US Contact: Susan Halkiotis
Phone: (919) 668-6031
E-mail: halkiotis@neuro.duke.edu
Web: www.nicolelislab.net

Brazil Contact: Beatriz Pegoraro
Phone: (11) 3872-1899
E-mail: comunica@aasdap.org.br
Web: www.aasdap.org.br

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Long-Term Rehabilitation Using Brain-Machine Interfaces Triggers Partial Neurological Recovery in Chronic Paraplegic Patients

On June 12th 2014, the Walk Again Project (WAP), a non-profit international research consortium, performed a unique scientific demonstration, during the opening ceremony of the Soccer World Cup in Brazil. During that demo, a young Brazilian man paralyzed from his chest down, delivered the opening kickoff of the World Cup by using a brain-machine interface that allowed him to control the movements of a lower-limb robotic exoskeleton, while receiving tactile feedback from the exo's feet.

Barely two years after its public demonstration, the Walk Again Project (WAP) is publishing its first clinical report, describing the findings obtained after the first year of training of the eight paraplegic patients, from January to December 2014. In this clinical study, the international team of neuroscientists, engineers, and neurorehabilitation personnel reports the discovery that the group of patients who have continued to train with the brain-controlled system, including a motorized exoskeleton, have regained the ability to voluntarily move their leg muscles and to feel touch and pain in their paralyzed limbs -- despite being originally diagnosed as having a clinically complete spinal cord injury, in some cases more than a decade earlier. The patients also regained important degrees of bladder and bowel control, and improved their cardiovascular function, which in one case resulted in a significant reduction in hypertension. As such, this is the first study to report that long-term BMI use may lead to significant recovery of neurological functions in patients suffering from severe spinal cord injuries.

The WAP researchers theorize that the long-term training regimen, which started in the early part of 2014, likely promoted brain reorganization and activated dormant nerves that may have survived the original spinal injury that occurred 3-14 years earlier.

The researchers, led by neuroscientist Miguel Nicolelis, director of the Duke University Center for Neuroengineering and principal investigator of the WAP, say that they do not yet know the limits of this clinical recovery since patients have continued to improve since the World Cup demo until today (a second manuscript will report on the continuous improvement from December 2014 to May 2016). However, they believe that the present discovery should change rehabilitation practices in paraplegic patients in the future by upgrading the status of brain-machine interfaces, from a simple assistive technology to a potential new therapy for spinal cord injury rehabilitation.

Nicolelis, who is also President of the Alberto Santos Dumont Association for Research Support, the non-profit Brazilian research society that coordinated the clinical study of the WAP, and other researchers from universities in the US and Europe published their findings in the August 11th issue of the journal *Scientific Reports*.

“When our lab at Duke, working with John Chapin’s lab in Philadelphia, created the current brain-machine interface paradigm in the late 1990s, the expectation was that, at the most, such an interface would allow people to regain mobility by artificial means—using prosthetic limbs or prosthetic exoskeletons controlled directly by their brains,” said Nicolelis. “We never predicted that by having patients interacting with these devices over a long period we might induce significant neurological recovery, including sensory, motor, and visceral improvements, all body functions lost due to a devastating spinal cord injury, such as the case of our eight patients.”

Until now, no clinical study that employed BMIs in patients suffering from severe spinal cord injuries reported any neurological improvement of their patients. Nicolelis believes that this happened because those studies were very short-termed, and usually involved a single human subject. In addition, in none of these studies did researchers perform any detailed neurological evaluation to search for any clinical improvement.

In the *Scientific Reports* study, the researchers trained eight paraplegic patients over a period of a year on what the scientists named the Walk Again Neurorehabilitation protocol. The patients had been completely paralyzed for 3 to 13 years due to a severe spinal cord injury. Seven had been classified as having a complete injury, according to the American Spinal Injury Association (ASIA) Impairment Scale, and one had been classified as an incomplete injury. None of the patients had shown any clinical improvement with traditional rehabilitation prior to enrolling in the WAP and all eight showed no movement below the level of their spinal cord injury.

The brain-machine interface used in this study consisted of multiple EEG recording electrodes embedded in a cap on the patients' scalp, fitted over the brain areas controlling movement in the frontal lobe. The training protocol was comprised of multiple components. In the virtual reality component, the patients wearing an Oculus Rift head-mounted display were shown a three-dimensional avatar of a person and asked to imagine movements of their own bodies so that they could make the avatar walk. All patients learned to use only their brain activity, recorded through the EEG, to move this avatar body that represented a soccer player walking in a stadium. They also received a continuous stream of tactile feedback, every time the avatar's feet touched the ground. This feedback was delivered through mechano-vibrating elements attached to the long sleeves of a shirt the patients wore in every session. Tactile feedback was delivered to the skin of the patient's forearms to ensure full tactile sensitivity. This haptic device was named the "tactile shirt".

In a second component, the patients used a Lokomat, a robotic gait orthosis, placed on a treadmill, which enables paraplegics to perform walking motions while suspended by a harness. In this component, the patients used the same EEG cap to trigger the Lokomat movements while receiving tactile feedback through the same "tactile shirt". This "haptic feedback" device received signals from pressure sensors placed on the patients' legs and feet, which vibrated in a pattern reflecting the patients' stepping movements.

In a third component, the patients—also wearing the EEG electrodes and the tactile shirt—operated a brain-controlled motorized exoskeleton custom designed for the project by an international team of roboticists. The exoskeleton is the same one the researchers demonstrated at the opening of the 2014 World Cup soccer tournament.

The combination of visual and haptic feedback was critical to the training paradigm, said Nicolelis. “The addition of tactile feedback that was coherent with the visual feedback created a very realistic walking illusion for the patients when they controlled a virtual avatar or the robotic exoskeleton”.

Over a training period of 12 months, the researchers recorded the changes in the patients’ EEG patterns, muscle contractions, voluntary limb movements, and somatic sensitivity in the region below their spinal cord injury. They found that all the patients showed signs of recovery of voluntary muscle function below their spinal cord injury. And all the patients progressed from almost total absence of touch sensation to experiencing tactile sensations, on average up to five segments below the spinal cord lesion. As a result of this neurological improvement, some patients regained the ability of producing multi-joint voluntary movements of their legs, something they had not experienced since their spinal cord injuries.

As an overall result of the 12 months of training, four of the eight patients who were classified as completely paralyzed (ASIA A) were upgraded to incomplete paraplegia (ASIA C) on the ASIA scale. The researchers also found that the patients’ gastrointestinal function improved, with the number of bowel movements directly correlated with the hours of upright walking.

Importantly, said Nicolelis, the researchers saw significant changes in the EEG patterns in the patients’ brains over the course of the study. “We began to see signs of plasticity in their cortical function, as they learned to use the system and progressed in their training,” he said. “Our interpretation of these changes is that we were documenting the reassertion of a representation in the patients’ brains of the lower limbs and their movement. Since they had been paraplegic for years, their brains had significantly reduced that representation." In the spinal cord, the combination of brain reorganization and muscle exercise may have also induced sprouting of new connections theorized Nicolelis.

"Our hypothesis is that this training triggered a combination of cortical and spinal plasticity because of the combined use of the brain-machine interface with virtual reality, physical leg movement and tactile feedback," he said. "When the patients are moving their legs and walking upright again, they are exciting the proprioceptors in their muscles, tendons and joints. And those proprioreceptors are sending signals back to the spinal cord."

"We also hope to take this protocol to other spinal cord centers around the world, to try to replicate and expand on our findings," said Nicolelis. "Currently, once people with spinal injuries receive a diagnosis of complete paralysis, rehabilitation consists mainly of adapting them to a wheelchair. We believe that our results with this long-term, sustained brain-machine interface training can be not only critical itself in triggering recovery in our patients, but it can also serve as an important motivator for spinal cord patients worldwide."

Besides Nicolelis, other co-authors on the *Scientific Reports* paper are Ana Donati, Solaiman Shokur, Edgard Morya, Debora Campos, Renan Moioli, Claudia Gitti, Patricia Augusto, Sandra Tripodi, Cristhiane Pires, Gislaine Pereira, Fabricio Brasil, Simone Gallo, Anthony Lin, Angelo Takigami, Maria Aratanha, Sanjay Joshi, Hannes Bleuler, Gordon Cheng and Alan Rudolph.

All clinical work was carried out in the Neurorehabilitation Laboratory of the Alberto Santos Dumont Association for Research Support (Associação Alberto Santos Dumont para Apoio à Pesquisa) in São Paulo, Brazil. Authors are with AASDAP, the Associação de Assistência à Criança Deficiente in Brazil (AACD), the Santos Dumont Institute in Brazil, the Ecole Polytechnique Federal de Lausanne in Switzerland, the University of California, Davis, the Technical University of Munich in Germany, Colorado State University and Duke University.

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