Logbook

December 17, 2023

In *Dynamics of muscle activation during tonic–clonic seizures*, Conradsen et al. recorded electromyography of the deltoid muscle during generalized tonic-clonic seizures (GTCS). Apart from some other findings in the paper, they “suggest that the same inhibitory mechanisms that contribute to GTCS termination counteract seizure initiation” and they suggest that “both active inhibition and mechanisms related to metabolic depletion act synergistically to stop the seizure.” In essence, they used muscle activity as a surrogate of brain activity to figure out what was happening during GTCS.

Active inhibition is the decreasing of neuronal activity by certain neuronal mechanisms. One of the most accessible neuronal mechanisms is proprioception, or kinaesthesia, which is the ability of the body to feel where it is in space, and to detect how much resistance each muscle has. Haptic feedback takes advantage of kinaesthesia and mechanoreceptors on the surface of the skin to produce illusory sensations; in one video game, the player is made to feel that there are marbles in side the controller, and they are to count the marbles by feeling the “collisions” between each one that they create by tilting the controller.

If the prior paper is correct, this means that wearable haptic feedback tools can be used in epilepsy to decrease seizure frequency, intensity, and duration. This would also mean that, even during seizures, certain components of motor control still remain that can be taken advantage of for therapeutic effect; these aspects can be considered “laws” of motor control that must always be obeyed by the body.

https://nba.uth.tmc.edu/neuroscience/s3/chapter01.html

https://www.sciencedirect.com/science/article/abs/pii/S0920121112002689?via%3Dihub

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8782545/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8004256/

email : https://scholar.google.com/citations?user=XA8NibUAAAAJ&hl=da

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5478113/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5997460/

https://pubmed.ncbi.nlm.nih.gov/12171130/

https://www.nature.com/articles/s41551-022-00918-x

https://en.wikipedia.org/wiki/Extended_physiological_proprioception

https://pubmed.ncbi.nlm.nih.gov/30140254/

https://pubmed.ncbi.nlm.nih.gov/21973264/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8018764/

December 28, 2023

The plan was to use a haptic piezoelectric buzzer (rather than the powerhap piezo because it was too expensive) to deliver haptic feedback to the musculotendinous area, where the majority of golgi tendon organs are. A similar technique is present in massages, where they press down on the musculotendinous area with 2lbs of force (about 1 Newton) for 60 seconds, forcing the muscle to relax (https://www.youtube.com/watch?v=Dip49xZzfsA). What we are aiming for is something that generally acts mildly to inhibit, but, in a seizure, increases the force to encourage inhibition.

What we need is the DRV8662 EVM (https://www.ti.com/tool/DRV8662EVM, about $170CAD at the time of writing) to drive the piezo buzzers, the piezo buzzers (something like this, https://www.amazon.ca/Buzzer-Piezoelectric-Ceramic-Loudspeaker-Aluminum/dp/B0B3HX9YDR), a power source (seems like 3-5.5 volts are required for the driver, section 7.3 of manual), and an Adafruit Gemma for the code (really just need a small controller board, https://www.adafruit.com/product/1222). We also need a breadboard and some resistors and amplifiers to act as a potential divider between the Gemma and the driver so that the gemma can safely sense the touch placed on the buzzers. Finally, it would be good to have something that conducts the force output of the piezo well, as well as something flexible so that it can go on the animal. PCBs are often used, so plastics could be tested for this application.

For the software, one model is Carl Bugeja's videos. In this video, he creates a haptic buzzer system that buzzes every time it is tapped (https://www.youtube.com/watch?v=egLA0GgF3xw, project files here: https://www.hackster.io/carlbugeja/haptic-piezo-buzzers-d47f96). For this project, something similar needs to be done, except that there needs to be a (light) constant stimulation of the sensor (buzz or something similar, although simulating balls like the 1, 2 switch game would be cool) and an increase in buzz when multiple stimulations happen, simulating the clonic part of a tonic-clonic seizure (the clonic portion is probably the easiest to detect; tonic is often more common, especially in children in absence seizures, so detecting that would make this project better). The latter part of the goals can probably wait until there is a proof of concept.

Resources not mentioned:

How to use a Piezo Buzzer (sound) with Arduino
https://www.youtube.com/watch?v=K8AnlUT0ng0

Haptic Neuroprosthesis with Beagle Bone Haptic Cape
https://www.hackster.io/cw-earley/haptic-neurohacking-with-the-beaglebone-haptic-cape-08ac18

January 1, 2024

Today, the investigation mainly centered around whether vibration would stimulate golgi tendon organs. Initially, it was found that golgi tendon organs were insensitive to vibration (https://link.springer.com/chapter/10.1007/978-1-4615-1935-5_64), and that muscle spindles were more sensitive to it. I thought this was bad for the project, as the stimulation of muscle spindles encourages the stretch reflexes, which contracts muscles. I then found that golgi tendon organs were sensitive to “High-Velocity, Short-Duration Loads” (Pickar and Wheeler, 2001) and “Suprathreshold Short Mechanical Pulses” (Fukami, 1980), which meant that clicks were effective to stimulate Golgi tendon receptors. One of the papers also stated that “High-Velocity, Short-Duration Loads” stimulate muscle spindles, so, by that point, I thought the project was gone. But then I found that, while muscle spindles may encourage contraction during a seizure, the literature suggests that, when stimulated by vibration, muscle spindles encourage a slow and metered contractions and relaxation through the stretch reflex, which may be beneficial for reducing the activity of muscle groups during a seizure and increasing inhibition of contractions (https://jnnp.bmj.com/content/31/3/207). This keeps the project afloat. Finally, in terms of modifications to the hardware, perhaps more actuators could help increase the effect. Am currently writing the Research Plan, and will hopefully finish building a prototype by next week, and start trials by mid-to-late January.

January 2, 2024

Today, I figured out more of the engineering of the project. I do not think that I will need a potential divider, as the piezoelectric device does not need to give information to the microcontroller. For the microcontroller, which is going to I will use the Adafruit Gemma m0, which is modeled off the discontinued Arduino Gemma. This will need alligator clip jumper wires to connect to the DRV8662 EVM, which contains the driver, the boost converter, and the amplifier, as high voltage is needed to run the piezo actuators. As for the actual actuator, I think I will use a 9mm powerhap piezo actuator. It is the right size for use on rats, and it can exert large force (~2 Newtons), which is ideal for stimulating golgi tendon organs (I will probably not stimulate them that much). I will design a covering for the 12.7mm powerhap piezo actuator and 3d print it out of Thermoplastic Elastomers, preventing the rat from getting shocked and increasing flexibility. I need to find some sort of adhesive for the 3d printed covering for the actuator. How will I 3d print this for the rat to make it wearable?

January 12, 2024

Previously, I had contacted some members of the clinical epileptology faculty at the University of Calgary. All who responded were intrigued by the project and assigned it a high probability of success. With theory out of the way as an obstacle, the only thing in the way is practice. How will I test this project? There are two ways to do this. The first, and the most effective, is to induce seizures in rats under the procedure laid out by Ferland. The second is to order an EEG and an EMG to figure out if the haptic feedback affects active inhibition processes, as theory states. This is a softer way to test the main goal of the project, so it less desirable. At the moment, I am contacting members of the University of Calgary faculty to see if they wish to provide lab space for the project. I have also submitted an ethics board application. Finally, have also ordered the requisite parts for the project.

January 16, 2024

Today, all the parts for the project arrived. This allowed me to build the first working prototype of the project! In essence, I just connected the DRV8662 EVM to the haptic actuator, and, using one of the DRV's existing modes, the actuator started buzzing slightly. I think that I may need a bigger actuator that can buzz more, as well as good housing that conducts vibration, which I want to be 3d-printed.

January 17, 2024

Today, I managed to connect the Arduino to the DRV using the ground pins on both, and pins 12 and 13 on the Arduino to the EXT pins on the DRV. I have not yet coded any signal. Also, the battery holder that I was using for the DRV broke, so I am going to have to order some new ones before the project can proceed.

January 20, 2024

Today, a rough prototype was finished, and some problems were solved with the initial build (battery holders arrived today). Initially, I had tried to run Carl Bugeja's code on the system, and it ended up not working, but then I realized that I had no input to the Arduino, so the code could not work. I wrote a code that I thought was going to work using the ENpin functions. I did not work. I then read the instruction manual for the DRV and I realized that I needed to connect pins 12 and 13 to the JP2 and JP3 pins on the DRV to drive a waveform. I did this, and still nothing came of it. After some troubleshooting in the code, I realized that I had failed to enable the DRV, and that was why the code was not working. The code now works by using Freqtoggle, which is a function that counts the amount of times another function has been executed. I chose for a series of 3 long buzzes and 5 short clicks. I worked very well, although I could really only feel it in my hands, not in less sensitive areas of the body, such as the biceps.

The main flaw with this code is that the frequency and duration of the waveforms generated by this code are intertwined. To understand this, you have to look basically at how a piezoelectric material functions. Basically, when mechanically deformed, one side of the piezo material will be more positively charged than the other, and one side more negatively charged. This creates a voltage potential between the two sides of the material. We take advantage of this by driving a voltage through the material and by artificially creating a positive and negative side to the material, the material moves slightly. This is what we are doing here in the code. The code involves one pin turning on while the other is off, creating positive and negative sides to the material, deforming it. If you repeat this enough times, the material moves back and forth across a position, creating a buzz. In the code, we can choose the duration of each half waveform cycle (e.g pin on and pin off), thus establishing a frequency for the piezo. This frequency is dependent on the length of the half waveform cycles, which is the problem. In the code, I would like to drive frequency and duration separately. It also looks cleaner and makes it easier for clinical use.

January 23, 2024

Unfortunately – or fortunately (?) – the CYSF ethics board denied my application, saying that I needed to work in a lab that regularly induces seizures in rats. I was discussing this issue with some of the faculty that I was planning to do the project with, and they have similar opinions. They said that the experiment was too expensive, and a little unfeasible. I agreed with them, and I was also starting to have my own doubts about the project. While I was planning to pay for the entire project, I could realistically do 5 trials total, as the gas, flurothyl was too expensive. This meant that the project could only be a feasibility study, and that it would have little statistical significance. I dp not want to put 3 rats through seizures for no real reason, no statistical significance. This means I need to develop something a little different. First, I want the study to be generalizable, which means scrapping the EEG/EMG plan and doing something a little different. There are two other goals for this new approach. The first is to prove that active inhibition mechanisms are activated by haptic feedback. The second is for it to have some sort of clinical/practical application. The plan is to use the same procedure that academics use to test proprioception and proprioceptive mechanisms: tendon vibration. This time, however, rather than a special tendon vibrator, a piezo electric one will be used to see if it works similarly. The common procedure is simple. A subject is blindfolded, arms out, facing up on a table, their elbows on some cushioning. A protractor will be placed between their arms. Their left arm will be raised by the experimenter to 30 degrees. Then, the haptic feedback device will be strapped onto their right bicep tendon, turned on, and they will be asked to match positions. For every subject, control will be the normal level of matching between their arms (That is, matching without proprioception). The absolute value of the difference will be taken for the control and haptic trials, and the difference will be taken as the angle deviation caused by the haptic feedback. If this causes sensory illusions, the same benefits associated with these illusions can be applied to this. Short pulses can cause an increase in strength output, which may be beneficial for sports. Longer pulses decrease strength output and may help with shaking in movement disorders and seizures in epilepsy. Both can probably be tested using a grip strength

task. The next step would be to create an app that could be used by clinicians, personal trainers, and physiotherapists to manipulated which pulses are released and when. This would result in a programmable app that everyone could use to increase strength output and decrease muscle shaking/seizure intensity in people.

January 24, 2024

Today, I designed an experiment based on the ideas from yesterday. This experiment will be performed on humans, and involve looking at the effect haptic feedback has on movement and muscle force.

I am the experimenter in these experiments. The first part to this experiment will be concerned with the notion of whether haptic feedback can stimulate deep tendon reflexes. If haptic feedback can do this, it can also stimulate active inhibition mechanisms. The experiment involves blindfolding the subject, who is sitting down. The subject has their arms out, their elbows on small cushions. The experimenter notifies that he is going to raise the subject's arm to a thirty degree angle, and, if the subject says yes, he raises the subject's left arm to a thirty degree angle, as indicated by a large protractor between the subject's arms. The subject will then be asked to raise their right arm to the same angle as their left one. The percent difference in angles between the arms will be compared.

The subject's blindfold will then be taken off, and, with their assistance, a Velcro strap will be placed snugly on their musculotendinous area of their bicep. They will be asked whether it is comfortable or not, and we will have a few moments for adjustment of the strap. Then, a similar procedure will be performed except that, 5 seconds prior and during the right arm raise to the same angle as the left arm, the haptic actuator will be turned on in the hopes of creating an illusion and therefore a mismatch between the two arms. The percent difference in angles between the arms will be computed. The difference between the percent difference of both trials will be analyzed. If it is positive (control – experimental), the experiment will suggest the null hypothesis that haptic feedback improves proprioception. If it is negative, the experiment suggests that haptic feedback supports the hypothesis that haptic feedback increases in accuracy. If the hypothesis is correct, and based on the mechanisms currently known, it is suggested that haptic feedback, at least in this case, works to activate proprioception via muscle spindle stimulation. A question will be asked at the end of the experiment: "Was your hand higher than you thought that it was going to be?" If yes, haptic feedback as active inhibition will also be proved.

The second experiment is about the effect different types of haptic feedback have on grip strength. The hypothesis we want to test here is the effect of long haptic pulses (40s) and no pulses on grip strength. To begin with the control experiment, a velcro strap will be placed on the subject's forearm so that the actuator has contact with the Flexor digitorum profundus muscle, which is one of the main controllers of grip strength. The subject will then be instructed to squeeze a grip trainer at about 50% strength for 10s. The displacement of the handles of the grip trainer will be calculated. For the experimental part of the experiment, the velcro strap with

the actuator will be placed on their forearm so that the actuator has contact with the same muscle. The actuator will be turned on 40s before the contraction. Crucially, vibration will be turned off during the contraction. In theory, long pulses decrease the firing rate of the motor neurons in the muscle, decreasing force output. Displacement will again be measured. The spring constant of the spring in the grip trainer will be calculated to determine the amount of force applied, as well as the percent difference, which will be used in analysis of the experiment.

For the number of people, we are aiming high at n=30, in order to ensure statistical significance. It is possible that we get a lower number than that, but, as long as statistical significance is reached, it is good.

Feb 1, 2024

I modified the code so that frequency and duration are independent, allowing anyone to work on it. Still waiting for ethics board response.

Feb 4, 2024

Started compiling documents and working on trifold.

Feb 8, 2024

Finished Trifold and presentation.

Feb 11, 2024

Qualified for CYSF. Working on improving sensing apparatus for project newly Christened NeuroPulse.

Feb 16, 2024

Ethics 2A form was approved, but directed to fill out 2B more of as a formality than anything else. Sensing apparatus works! Working on starting testing soon.

Feb 23, 2024

2B filled out. Hoping for a response.

Mar 8, 2024

Starting testing.

Mar 13, 2024

Finished testing and data analysis today. Working on getting everything ready for CYSF online portal.