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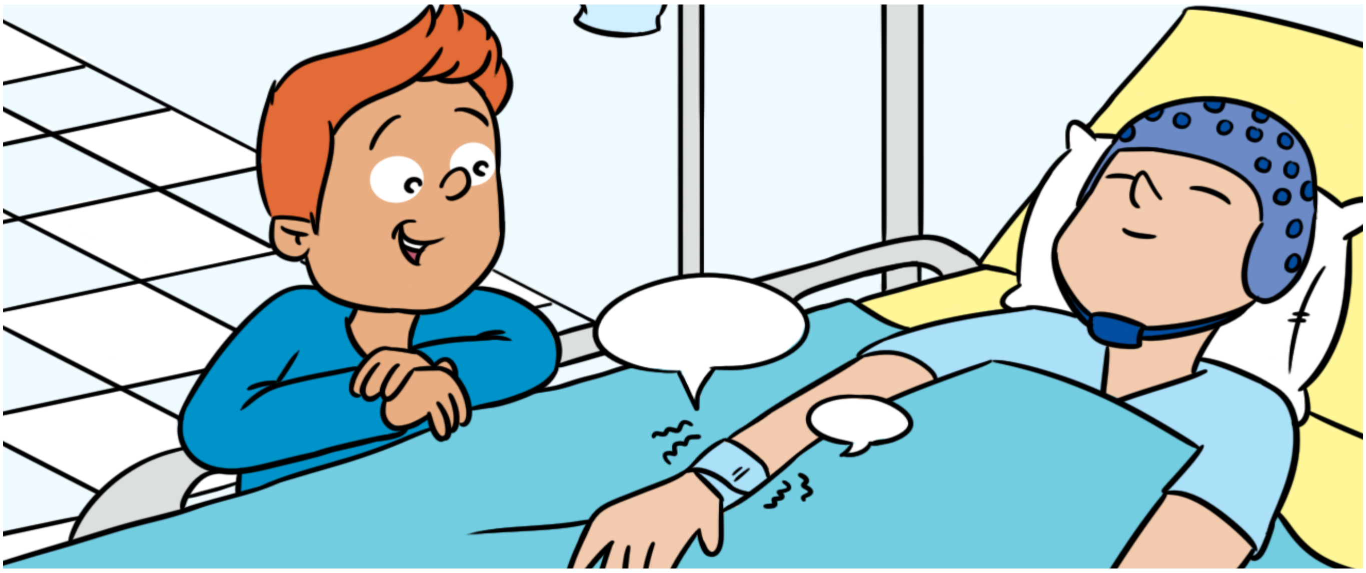

HOW CAN COMPLETELY LOCKED-IN PERSONS COMMUNICATE WITH A BRAIN–COMPUTER INTERFACE?

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People with complete locked-in syndrome have lost the ability to control any kind of movement. They can't speak, move their hands, or even choose to blink or move their eyes, but the brain is working. Therefore, communicating with these patients can be very difficult. Many groups have developed brain–computer interface (BCI) systems that can provide communication for people even if they cannot move. The BCI system can translate the user's brain activity into signals for communication, such as answering YES or NO. Unfortunately, most of these systems do not work for patients who cannot see. Here, we introduce new results with a system that uses little vibrators. The mindBEAGLE system can vibrate the left and right wrists, and the patient can answer YES or NO by silently counting the stimulations on one wrist or the other. The system is using the wrist, because they are easy to distinguish for the patient. We tested this system with 12 locked-in patients, and we established successful communication

with nine of them. We were even able to get two completely locked-in patients to communicate. The successful communication was promising and had a strong impact on some patients' lives.

WHAT ARE COMPLETELY LOCKED-IN PATIENTS?

Completely locked-in patients cannot move any part of their bodies, and so they cannot communicate with their families and friends. Many of these patients have an illness that is called amyotrophic lateral sclerosis, which makes them lose control of their muscles. Before becoming completely locked in, these patients are in a less locked-in state, which means that they can still use some of their muscles and can do things like blink. In this state, blinking can be used to establish communication. There are many devices that can help patients to communicate by using their breathing, blinking, cheek muscles, or other muscle activities they can still control—even if they cannot type or speak. But, when patients can no longer control any movement, they may feel very isolated. Even doctors and family members may not know what these patients want or even if they are still mentally healthy enough to communicate.

BRAIN–COMPUTER INTERFACE (BCI)

A system that can translate the user's brain activity into signals for communication.

ELECTROENCEPHALOGRAM (EEG)

Measures the electrical activity of neurons (nerve cells) in the brain.

These completely locked-in patients need new ways to help them establish communication. For that reason, researchers started to develop **brain–computer interfaces**, which are also called **BCIs**. To learn more about BCIs, we recommend the books by Wolpaw and Wolpaw [1], and by Nam and colleagues [2].

Brain–computer interfaces can identify specific brain activities through the patient's **electroencephalogram (EEG)**. EEG measures the electrical activity of neurons (nerve cells) in the brain. Whenever you think, feel, make decisions, or do anything with your brain, your brain's electrical activity changes. If many millions of neurons are working together, the resulting changes in electrical activity are large enough that we can measure them with little metal disks, called electrodes. These electrodes can be placed in an electrode cap, which is worn on top of the head. This doesn't require any surgery or pain. The electrode cap just sits on top of the head, much like a baseball cap.

Electrode caps are designed so that each electrode is positioned over a certain brain region. So, electrodes measure brain waves and brain activity over different parts of the brain. By examining brain activity under different electrodes at different times, the BCI can transform some of this information into control signals for different kinds of devices. For example, BCIs have been used to control robotic devices, play computer games, move a cursor on a computer screen, and provide communication. BCIs are typically much slower than other devices used for communication and control, such as keyboards, mice, or game controllers. That's a major reason why most people today don't use BCIs. But, for people who have lost the ability to move, BCIs can make a huge difference in their lives.

HOW CAN A BCI USE BRAIN WAVES TO CONTROL A COMMUNICATION DEVICE?

For many years, researchers used movement imagery-based BCIs to establish communication with locked-in patients. For example, the patients were asked to imagine movements of their left or right hands. Imagining a left-hand movement activates the right side of the brain. Imagining a right-hand movement activates the left side of the brain. Then, the BCI system determines whether the patient imagined moving the left or right hand. The BCI system then uses the patient's brain activity to move a cursor to the left or right side of a computer screen, for example.

P300

Little wave that can be seen in brain wave recordings.

Another type of BCI uses a certain type of brainwave called the **P300**. The P300 is a type of brain wave that is larger when a person is paying attention to a sudden event. This event can be a flashing symbol on a computer screen. In this example, all characters of the alphabet and all numbers are shown on a screen. Some of the characters then flash (see Figure 1). The patient's task is to look at the character that s/he wants to say, and when this character flashes, the brain produces a P300. This means that the brain wave shows a little peak shortly after the flash, which allows the BCI to "know" which character the patient is trying to communicate.

WHY DO WE NEED A NEW TYPE OF BCI SYSTEM FOR LOCKED-IN PATIENTS?

There are problems with the two types of BCI systems described above. The movement imagery BCI is not very reliable and requires a lot of training.

FIGURE 1

FIGURE 1

A P300 brain–computer interface (BCI) that allows the patient to write words and sentences using brain waves only.The patient focuses on the character that she or he wants to write, called the target character, and silently counts each time it flashes. Every time this character flashes, the brain produces brain-waves including the P300. The BCI then tries to identify the target character by identifying which flashes produced the P300. This way, letters can be selected one after the other. In this example, the patient had already written WATCH YOUR BRAI. The next letter in the word BRAIN is "N," so that letter is highlighted in this example. The column highlighted in white shows what the screen looks like when one column flashes. Since the flashing column does not contain the target letter, the patient would ignore this flash, and it would not produce a P300. Our work uses a similar concept, but with vibration, not visual stimuli.

Locked-in patients may have trouble concentrating on a task and may get tired very quickly, so training can be difficult or impossible. P300 BCIs require no training for users, but most P300 BCIs use visual stimuli, like letters on a screen, as mentioned above. Since completely locked-in patients often cannot see, they need a BCI that doesn't require vision. Therefore, researchers have been looking for BCIs that do not require extensive training and that work for people who can't see. Many completely locked-in patients can still feel vibrations on their wrists and other touch stimuli, and both our group and other groups have proven that P300 BCIs based on feeling vibrations are possible to create.

VIBRATION-BASED BCI SYSTEM

To develop a BCI that is practical for completely locked-in patients, we decided to use little vibrating devices. In this case, the vibrating device (like the one in your cell phone that is activated when someone messages or calls) is placed on the right wrist, another vibrating device is put on the left wrist, and another one on the patient's leg (see Figure 2, middle). Then, each of the devices is switched on for a very short time. The important point now is that we ask the patient to count the number of vibrations in a certain location, such as the left wrist. When the patient counts the vibrations on the left wrist, this produces a P300, like the P300 from the flashing characters in Figure 1. Since the patient ignores the vibrations on the right hand and foot, these vibrations produce much smaller P300s. This allows

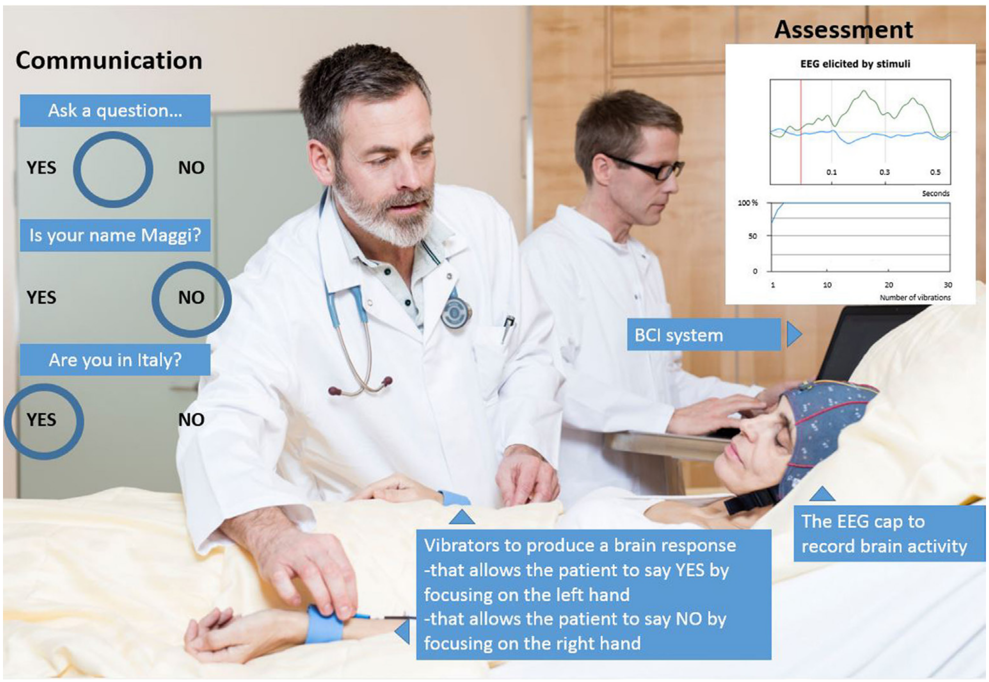

FIGURE 2

FIGURE 2

Vibrating devices are attached to the patient's right hand, left hand and a leg and are randomly switched on very briefly. The patient is connected to the brain–computer interface (BCI) system with electroencephalogram electrodes in a cap worn on the head. Top right (Assessment): The brain responds with a P300 wave to the vibrations that the patient counts (green line) within 0.5 seconds. There is only a very small response for the other vibrations (blue line). The BCI system finds the differences between the green and blue lines. Just below these brainwaves, another image shows the BCI accuracy. After only one target vibration, the system's accuracy would be a little less than 75%. This is why we repeat the vibrations multiple times and combine the results to increase accuracy. In this example, the system reaches 100% accuracy after about three vibrations and keeps at 100 % also after 10, 20, and 30 vibrations. In locked-in patients, we often require more than three tries to attain good accuracy. Left (Communication): After high accuracy has been achieved, the caregiver can ask the patient questions. The patient just silently counts the vibrations to the left hand to say YES and on the right hand to say NO. Then, the little circle suddenly moves to YES or NO, and the family sees the answer!

the BCI system to identify that the patient counted the vibrations on the left wrist only.

Patients can use this approach to answer questions, even if they can't see. If a mother of a patient asks, "Are you in Italy?" (see Figure 2, left), the patient could choose to count the vibrations on the right hand to say YES. If the patient is not in Italy, then counting vibrations on the left hand will say NO. The patient never counts the vibrations on the leg, because these stimuli are just needed to make the vibrations on the hand stronger. The BCI system also needs to repeat the left and right wrist stimulations several times to make an accurate decision about what the patient is trying to communicate. This is because the brain signals are very weak and noisy.

TASKS OF THE BCI

All these tasks are done by a system called mindBEAGLE. The beagle is a dog that is famous for its sense of smell. Beagles are legendary for finding people who are lost, rather like we are trying to do here. Of course, we're not trying to find people through smell, but rather by proving that they have the ability to communicate and by providing communication. The HMS Beagle was also a famous ship in the history of science. Charles Darwin studied a wide variety of different species while he traveled on the HMS Beagle, which helped him develop many theories about evolution.

The BCI system has to do a lot of different tasks to interpret the brain waves correctly. First, it must amplify the brain signals, because the signals coming from the brain are very small. Then, the signals are sent to a computer that does a sequence of calculations. In this way, the BCI system learns what the brain waves look like for left wrist, right wrist, and leg vibrations. This information is used to train the system for every patient. Figure 2 (right) shows the brain response while the patient counted vibrations to the left hand (green line). This figure also shows the response to right-hand vibrations, which the patient did not count (blue line). This training procedure takes 2.5 min. The BCI system provides an accuracy score that tells the scientist how well the system can identify which side the patient is counting the vibrations on.

RESULTS

If the accuracy score of the BCI system is 100%, which means the system works perfectly (Figure 2, right side, Assessment). This tells the scientist that the patient's brain is fully able to do the task and that the patient has the necessary brain functions to count the vibrations and generate a P300. If the accuracy is 0%, then this might mean that the patient is sleeping, or it could mean that the patient has permanently lost the ability to perform the mental tasks needed for this BCI. That is why the procedure must be repeated several times. If someone does not perform well, it might just mean that we did the test at the wrong time. With completely locked-in patients, even doctors can have trouble determining whether patients are awake or responsive at the time the test is being done.

If the accuracy score is above 60%, then the BCI system can be used to help the patient answer questions. In this case, we ask the patient 10 different questions for which we know the answers. We also ask questions that should be very easy and can be answered with a yes or no, such as: "Were you born in Italy?" or "Is your name Rossella?" Then, we count how many answers are correct. This shows us whether the system is working properly and whether the patient can use it. We can then switch to asking yes/no questions in which we don't know the answers, such as "Are you cold?" or "Do you want to try another BCI communication session tomorrow at 10:00 a.m.?"

Recently, we had a very exciting case! A mother used the BCI system after being completely locked in for more than 10 years. Suddenly, she answered 9 out of 10 questions correctly. This showed us that she could still understand what was going on in her environment. Her family was very excited to know that she could understand them. Furthermore, this will allow her family to ask her more questions in the future.

Another patient could answer 7 out of 10 questions correctly. The system made one mistake, and twice the system was unsure about what the patient wanted to say. For another completely locked-in patient, the system could not establish communication at all. In this case, the system must be used at a different time on the same patient to see if the results are different.

In total, we tested the system with 12 locked-in and completely locked-in patients, and 9 out of 12 patients could answer questions correctly. In three patients, we were not able to establish communication, and therefore, we will repeat the procedure.

FUTURE WORK

In the future, we will keep making the BCI system smaller and easier to use. We will also use new ways to interact with patients to learn about their brain activity and to provide better communication. For example, we want to go beyond yes/no communication by adding more vibrators on other areas of the body, which could help patients select "multiple-choice"-style answers, or even to spell. Finally, we plan to have technology available that can be used at home to allow family members to communicate whenever they want, without requiring experts to help them with the BCI system.

ORIGINAL SOURCE ARTICLE

Guger, C., Spataro, R., Allison, B. Z., Heilinger, A., Ortner, R., Cho, W., et al. 2017. Complete locked-in and locked-in patients: command following assessment and communication with vibro-tactile P300 and motor imagery brain-computer interface tools. *Front. Neurosci.* 11:251. doi:10.3389/fnins.2017.00251

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CONFLICT OF INTEREST STATEMENT: The BCI system mentioned in the publication is called mindBEAGLE. It is produced by a company called g.tec in Austria. CG is the CEO. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

REVIEWED BY

ANIRUDH, AGE: 12

I am 12 years old, and I live in Melbourne, Australia. My favorite subjects in school are science and Japanese. When I grow up, I would like to study neuroscience because there is so much to learn and discover, and so you'll never get bored! I have written a few neuroscience articles for school competitions and I'm planning to do more in the future! I also enjoy reading books, listening to music, playing with my younger brother, and playing tennis with my friends.

AUTHORS

CHRISTOPH GUGER

Christoph Guger is from a small town in the mountains of Austria, a couple hours south of Germany. He loves hiking, skiing, and other mountain sports. He earned his Ph.D. in Biomedical Engineering in 1999 at a top Austrian technical university called the Technical University of Graz (TUG). He started g.tec medical engineering GmbH and has been the CEO there ever since. He studies and develops BCIs for different people, including patients with stroke or disorders of consciousness (DOC). He also runs several international research projects with people from different countries, which helped us do the research in this paper. *guger@gtec.at.

ROSSELLA SPATARO

Rossella Spataro is a doctor from Agrigento, Sicily, which is in southern Italy. She has worked in Palermo for many years. She is clinical neurologist, meaning she specializes in helping patients who have brain injuries or disorders. She has worked with many patients who have a disorder of consciousness (DOC) or locked-in syndrome (LIS). In the past few years, she has begun using BCI systems with these patients, which led to the work in this paper and other recent publications.

BRENDAN Z. ALLISON

Brendan Allison was born in southern California and earned his Ph.D. in Cognitive Science at UC San Diego. He has been working with BCIs for over 20 years. For most of his career, he was involved with BCIs to help locked-in patients. He also works on BCIs for other types of patients, including people with disorders of consciousness (DOCs) as described in this paper. BCI research requires experts with different skills, including brain science, engineering, psychology, and medicine, and Brendan enjoys working with people from different backgrounds.

ALEXANDER HEILINGER

Alexander Heilinger studied biophysics, which is a research field that helps us understand how brainwaves work. He is also an experienced programmer. Mr. Heilinger works at g.tec and is also finishing his Ph.D. at a nearby university. His Ph.D. research involves new types of EEG-based BCIs for disabled users, including testing how well they work with different patients. He has helped to analyze and interpret EEG activity in several research projects that involved collaboration with different hospitals in different countries.

RUPERT ORTNER

Rupert Ortner is one of the top programmers at g.tec and has worked with EEG-based BCIs for many years. He leads several programming and development projects, including work with patients who had a stroke or were diagnosed with a disorder of consciousness (DOC). Dr. Ortner earned his Ph.D. at TUG in Austria, like Dr. Guger. During his Ph.D. work, he developed different non-invasive BCIs for disabled people. For example, he developed an SSVEP to control an orthosis, which is a device that helps disabled people move their arms. Dr. Ortner also enjoys skiing and travel.

WOOSANG CHO

Woosang Cho is from Korea and recently earned his Ph.D. through a university in Germany. He joined g.tec's research department in 2016, where he works on BCIs to help people recover movement. He studies how feedback and brain stimulation can help people learn to move again. People with stroke, injuries, or other conditions may have healthy bodies, but their brains can no longer control movement correctly. Dr. Cho hopes to help people use BCIs and other technologies as part of future therapies that could help people walk, grasp, or speak again.

VINCENZO LA BELLA

Vincenzo La Bella is also a neurologist from the island of Sicily, like Dr. Spataro, and they work together at the University of Palermo. Dr. La Bella has also worked in the US and France and is now the Director of the ALS Clinical Research Center at the University of Palermo. He studies some of the reasons why some people lose the ability to move. He works with many patients who cannot move, including people with a disorder of consciousness (DOC).