Developing Wearable Headband for Enhancing Slow Wave Sleep in Alzheimer's Patients
(Technical project)

Investigating Normalizing Bias in Cochlear Implant Regulations
(STS project)

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On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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Introduction

Medical devices are any apparatus, machine, software, or instrument used either alone or in combination with medical procedures to diagnose, prevent, screen, or monitor illnesses and treatments to those who have various degrees of healthcare needs. Within the US, the Food and Drug Administration (FDA) is an organization responsible for the selection and regulation of which devices are approved for use. According to the Center for Devices and Radiological Health (CDRH) at the FDA, there were approximately 18,800 device submissions received in 2022 alone, and the selection criteria for these depend upon the categorization of these devices ("Center for Devices", 2022). These three categories are Class I, II, or III devices, which are lowest to highest risk respectively, based on how many regulatory controls are required to provide safety assurance.

However, these regulatory controls often hinder access to approval for device marketing, and so there are many ways that medical device companies, who likely prioritize making a profit by marketing the device as quickly as possible, may manipulate these regulations to their benefit. Class I and II devices have less detailed regulatory processes and require only general preclinical and clinical data; however, Class III devices which pose a genuine risk to patient safety often have much more strict design and testing requirements, including the need for clinical trials. However, there are some ways in which these Class III devices may be reclassified as either Class I or II devices to avoid more strict testing requirements. For example, the pre-market approval (PMA) required during the testing process of Class III devices may be avoided if the device is similar to a predicate device, equating the device to that of a lower risk level when it (Van Norman, 2016). Moreover, some devices which qualify for "exempt" status need no proof of safety or efficacy, which is true for 75% of Class I devices as well as some Class II devices.

Considering the possible workarounds to the so-called regulations for FDA approval, it is important to study the degree of bias within these regulations to understand how the approved devices may disproportionately and negatively affect any marginalized groups. These biases can contribute to the marketing of devices which are "normalizing", or catered towards helping people from certain marginalized social groups fit in with the "mainstream". One such normalizing device is the cochlear implant (CI), which is a device that is surgically installed into a region above the ear to stimulate the auditory nerve and allow for pseudo-hearing. As they require surgical intervention, CIs are classified as a Class III medical device, and have become a common option for restoring partial hearing in those who are hard of hearing or deaf (Eshraghi, 2012). However, it is important to highlight that an essential bias within the regulations of CIs is that they assume that being a hearing person is "normal" and desirable, while being deaf is not.

Issues with device regulations are further propagated by the fact that testing devices for racial and ethnic biases is not required by the FDA, which leads to a lack of transparency within the data used to market the device to the general public (Grant, 2023). Another critical point of possible bias is socioeconomic status (SES) of patients who are affected. Based on a study of randomized clinical trials in the U.S., it was found that less than 15% of studies considered or reported the SES of the trial participants (Alegria, 2021). As such, there are several avenues through which these regulations may be examined for biases which disproportionately affect different groups within society.

In my technical project, I will be focusing on developing a medical device which aligns with FDA regulations and affects a similar marginalized group; elderly patients who are affected by Alzheimer's disease. In my STS project, I will be analyzing the historical bias within FDA regulations affecting cochlear implants to understand how these have impacted the social and

cultural development of deaf people. These projects both aim to consider how FDA regulations have an indirect effect on the development of communities within two marginalized groups of society.

Technical Topic

Alzheimer's disease (AD) is a form of dementia resulting in progressive memory loss which affects over 6 million Americans. AD can also be fatal in some cases, killing 1 in 3 of those affected ("Alzheimer's Disease", n.d.). Currently, there are no cures or treatments for patients that target the root cause of the disease in the early stages of memory loss, as the exact mechanisms of AD-related neuropathology are unknown. Generally, it is known that AD is caused by a buildup of amyloid-beta proteins around brain cells, better known as plaque, which leads to neuronal toxicity in the central nervous system (CNS). This affects neural processing, and thereby memory retention ("How Is Alzheimer's", 2023).

A critical phase of sleep responsible for the clearing of these plaques is slow-wave-sleep (SWS), which is the deepest and most restorative phase in terms of maintaining memory strength. This works through cerebrospinal fluid (CSF) flow, a biological mechanism which synchronizes with blood flow during the clearing process. In patients with Alzheimer's disease, CSF clearance abnormalities have been found in extracranial CSF samples (de Leon, 2017). One key marker of cognitive decline is decreased slow wave activity (SWA) in old age, which is bidirectionally linked to amyloid-beta presence in the brain. SWA can be measured through the use of electroencephalogram (EEG) readings, which measure electrical activity emitted by brain cells through electrodes attached to the scalp (Wunderlin, 2020).

Auditory stimulation through pink noise has been found to increase memory consolidation in patients with mild cognitive impairments (MCIs) by increasing the amplitude of

slow oscillations (SOs) during SWA (Harrington, 2021). Pink noise is best described as constant ambient sound, which has a lower frequency and deeper pitch than white noise; this allows for filtering out of higher frequency sounds which may disturb sleep, thereby inducing a constant phase of sleep (Robinson, 2022). As such, the primary goal of the technical project is to target memory retention in patients with Alzheimer's disease through the development of a wearable device that delivers in-sleep acoustic stimulation. There are three major components of the project. The first is to complete a form factor design of the wearable device, with the required electrodes and wireless hardware for EEG data collection. The second is to develop and test the closed-loop EEG system, which is a machine learning algorithm that detects SWA patterns during sleep and predicts the occurrence of the next SO to deliver acoustic stimulation accordingly. Finally, a supplementary mobile application will be developed in order to display tracked sleep data and increase patient usability of the device.

The technical question I will be answering in this project is: how do we make sure that the device design specifications align with FDA regulations and are able to be used by all AD patients? Broadly, these design specifications include factors such as comfortability, useability, connectivity, safety, and accuracy. As this device is external, it would be regulated as a Class II medical device, meaning that it is not as heavily tested as more invasive Class III devices. Due to this, it is important that the SWA prediction algorithm and materials used in the form factor of the device are studied for potential bias during the research and development stage, particularly in terms of lack of previous testing on a specific ethnic or socioeconomic group. By considering both required and unseen factors, the device deliverable will ideally be able to effectively provide treatment to and improve the diagnosis of any patient affected with AD.

STS Topic

Cochlear Implants (CIs) are historically highly controversial within deaf communities, as it is implied that they are "corrective" devices for hearing disabilities, contributing to the normalization of being a hearing person, and the marginalization of deaf people. There has also been much debate surrounding the effect of CIs on the deaf experience, as deaf people do not consider hearing loss a disability that needs to be "fixed". Although one may assume that being deaf can be an alienating experience, most deaf people are well integrated into the deaf community, which shares a strong culture of self-sufficiency based on the usage of American Sign Language (ASL). Hearing is not sought-after because communication is not a barrier within this community, and deaf people are able to lead productive lives regardless (Erting, 1996).

In the 1980s and 1990s, parts of the deaf community within the United States protested the use of CIs on behalf of children, rooted in the conception that CIs often force deaf people to assimilate into a hearing world without giving them the ability to hear at the same level of a hearing person (Sparrow, 2005). A review of articles on CI user feedback determined that the average hearing perception ability improved from 8.2% to 53.9%, demonstrating that physical hearing is not fully restored as a result of the device (Boisvert, 2020). Consequently, deaf people who use CIs are often stuck between deaf and hearing culture, causing them to be unable to fully identify with either and significantly affecting their sociocultural development (Sparrow, 2005).

To understand this effect, CIs and their regulations must be firstly analyzed in terms of their effects on social development of deaf children as this is likely the earliest or most common instance at which CIs are able to impact the development of an individual deaf person. Parents are often forced to decide whether or not to implement a CI when their children are very young, as this provides a higher likelihood for more significant hearing improvements. Accordingly,

both the FDA and medical specialists recommend early implantation of CIs ("Mayo Foundation", 2019). However, despite professional advice regarding the detrimental consequences of CI usage to social factors such as deaf identity, communication, and educational implications, it was found that parents were more inclined to carry on with implementation at a younger age based heavily or solely on medical advice stemming from CI regulations (Hardonk, 2011). Relatedly, a study evaluating the self-esteem and social wellbeing of children with and without CIs found that 68% of the children with low self-esteem were children with CIs who attended deaf schools (Percy-Smith, 2008). This demonstrates how the use of cochlear implants at such a young age may impact the potential quality of life of deaf children, who develop into deaf adults facing the same social issues; in this way, CIs may be hindering the social adaptation of deaf people throughout their lives.

Another power structure that significantly impacts the implementation of CIs is socioeconomic status (SES), as CI cost ranges from $50,000 to $100,000. Despite this cost being covered in part by federal health insurance programs such as Medicare and Medicaid, difference in access to healthcare between those of different SES plays a clear role in which deaf people are even able to receive a CI ("Duke University", 2023). Within families where deafness is genetic, unemployment rates are often as high as 16.1% (Gallaudet, 2022). One study found that over 70% of children who received CIs lived in above-average SES areas. Additionally, despite white children making up 51.1% of patients with severe hearing loss, they accounted for 73% of cochlear implant recipients, while Hispanic, Asian, and black children made up less than 9% each (Stern, 2005).

Historically, literature surrounding FDA regulations of cochlear implants is published by the FDA itself and paints these regulations ensuring safety, effectiveness, and constant

innovation within the CI field (Sauberman, 1983). Current research regarding CIs also revolves around the influence of their design and use on deaf communities, rather than the root of how this design came to be through testing and regulation. However, to truly identify how the technological and social aspects of CIs are connected, these regulations must be deciphered. Thus, the research question I aim to answer is: how have regulations set for cochlear implant approval by the U.S. Food and Drug Administration (FDA) demonstrated a normalizing bias historically?

To elucidate how FDA regulations play into societal power structures that determine which CIs and their associated recommendations for use are approved, I will be conducting a literature review of these regulations and highlighting the inherent bias within each. This includes the aforementioned recommendations surrounding age as a result of the approval of specific CI devices, as well as how those have changed historically; for example, criteria for adult candidates has expanded significantly in accommodations since 1990, while the age and speech perception criteria for children who are CI candidates has only changed with a reduction in the minimum age from 24 to 9 months in the past 30 years (Park, 2021). This investigation will be continued through a thorough analysis of regulations surrounding Class III devices from the FDA database on requirements which were enacted by the Federal Food, Drug, and Cosmetic (FD&C) Act. This includes information on general controls listed under specific sections within the act, applications which must be submitted such as premarket notifications (510k), and limitation and exemption rules. Additionally, special controls and PMAs will be studied that apply to cochlear implants, as these are specific to the device and will exemplify what the true requirements are currently (“Center for Devices”, 2018).

Conclusion

In my technical project, we will be creating and testing prototypes of an in-sleep acoustic stimulation headband for patients with AD, to ultimately increase memory retention of these patients. The holistic consideration of design specifications for the device will be utilized in future developments so that the possibility of device usage and effectiveness is equal for all patients. In the STS deliverable, I will be investigating normalizing bias within FDA regulations to understand how this has led to the socioeconomic and cultural impacts discussed. By investigating the roots of the bias and outlining specific regulatory gaps, we can gain a better understanding of how FDA regulations are formed to create solutions that will prevent marginalizing effects of future medical devices.

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