Thesis Project Portfolio

Computationally Modeling Spreading Depolarizations' Impact on Intrinsic Patterns of Brain Activity

(Technical Report)

Diversifying the Knowledge Base: The Strive for the Inconceivable True Objectivity

(STS Research Paper)

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Executive Summary

Migraine, a disabling neurological condition that is often confused with headache, is known to induce spreading depolarizations (SDs) or periods of brain activity suppression that travel across the surface of the brain that acutely worsen prognosis and may lead to death. In order to identify SDs, electrocorticography (ECoG) – a highly invasive technique requiring burr holes in the skull – must be used as electroencephalography (EEG) is not sensitive enough to depict the abnormal spikes that characterize SDs. As not every patient with SDs will consent to this invasive technique, a non-invasive method must be developed. Migraines are much more prevalent in women than men (20.7% versus 9.7% globally) and have a misdiagnosis rate of 44.0% when consulting a primary care provider (PCP) (Kim et al., 2024; Rossi et al., 2022). This misdiagnosis rate is seemingly exacerbated by the fact that this is a feminized disorder. This lack of urgency in ensuring proper care can only be rectified by focusing research on women's health. Since migraine sufferers likely won't consent to an invasive ECoG, developing a way to show the severity of SDs in migraine non-invasively is of utmost priority.

In order to work towards a non-invasive method of identifying SDs, predictors of SD must be found. To do this, data from intensive care unit (ICU) patients with SD from the University of Virginia (UVA) was processed using a bandpass filter (0.5 Hz – 100 Hz) to look at overall activity, a notch filter (60 Hz) to remove 60 Hz noise, and a highpass filter (0.01 Hz) to remove low frequency noise and normalize the baseline. These waves were then overlayed to identify SDs via finding the sharp negative DC shift characteristic of SDs. Each SD was then characterized by amplitude and duration. The Hilbert transform was used to extract the phase (using the angle function from MATLAB) and the amplitude (using the absolute value function from MATLAB) from the bandpass data to calculate the cross-frequency coupling (CFC)

metrics. Additionally, the bandpass data was also filtered within each wavelength range (delta, theta, alpha, beta, gamma), and the extract alpha and delta waves were used to calculate the alpha-delta ratio (ADR) (Finnigan et al., 2016). Multiple metrics of CFC were used to quantify phase-amplitude coupling (PAC) and one metric was used to quantify amplitude-amplitude coupling (AAC) (Penny et al., 2008; Tort et al., 2010; Zhang et al., 2013). These metrics were graphed against time as well as against each wavelength combination used in the respective calculation. Correlation and significance testing was conducted to determine if any patterns were present.

It was found that SD disrupt coupling during and well after resolvement. There was a higher correlation of coupling disruption where delta was implicated for the modulation index (MI) and the phase-locking value (PLV) metrics. The AAC was measured using the amplitude-envelope correlation (r_{AEC}) metric which revealed more disruption in the faster bandwidths (beta, and gamma primarily). To determine if there is any correlation between the coupling metrics and SD duration, the percent change in the metrics between before and during SD onset were graphed. It was found that the ADR did not corroborate past studies as it increased in value during SD onset rather than decrease. Additionally, MI was found to change the most when the delta phase was used with the theta and alpha amplitude, regardless of SD presence. PLV was found to change the most when the high gamma (HG) or the delta phase were impacted. r_{AEC} was found to change the most when the gamma amplitude was impacted and the theta, alpha, or beta amplitude was not impacted. Overall, there was a loose correlation for all coupling metrics between SD duration and percent change between before and during SD onset. The longer the SD was, the greater the metric became during SD onset. Further studies on different correlations

such as SD amplitude as well as different injury types must be done in order to fully understand the effect SDs have on the brain.

In order to create truly objective, non-discriminating research, focus towards those who have been discriminated against is necessary. This focus levels the playing field of understanding, ensuring that future steps are on even ground. Migraine can be used to highlight discrimination and stigma that surround 'women's diseases' due to the higher prevalence in women whilst still having a substantial prevalence in men. Using Donna Haraway's thesis on objectivity, research articles were analyzed. The research papers used were fully-accessible (no paywall or subscription), in English or translated to English, did not focus solely on social class or location, and no literature reviews, book reviews, commentaries, case studies, or papers with a study size less than one were used. With this criteria, only eight studies were used.

Of these eight studies, only two briefly considered social class or race but no true discernment between these parties were considered. Only three of the eight studies explained and differentiated the differences between presentation of the different types of migraine. The generalization across all types of migraine is inaccurate as each type requires a different level of treatment and diagnostic criteria. Additionally, three of the eight studies were surveys which introduced response bias. With the intention of educating the public, these fully-available studies fall short with explaining the effect society has had on the state of migraine research today. Many of these studies do not acknowledge the discrepancies or discrimination that people of color and women face. The main motivator to study migraine is the lack of understanding of migraine with little mention as to why we have this gap in the first place. Not acknowledging the issues that give rise to discrimination allows for more discrimination to occur. In order to work

towards truly objective research, where everyone is properly considered, we must hold each other accountable by acknowledging the past and focusing on bridging the gaps in knowledge.

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