Accepted for publication in

Biomedical Instrumentation and Technology

on 28 March 2018

DRY-ELECTROENCEPHALOGRAM AND SUPPORT VECTOR FOR OBJECTIVE PAIN ASSESSMENT

Disclosure: The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Authors

Chika Okolo, B.Sc., Biology and M.Sc. Biomedical Engineering

Dr. Ahmet Omurtag, Senior Lecturer in Biomedical Engineering, Engineering Department, Nottingham Trent University, United Kingdom

ABSTRACT

Our primary goal was to objectively quantify pain. The experiment we designated for this task was via dry electroencephalography (EEG) in conjunction with a support vector machine classifier (SVM).

Normal gel-based electrode EEG has been validated as reliable in pain measurement. Yet, to date, there are few documented trials that use dry-EEG for pain quantification. In addition, SVM classifiers have proven accurate when classifying pain intensity. Therefore, we believe EEG combined with SVM could increase the statistical power of pain assessment.

However, due to the subjectivity of pain, currently clinicians mainly rely on verbal reports. This research could offer a method to objectively monitor pain, eliminate observer error and individualize treatment.

Pain Background

Definition

Acute pain results directly from injury, such as stubbing a toe or falling on ones face. Chronic pain is from an underlying disease, or untreated condition; and is normally treated using NSAIDS, non-opioid and opioid medications.

Economic Burden of Pain

Due to the medications, social losses, rehabilitation and decreases in work productivity etc., chronic pain conditions constitute a growing burden on the healthcare system. Its annual cost in 2010 was estimated to range from $560 to $635 billion, surpassing that of diabetes ($188 billion), cancer ($243 billion) and heart disease ($309 billion) [1]. Furthermore, in 2011 chronic pain sufferers in the United States numbered up to 100 million, compared to those diagnosed with diabetes (25.8 million)[2], coronary heart disease (16.3 million)[2-4] or cancer (11.9 million)[5].

Undertreatment of Pain

Untreated pain can lead to increased risk of myocardial infarction and ischemia.[6] Other issues include loss of sleep, mobility and strength.

Aim of work

Human pain has been analyzed using various non-invasive, medical imaging devices. Examples include: positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). [7.] Due to the high temporal resolution of electroencephalograms (EEG), some researchers have concluded that EEG is the most effective neuroimaging device for pain diagnosis. It also can capture real-time, dynamic changes within the brain. Therefore, our primary goal was to design an experiment that could objectively quantify pain sensation using this device. In comparison to normal gel-electrode EEG, dry EEG is more convenient and feasible in a clinic setting.

We implemented a support vector machine classifier (SVM) which uses supervised machine learning to predict offline and real-time changing levels of pain stimulus. The data we used was frequency band power (described further down) obtained during EEG recordings. We processed the raw data using power spectral analysis and used results as input (i.e. features) into our support vector machine algorithm.

Dry EEG vs. normal gel-electrode EEG

Quick-20 Dry EEG (19 channels) differs from normal EEG in that it doesn't use gel-based electrodes.

It has the advantage of quicker setup time, increased versatility and mobility. It also has increased resistance against movement and electrical artifacts and can measure impedance in real-time. Previous results show that this device has the same quality of raw data collection as the current gold standard, wet EEG.

On the adverse side: recordings include more impedance due to the lack of gel which is normally used to fill gaps in between electrodes and the surface of the scalp. In addition, the dry system must overcome shortcomings pertaining to sensor design, mechanics and electronics. [24]

Power Spectral Density

Variations in brain neural activity causes increases and decreases in the power of EEG waves. Power refers to the energy of these waveforms, seen as variations in amplitude of EEG signals in the time domain. In signal processing, power is defined as the average of the magnitude of a signal, squared, and spectrum refers to the variations in frequency of an entire wave signal. [8]

Therefore, power spectral density (PSD) can be used to characterize brain activity by tracking changes in amplitude of frequency waves. Figure 1 shows EEG time signals converted to the frequency domain.

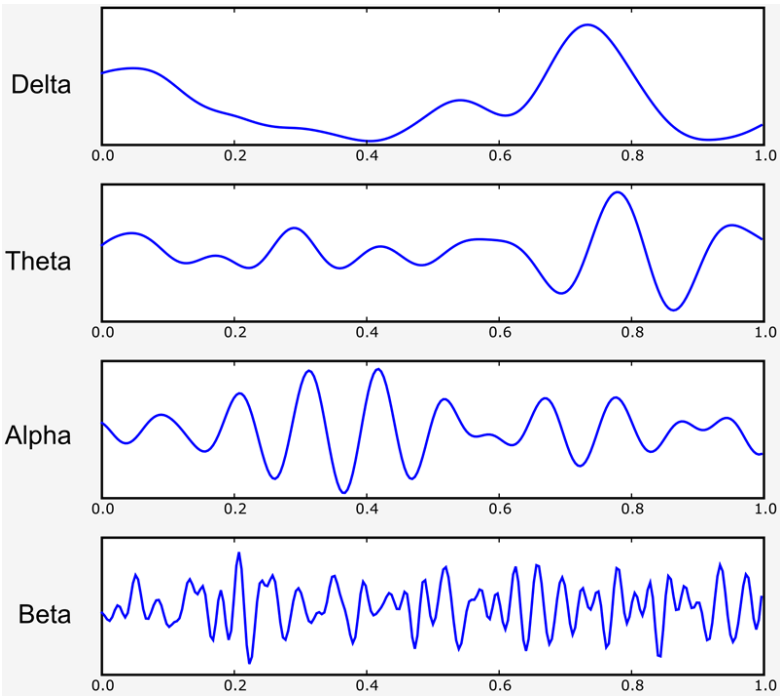

Figure 1: Example of EEG waveforms in the frequency domain. Displays δ (1–4 Hz), θ (4–8 Hz), α (8–12 Hz) and β (12–28 Hz) frequency bands. [9]

The significance of each frequency band above is that each relate to specific brain functions. The brain contains billions of specialized cells called neurons, which are recruited in populations numbering in the thousands to perform a specific task. Neuron rate of recruitment, or "firing rate," is displayed as power fluctuations in EEG data. For example, high α frequency-band power has been shown to be associated with processing painful stimuli. [10]

Null Hypothesis

We believed all people experience pain differently. Therefore, the null hypothesis was that everyone's pain experience would be similar when exposed to the same modality and magnitude of pain stimuli; thus, there would be no significant differences in EEG data.

Methods

We started with a pool of 15 subjects but selected only a sample size of nine due to noisy data. This is data that is convoluted with meaningless information which is common during EEG recordings since it is highly sensitive to movement (i.e. blinking, muscle twitch, person walking near device etc.). We chose seven males and two females placed into three age categories, youngest (age 20-29, n=5); middle (age 30-39, n=2) and; mature (age 40+, n=2). When choosing subjects, the exclusion criteria was that no pre-existing injury could be present in either hand due to the examination method. A pre-consent form approved by the IRB committee was given to each subject before testing began.

Subject Comfort

Participants were tested in an isolated, temperature-controlled room. The experimenters' instructions were for the subject to relax in a comfortable chair with both of their hands placed palm down on a table in front of them. The Adductor pollicis muscle of both subject's hands were marked to ensure accurate and consistent pressure stimulus application. Wireless, dry EEG was connected to the subject's scalp while instructions were read (figure 2). Subjects were told to hold a time-sensitive trigger throughout the test. They were instructed to press the button when: 1) Initial signal, "press trigger" was given, 2) discomfort was first experienced (threshold), and when 3) stimulus pressure became unbearable. Subjects could opt out at any time.

Figure 2: Subject awaiting pressure stimulus test. Dry quick-20 EEG device is connected in testing room; with hands (adductor pollicis) marked using dry erase marker for points of stimulus and with Quick-20 Dry EEG connected to detect brain waves.

Experimental Procedures

Tactile stimulation was performed using a Wagner pressure gauge. During the baseline trial: The pressure gauge was placed on the surface of subjects' hand, but no pressure was applied. Afterwards the tester applied pressure with the 1 cm^2 tip while monitoring the pressure with an algometer. Pressure was slowly increased during each trial at a fixed rate of 1 kg (2.20 lbs) every 30 seconds to a maximum of 5.5 kg (12 lbs). Results were recorded in pounds.

Measures

There was a one-minute interval of rest in between each trial to avoid pain wind-up [11]. There were four trials (excluding baseline), each included step two-four below:

1. Baseline (no stimulus/beginning of experiment);
2. Low stimulus (beginning of trial to threshold);
3. Max stimulus (threshold to maximum tolerance/end of trial);
4. Rest (no stimulus in between trials).

Data was separated into time epochs then analyzed in MATLAB [12] using support vectors to categorize pain.

Pre-Processing

EEG-signal data were sampled at 500 Hz. Preprocessed signals were visually examined for high amounts of convoluted data and if present, omitted from the study. Butterworth and notch filters were used to eliminate noisy data.

Supervised Machine Learning with SVM

Feature Extraction

This study was performed using eight frequency band powers captured in the 19 channels as features (8*19=152 features): δ (1–4 Hz), θ (4–8 Hz), α (8–12 Hz), β1 (12–16 Hz), β2 (16–20 Hz), β3 (20–24 Hz), β4 (24–28 Hz), and low γ (28–32 Hz) bands. The label vector was supplied to the machine learning algorithm, which included stimulus levels: no stimulus, low stimulus, and max stimulus. Time epochs occurring before baseline and after the end of the final trial were discarded.

Classification

We constructed feature vectors containing frequency band powers obtained through PSD for 19 channels. Then a label vector for pressure stimulus levels was created

for each row (no stimulus, low stimulus and high stimulus). Afterwards, SVM was used to compare each individual observation.

Type of classification - Linear classification was performed using SVM to predict a maximum margin classifier for: 1) rest vs. low stimulus; 2) rest vs. max stimulus; and 3) low vs. max stimulus. The support vector machine algorithm is determined by a binomial classifier

$$(c) = \sum a_i \, k(s_i, x) + b, \qquad (1)$$

where c is used to classify observations in vector x. When $c \geq 0$ then x is classified in the 1st group, and when $c<0$, x is placed in the 2nd group. Contributions of each x vector is explained by a_i. The kernel function is k which becomes a dot product when using a linear kernel. The support vectors are represented by s_i and the bias by b.[13]

Validation

Efficacy of the SVM algorithm was assessed using rate of true negatives (specificity), true positives (sensitivity) and correctly identified observations. This is known as accuracy. Standard error and p-values were calculated for individual and group classifications using a binomial test.

Results and Discussion

Channel and Subject Averaged Relative Band Powers- Figure 2 displays results for relative EEG band power. Height of each bar represents relative band power taken as the mean value during the three conditions.

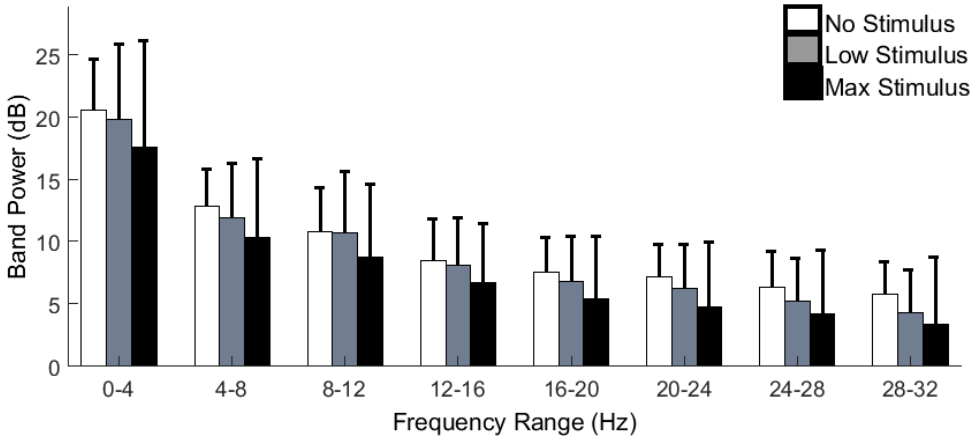

Figure 2: Relative EEG frequency band power in multiple frequency ranges for window size = 6 s Averaged across observations, channels, and subjects. All changes in relative band powers were significant at the 5% level.

We used a one-sample t-test to determine any significant changes. Standard error bars describe the amount of variability in each result from 10-fold cross validation.

Results show that relative change in each frequency band power from rest to painful states decreased significantly at the 5% level: δ ($p = .002$), θ ($p = .004$), α ($p = .005$), β1 ($p = .005$), β2 ($p = .009$), β3 ($p = .013$), β4 ($p = .015$), and low γ ($p = .024$). This means there is only a 0.05 or a 5% chance of incorrectly assuming these differences in brain activity resulted from test conditions. Results indicate that neural activity decreased throughout the cortex because of increasing pain stimulus.

The significance of these results, taken in retrospect to previous studies, is that increased pain normally leads to decreased average power density in δ, θ, α and β ranges (2 - 25 Hz). [14,15] Our results for δ and θ were similar to a previous study involving cold pain, where these powers were highest [16].

Subject average topographical distribution of difference of band powers- Figure 3 shows difference between subjects' band power for each condition. For example: rest = band power during low stimulus minus band power during no stimulus. Red indicates that an increase occurred in power for the frequency band; blue represents a decrease occurred; and green represents no change in power of frequency occurred during changing stimulus level.

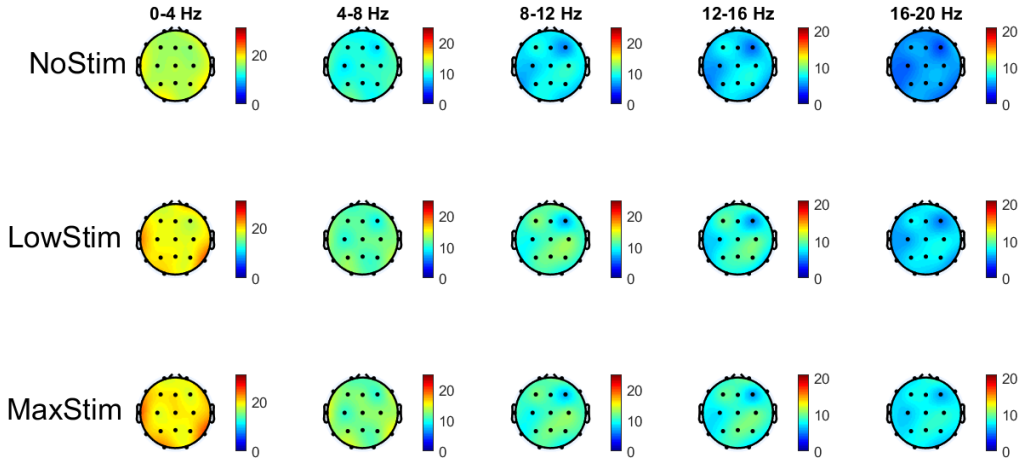

Figure 3: Topographic distribution of frequency band power. Window Size = 6 sec. Averaged across subjects and observations.

Changes in frequency power appeared consistent for each condition. Power was high for lower frequency bands (i.e., δ and θ) then decreased with rising frequency. These results indicate that the entire brain response to pressure pain stimulus is relatively the same.

Static changes in resting state EEG have been reported in previous experiments dealing with pain [16]; this does not indicate unusable data but could reflect brain activity not explicitly studied. Alpha band (1-4 Hz) and θ bands (4-8 Hz) once again had the highest average power. Both have been shown to be highly associated with pain. [17, 18]

Classification accuracy for subject specific trained SVM: Figure 4 displays accuracy of binomial classification using the SVM algorithm to determine moments of: rest vs low stimulus; rest vs max stimulus; and low stimulus vs max stimulus for individual subjects. Height of bars represent accuracy as a percentage. Each comparison was completed with changing window sizes of two, four and six seconds.

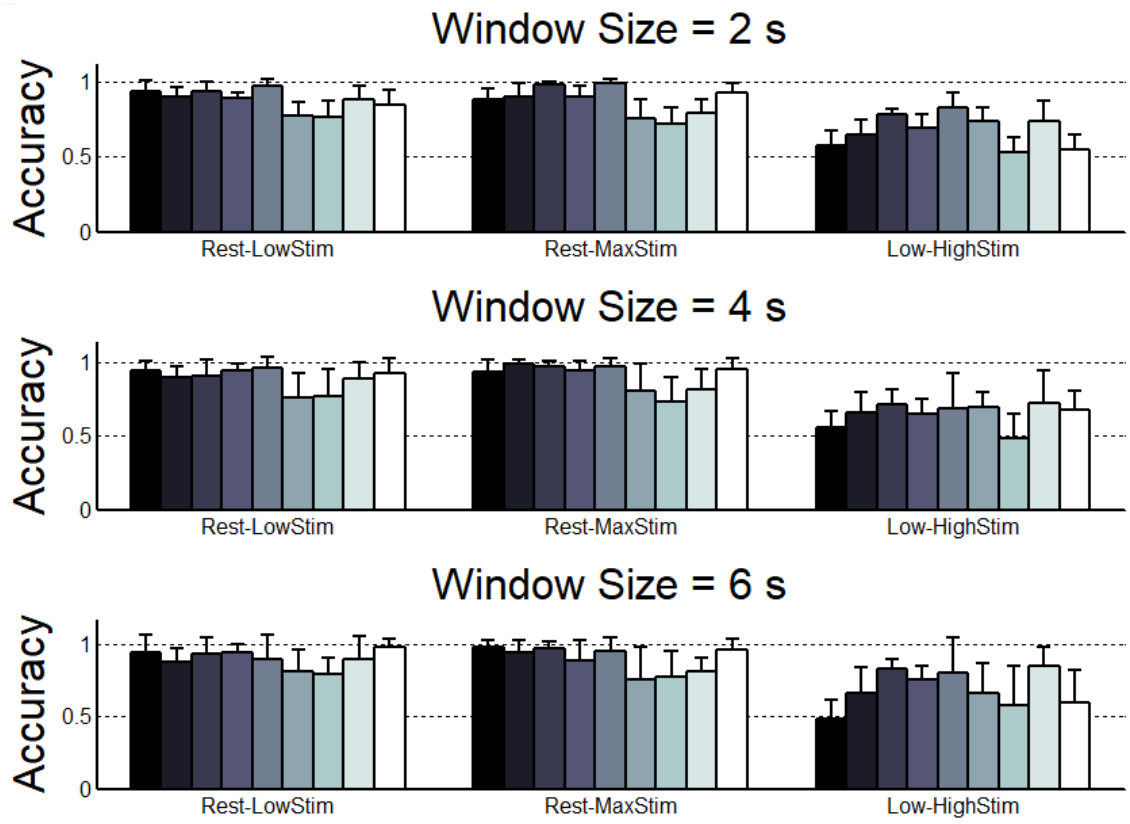

Figure 4: Accuracy of binomial classification for multiple window sizes.
Subject specific SVM (i.e., SVM trained for individual subjects).
Every bar represents one subject.

We achieved accuracy near 100% during individual trials when classifying for each condition. The maximum classification accuracies were as follows: low vs max stimulus was 85% (± 27%), rest vs. low stimulus was 98% (± 17%), and rest vs. max stimulus accuracy was 98% (± 23%). Lowest accuracy occurred for low vs maximum stimulus (20%). Accuracy was calculated as the area under a binomial density curve.

Table 1 shows mean classification accuracy along with standard deviation (SD) for each comparison.

Table 1: Mean classification accuracy for nine subjects and three binary classifications.

Low vs Max Stimulus	***SD* +/-**	**Rest vs Low Stimulus**	***SD* +/-**	**Rest vs Max Stimulus**	***SD* +/-**
48.00%	*13.27%*	94.33%	*12.48%*	98.33%	*5.00%*
66.61%	*17.95%*	87.78%	*9.70%*	94.67%	*8.19%*
83.27%	*6.74%*	93.33%	*11.06%*	97.09%	*4.79%*
75.28%	*9.72%*	94.56%	*5.45%*	89.00%	*14.28%*
80.00%	*24.49%*	90.00%	*16.58%*	95.00%	*10.00%*
66.67%	*20.71%*	81.00%	*15.78%*	75.50%	*22.85%*
57.50%	*27.25%*	79.00%	*11.58%*	78.00%	*17.46%*
85.50%	*13.12%*	90.00%	*15.28%*	81.67%	*8.98%*
60.00%	*21.91%*	98.00%	*6.00%*	96.33%	*7.37%*

Since we were able to use SVM classification to achieve accuracy near 100% for individual EEG recordings, this proves that wireless, dry-EEG was successful in capturing changing brain patterns resulting from rising pain stimuli.

Limitations

Due to our small sample size, all results should be considered theoretical and not based on concrete evidence.

Conclusion

We used support vector machines to showcase frequency band changes that showed significance at the 5% level. With relative band power, we were able to show that at rest, and during pain states, EEG power tends to be increased at lower frequencies such as δ (1-4 Hz) and θ (4-8 Hz) bands. Results demonstrate that a dry, wireless, quick-20 EEG can effectively capture changes in brain activity resulting from pain.

Results from similar studies vary. In two different experiments, both using cold pain, Hadjileontiadis et al., used quick-20 dry EEG to discover changes in frequency band power due to stimulus condition can be non-significant (all frequencies F statistic < 3.17 and "p-value> 0.10," except for β1); whereas, Gram et al., used gel-electrode EEG and found significant increase in EEG power for δ (1–4 Hz), β (18–32 Hz) and γ (32–72 Hz) ranges and decrease in θ (4-8 Hz), α1 (8–10 Hz), and α2 (10–12 Hz) bands.[16,19]

One cause for these differences was answered by Pinheiro et al., in their recent literature review regarding pain assessment with an EEG: Changes in band power depends on the type of injury and stimulus producing discomfort [20]. For instance, θ power has been shown to increase from rest for patients enduring neuropathic pain and migraine, but not in fibromyalgia patients or those with back pain. [21,22] It was noted that majority of these studies also found that θ and α band changes were in highest correlation with pain, and it was suggested by Pinheiro et al. that increases in θ band power could serve as a biomarker in severe neuropathic pain.[23, 20] We saw similar changes in all frequency bands. Yet, due to our sample size, it will take conducting a larger study perhaps with more than one pain modality to make any valid conclusion.

REFERENCES

1. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. (National Academies Press (US), 2012).
2. Committee on Advancing Pain Research, Care, and Education, Board on Health Sciences Policy & Institute of Medicine. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. (National Academies Press, 2011).
3. Heart Disease and Stroke Statistics—2011 Update: A Report from the American Heart Association. Circulation 2011, 123: e18-e209, page 20. http://circ.ahajournals.org/content/123/4/e18.full.pdf. (Accessed: 31st January 2018)
4. Roger, V. L. et al. Heart disease and stroke statistics--2011 update: a report from the American Heart Association. Circulation 123, e18–e209 (2011).
5. The American Cancer Society. The American Cancer Society's Principles of Oncology: Prevention to Survivorship. (John Wiley & Sons, 2018).
6. Nir, R.-R., Sinai, A., Raz, E., Sprecher, E. & Yarnitsky, D. Pain assessment by continuous EEG: association between subjective perception of tonic pain and peak frequency of α oscillations during stimulation and at rest. *Brain Res.* **1344,** 77–86 (2010).
7. Ingvar, M. Pain and functional imaging. Philos. Trans. R. Soc. Lond. B Biol. Sci. 354, 1347–1358 (1999).
8. Press, W. H. Numerical Recipes in C: The Art of Scientific Computing. (Cambridge University Press, 1992).
9. CEC — eContact! 14.2 — A Brief History of Biosignal-Driven Art: From biofeedback to biophysical performance by Miguel Ortiz. CEC | Canadian Electroacoustic Community Available at: http://econtact.ca/14_2/ortiz_biofeedback.html. (Accessed: 17th July 2017)
10. Nir, R.-R., Sinai, A., Raz, E., Sprecher, E. & Yarnitsky, D. Pain assessment by continuous EEG: association between subjective perception of tonic pain and

peak frequency of alpha oscillations during stimulation and at rest. Brain Res. 1344, 77–86 (2010).

11. Xu, F. & Lu, T. Introduction to Skin Biothermomechanics and Thermal Pain. (2011).
12. MATLAB® and Simulink Toolboxes. in Matlab 565 (2017).
13. Andrew, A. M. AN INTRODUCTION TO SUPPORT VECTOR MACHINES AND OTHER KERNEL-BASED LEARNING METHODS by Nello Christianini and John Shawe-Taylor, Cambridge University Press, Cambridge, 2000, xiii 189 pp., ISBN 0-521-78019-5. Robotica 18, 687–689 (2000).
14. Sarnthein, J., Stern, J., Aufenberg, C., Rousson, V. & Jeanmonod, D. Increased EEG power and slowed dominant frequency in patients with neurogenic pain. Brain 129, 55–64 (2006).
15. Stern, J., Jeanmonod, D. & Sarnthein, J. Persistent EEG overactivation in the cortical pain matrix of neurogenic pain patients. Neuroimage 31, 721–731 (2006).
16. Gram, M., Graversen, C., Olesen, S. S. & Drewes, A. M. Dynamic spectral indices of the electroencephalogram provide new insights into tonic pain. Clin. Neurophysiol. 126, 763–771 (2015).
17. Gram, M., Graversen, C., Olesen, S. S. & Drewes, A. M. Dynamic spectral indices of the electroencephalogram provide new insights into tonic pain. Clin. Neurophysiol. 126, 763–771 (2015).
18. Taesler, P. & Rose, M. Prestimulus Theta Oscillations and Connectivity Modulate Pain Perception. J. Neurosci. 36, 5026–5033 (2016).
19. Hadjileontiadis, L. J. EEG-Based Tonic Cold Pain Characterization Using Wavelet Higher Order Spectral Features. IEEE Trans. Biomed. Eng. 62, 1981–1991 (2015).
20. Pinheiro, E. S. dos S. et al. Electroencephalographic Patterns in Chronic Pain: A Systematic Review of the Literature. PLoS One 11, e0149085 (2016).
21. Vuckovic, A. et al. Dynamic oscillatory signatures of central neuropathic pain in spinal cord injury. J. Pain 15, 645–655 (2014).

22. Bjørk, M. H. et al. Interictal quantitative EEG in migraine: a blinded controlled study. J. Headache Pain 10, 331–339 (2009).
23. Vécsei, L., Majláth, Z., Balog, A. & Tajti, J. Drug targets of migraine and neuropathy: treatment of hyperexcitability. CNS Neurol. Disord. Drug Targets 14, 664–676 (2015)
24. Cognionics. (2018, March 21). *Quick-20 Dry EEG Headset*. Retrieved from Cognionics: http://www.cognionics.com/index.php/technology