripler Army Medical Center in Honolulu; Baylor/Michael E. DeBakey VA Medical Center in Houston; Yale/VA Connecticut Healthcare System in West Haven; and Harvard/VA Boston Healthcare System in Boston); with Posit Science in San Francisco as the study coordination center.

### **How was the study conducted?**

BRAVE enrolled 83 participants with a history of mTBI and diagnosed with cognitive impairment, and randomized subjects into a treatment group (BrainHQ) and an active control group (computer games). Both activities were plausibly expected to have some positive impact due to their demands on cognitive realms, such as attention, memory, and reasoning. Each group self-administered training in their own homes, with telephone supervision from trained coaches, and were asked to train for one hour per day, five days per week, over twelve weeks. Comprehensive cognitive assessments were performed before training, after training, and after a twelve-week, no-training, follow-up period.

### **Who was in the study?**

Study participants had an average age of 33 years and were 81% male. Before training, they showed meaningful cognitive impairment, testing about 2 standard deviations below normal scores on the ANAM (a standardized cognitive test used by the military to screen for cognitive impairment). Typically, participants had been deployed to combat areas and, on average, had their most recent mTBI more than seven years earlier. Across a standardized set of emotional and psychological health measures (including depressive symptoms, PTSD symptoms, and cognitive symptoms), participants scored in the mild-moderate impairment range. On the whole, these participants were representative of service members with a history of mTBI who then seek treatment for their cognitive issues so they can re-integrate with, and contribute to, society.

### **What did the study show?**

Statistical analysis showed that the BrainHQ group had a statistically and clinically significant improvement on overall cognitive function compared to the computer games group, and this benefit persisted for at least twelve weeks after training ended. Cognitive function improvements were 3.9 times larger in the BrainHQ group than the computer games group, as measured immediately following training, and 4.9 times larger when measured again 12 weeks later.

Twice the percentage in the BrainHQ group showed reliable improvements compared to the computer games group – with 77% in the intervention group experiencing clinically significant

change compared to 38% in the active control; and with 37% in the intervention group experiencing a full standard deviation of change compared to 18% in the active control.

On average, participants in the BrainHQ group improved on the cognitive performance composite measure by 24 percentile ranks – as though they went from the 50th percentile to the 74<sup>th</sup> percentile.

While results on the primary cognitive measure were significant, analysis of functional and self-report measures did not show significant between group differences. However, on many measures both groups showed improvement, suggesting general benefits of cognitive engagement and study inclusion.

### **What are the implications?**

Treatment of post-concussive syndrome following mTBI is complex, and patients typically manifest distinctive sets of physical, mental, emotional and cognitive symptoms that require individualized courses of treatment.

This trial provides significant evidence that this specific form of self-administered brain-plasticity-based cognitive training can be incorporated as part of an evidence-based treatment plan to improve cognitive function in people with cognitive symptoms following mTBI.

This is the first broadly-applicable and highly-scalable approach in an mTBI population shown effective in a randomized controlled trial.

This is the first such approach applicable even in remote locations.

The reliance on cloud-based software to deliver the intervention should make this approach relatively inexpensive. The retail price for the software portion of the intervention used in the study is \$8-14 per month, plus there was cost for weekly telephonic coaching supervision provided in the study by personnel at a military/VA hospital.

### **When will this be available as a treatment for service members with mTBI?**

BrainHQ has been used in dozens of military and Veterans' facilities for cognitive rehabilitation, under the supervision of healthcare professionals. With the publication of these results, Posit Science, the maker of BrainHQ, has indicated it intends to work with clinicians, payors, and regulators to make this widely available, as quickly as possible.