Electricity – A Bright Future for Mental Health Care and Medicine

A Research Paper submitted to the Department of Engineering and Society

Presented to the Faculty of the School of Engineering and Applied Science University of Virginia • Charlottesville, Virginia

> In Partial Fulfillment of the Requirements for the Degree Bachelor of Science, School of Engineering

Pierson Shamaiengar

Spring 2023

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

Advisor

Bryn E. Seabrook, Department of Engineering and Society

STS Research Paper

Introduction

The accepted answer to many of today's modern medical ailments, especially mental health disorders, is medication, but should it be? For more than a century, alternative medical treatments that focus on the electrical component of human biology rather than the chemical component have shown great promise in curing a variety of illnesses. Many of these treatments are now approved and available to the public but their existence and efficacy remain largely unknown. In particular, transcranial magnetic stimulation (TMS) and electroconvulsive therapy (ECT) have had significant success in treating drug-resistant depression with few adverse side effects (Mayo Foundation for Medical Education and Research, 2018). The question remains, however, whether these treatments are viable candidates to replace current solutions offered by the pharmaceutical industry. Whether this is possible, and whether it should be done, is answered with an analysis of these treatments through the lens of technological momentum.

Methods

This work employs the primary research methods of documentary analysis and discourse analysis. Documentary analysis involves the study of primary sources which, in this case, largely consists of collecting data and evidence from a variety of medical journals and studies that evaluate these treatments as well as pharmaceutical alternatives. Examining these sources is necessary to understand the efficacy of electrically-based treatment methods because the results have to be scientifically verifiable to compare to them with competing treatments. The second method, discourse analysis, is similar to the former but is used to gather evidence from more diverse sources and understand the whole of the dialog surrounding these treatments potentials.

Expanding the breadth of the search is necessary because not all of these treatments have rigorous studies behind them yet. Nonetheless, a large volume of anecdotal evidence supports and opposes a variety of these technologies and any attempt to forecast the future of medicine in this up-and-coming area needs to consider those options for which research has not been published.

Background Information

The history of bioelectric medicine is an ancient one. It dates back to at least the Greek and Roman Empires, long before the phenomenon that would later be named electricity had any hope of being understood. In these primitive times, Hippocrates and Scribonius Largus, along with other noted physicians of their eras prescribed use of the torpedo fish - now known as the electric ray – to treat headaches, gout, prolapsed anus, and even to numb pain during childbirth and medical operations (Tsoucalas et al, 2014). True understanding of this practice eluded humans for nearly 2000 more years until 18th century scientists began the formal study of electricity. One of the first in this generation of experimenters who applied these studies to biology was Luigi Galvani who famously observed a frog's leg twitching from the discharge of an electrical machine and coined the term 'animal electricity' (Livesey, 2019).

The work of Galvani and his contemporaries laid the foundation for what would become modern field of electric medicine. Today, perhaps the most well-known technologies in this class of medical techniques are those used for depression, specifically ECT introduced in 1938, and TMS, which arrived in 1985. The treatments have been shown to be effective and safe for treating a very common condition, which has shifted them into the public eye, but they are not the only therapies currently being offered by electric devices, and depression not the only condition being remedied. In the 1980's, neurosurgeon Kevin Tracey led a team of researchers at

Weill Cornell Medical Center that discovered the inflammation producing molecule Tumor Necrosis Factor (TNF), which can lead to death if overproduced (*Kevin J. Tracey, MD.*, 2021). This finding led to the development of monoclonal anti-TNF, a drug used to halt the production of TNF in the body which has been used successfully on a variety of inflammatory conditions. However, Tracey would later discover that electrical stimulation to the vagus nerve, which plays an important role in TNF production, stopped the creation of the molecule faster and more precisely than the drug that had been developed (Fox, 2017). He would go on to found Setpoint Medical Corporation which develops devices for this purpose (Balch, 2022).

Tracey's work on TNF is but one of numerous examples where new advances in bioelectric medicine are outperforming their pharmaceutical counterparts. In fact, his research is not the only modern use of vagus nerve stimulation (VNS), nor the only device the implements it. VNS has been studied for over 20 years in the treatment of numerous health complications including autoimmune disorders, sepsis, and epilepsy (González, Yengo-Kahn, & Englot, 2019). Similar treatments are also being studied in patients with post-traumatic stress disorder and, more recently, long COVID-19 (Lamb, Porges, Lewis, & Williamson, 2017; *Pilot study suggests long covid could be linked to the effects of SARS-COV-2 on the vagus nerve, 2022).* So, although this paper specifically addresses depression, the precedent is set for similar technologies to influence a wide range of medical fields in the coming years.

STS Framework

To answer the research question, the various technologies, devices, and the general concept of electricity as medicine are being analyzed through the lens of technological momentum. To better understand this theory, one must understand the gap that its creator, Thomas Hughes, sought to bridge between two prior theories: technological determinism and social construction. Technological determinism is "the belief that technical forces determine social and cultural changes," while social construction asserts that "social and cultural forces determine technological change." Each of these frameworks establishes either technical forces or social forces as dominant over the other. Hughes, in his objection to these one-sided stances, created technological momentum positing that "social development shapes and is shaped by technology" and that momentum is time dependent (Hughes, 1994).

Hughes and technological momentum are not without their critics, however. In particular, opponents of the theory argue that it is still centered on determinism because it places technology at the center of historical process, intertwined with everything else. One such critic, Alessandro Colarossi wrote a critique stating that "[technological momentum] appears to be simply a matter of rewrapping some concepts of [social construction and technological determinism] into a different package, albeit one that is largely derivative." This assertion follows Colarossi's analysis that Hughes's attempt to delineate technological momentum from determinism fail because both frameworks incorporate time dependence and a cause-and-effect formula which Hughes believes to be separating characteristics (Colarossi, 2020).

While this critique may have some validity in acknowledging undeniable similarities in between the two frameworks, it does not any way discount its ability to be applied to this research given that technological momentum incorporates any technologically deterministic aspects that will be used in the analysis. This work is also not the first application of technological momentum to the medical field. A similar approach was employed by Victoria Hinchberger in her 2020 research paper "The Technological Momentum of Cosmetic Procedures". Hinchberger acknowledged similar critiques and came to the conclusion that "the argument [of technological determinists] is not applicable to the analysis because the focus is not about whether society or technology has shaped the growth of cosmetic procedures, but rather the dangers of the continual growth." (Hinchberger, 2020) In the same way, technological momentum will be used here to forecast the continual use and expansion of electric medicine rather than societal shaping.

Results and Discussion

Can the people of the world overcome their depression by watching Netflix with a magnet next to their head? That is a peculiar question that one might ask themselves before understanding the data surrounding TMS treatments. The idea of it seems unbelievable and to many it appears little more than science fiction. However, given that many have had this very experience in TMS clinics across the country, the answer to that question is undoubtably yes, at least for some. The answer to the research question, on the other hand, is more nuanced. The reality is that both ECT and TMS have achieved a level of efficacy that is comparable to or better than the existing drug options. However, the conclusion cannot and should not be that these treatments replace antidepressants because the real issue facing mental health care is not which treatment is edging the others out in terms of remission but rather that on the whole there is not enough mental health treatment available. The conclusion of this analysis is that TMS and ECT should no longer be relegated to secondary treatments and that, along with drug therapy, all three should be offered as a first line of defense against the mental health epidemic.

If the goal is to assess the future of medicine, there a few places better to start than the issue of mental health which, for the past few decades, has plagued the world more with every passing year. According to the World Health Organization, "depression is one of the leading

causes of disability," "20% of the world's children and adolescents have a mental health condition," and "suicide [is] the second leading cause of death among 15-29 year olds" (World Health Organization). The issue is a rampant and systemic one that effects every area of the world and every area of one's life. Those effected suffer from decreased performance, difficulties with relationships and family, and inability to work and participate in the economy. It is no understatement to say that the world will struggle to meets its development goals without an effective answer to this issue. As it happens, electric medicine has resulted in a variety of answers to this troubling problem and they need to be evaluated.

First, to understand how well any of these new-age treatments work, they have to be compared to a baseline of common treatment options. Mayo Clinic lists the first treatment option for major depressive disorder (MDD) as medication and lists a variety of the options currently available: selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and monoamine oxidase inhibitors (MAOIs), among others (Mayo Foundation for Medical Education and Research). When evaluating the efficacy of depression treatments, the primary metric for comparison is remission rate and given that there are dozens of medications that fall into these categories, it is not feasible to provide this figure for all of them. However, a retrospective study which analyzed the experiences of 3,678,082 patients with 15 mono-treated antidepressants can help establish upper and lower bounds. Among these drug therapies, the prevalence of remission ranged from 3.1% with Amitriptyline, a TCA, to 49.3% with Sertraline, an SSRI, with an average across all 15 of 29.2%. It is also worth noting that the highest remission rate from any of the drugs for any gender and any age group was 58.61% with Fluoxetine, an SSRI, in women ages 65-79 (Alemi et

al, 2021). In terms of comparison, the overall average of 29.2% will be considered the value other treatments need to approach or surpass to be competitive with pharmaceuticals.

ECT

The first electric therapy that will be examined is also perhaps the most well-known – although the association is rarely positive. ECT is a depression treatment that has been in use since 1938 and is still one of the most effective treatments available today. Its effectiveness is so well established that Kar and Somani, in their 2019 comparison of ECT to TMS stated that "the place of ECT in the treatment of severe depression, psychotic depression, depression with self-harm or treatment-resistant depression is well known and does not need any elaboration or reference. ECT remains the treatment of choice in all patients where there is a need for early response because of the risk of harm to self or catatonia" (Somani and Kar, 2019). Put simply, to those within the medical community, there is no question about the effectiveness of this treatment. The public, on the other hand, is largely unaware of this success.

General perception of ECT is so poor that it was rated as the least helpful mental health treatment in a Swiss survey, where only 1% of participants considered it to be effective (Maughan & Molodynski, 2016). Another survey found a similar 1.2% of the public favored its use while 57% considered it to be a harmful treatment (Maughan & Molodynski, 2016). Despite this gap, the results are undeniable and the efficacy of ECT can be easily demonstrated scientifically. For example, a study of acute ECT courses on both psychotic and nonpsychotic depressed patients found that the overall remission rate between the two groups was 87%, with separate group remission rates of 95% and 83%, respectively. The study researchers concluded that "ECT was effective in relieving severe major depression" (Petrides et al., 2001). Similarly, another study found that when comparing ECT against paroxetine, a commonly used SSRI, for

treatment-resistant depression, ECT was "superior to paroxetine in medication-resistant major depression, in terms of both degree and speed of response" (Folknerts et al., 1997). With remission rates well above 80%, which outpaces any drug therapy and the 29.2% metric, it is clear from these two studies alone that ECT is a promising treatment – but these two studies are not alone, and meta-analyses paint a more complete picture.

A first meta-analysis conducted in 2003 concluded that over 18 trials with 1144 participants, ECT was significantly more effective than pharmacotherapy (*The Lancet*, 2003). Then in 2004, a second meta-analytic review of randomized controlled ECT trials found "a significant superiority of ECT in all comparisons: ECT versus simulated ECT, ECT versus placebo, ECT versus antidepressants in general, ECT versus TCAs, and ECT versus MAOIs" (Pagnin, 2004). As one might imagine, and as Somani and Kar noted, it is hard to overstate the effectiveness of this treatment. So, the question becomes why is ECT not at the forefront of depression treatment given that its remission rates equal or exceed virtually all other treatments? The answer to this question is that, regardless of the effectiveness of a technology, the influence of society matters, and its effect on ECT has been bleak.

For many, the first association with ECT is time in history when the treatment was not only an overused one but a painful one that was often forced on patients. Depictions of this can be found throughout various media, especially in Hollywood films from the past 70 years where a review of 22 them which found negative depictions in 18. A similar review of Hindu cinema found depictions of forced ECT in all of the 13 films that were reviewed (Maughan & Molodynski, 2016). The most prolific of these films is One Flew Over the Cuckoo's Nest which famously won the "Big Five" Academy Awards and was deemed "culturally [and] historically ... significant" by the Library of Congress (The Library of Congress, 1993). As such, these historical and popular culture influences irreparably damaged ECT's public reputation and created a substantial stigma surrounding use of the procedure.

Along with this stigma there are two other notable factors that contributed to the decline in ECT use: side effects which, while significantly less than media depictions, are still present, and limited availability. The primary side effects are amnesia – including retrograde amnesia, which affects memories of the past, and anterograde amnesia, which hinders ability to remember new information – temporary headache, and muscle aching (Duke Health, 2013). In a study of 157 participants, the rates of these more common adverse effects are reported to be 19.1% while the incidence rate of potentially life-threatening adverse events, which many associate with the procedure, is 0.097% (Hajak et al, 2021). Also, in support of the safety of the procedure, significant scientific research "has not found any evidence of physical brain damage in patients who have had ECT. There is no increased risk of epilepsy, stroke or dementia after ECT" (Royal College of Psychiatrists, 2022). In terms of availability, ECT faces additional challenges because it is a medically intensive procedure that requires multiple providers with advanced training to administer correctly as well as using highly contested facility space in overcrowded hospitals (Cleveland Clinic, 2022; Wilkinson et al, 2021).

TMS

While a variety of factors hold back the use of ECT, other technologies press forward and have been able to make significant strides publicly and within the medical community; TMS is among the most promising of these. In a study of 307 patients across 42 TMS clinics, the clinician-assessed response rate to treatment was 58.0% and remission rate was 37.1% which, while significantly less than ECT, is comparable to antidepressants on average (Carpenter et al, 2012). In addition to remission rate, rTMS (repetitive TMS), when compared with

pharmacotherapy, was found as the dominant and more cost-effective alternative for patients suffering from treatment-resistant MDD. The model used in the study predicted higher quality-adjusted-life-years, the academic standard for measuring how well all different kinds of medical treatments lengthen and/or improve patients' lives, as well as reduced costs versus antidepressant medication (Nguyen & Gordon, 2015; ICER, 2021). While these findings are important in establishing the efficacy of TMS, the most promising aspects of current TMS therapy are not that it is more effective than other options but that it is as effective while being safer, faster, less obtrusive, and offering remarkable potential for future development.

One of strengths of TMS is that it is safe, has an extremely low side effect rate, and "is generally exceptionally well tolerated as compared to the side effects often seen with medications and ECT" (Stern, 2020). As discussed, the side effect rate for ECT is one of the major factors in its inability to become the preferred MDD treatment, but how do antidepressants fair? In a study of SSRI's, the most commonly prescribed class of antidepressants, 38% of the approximately 700 patients reported side effects. Of those 229 patients who listed at least one, the most commonly mentioned issues were sexual functioning, sleepiness, and weight gain. In terms of severity, 26% of these 229 patients identified the side effects were "very bothersome" or "extremely bothersome" (Cascade et al, 2009). More recently, a second study also evaluated SSRI's, stating that side effects are often underrepresented in clinical trials. In this case, the most common side effects reported by patients were flatulence (64%), drowsiness (59%), memory impairment (51%), decreased concentration (50%), yawning (47%), fatigue (45%), dry mouth (45%), weight gain (45%), light headedness (43%), and sweating (38%) (Anagha et al, 2021).

TMS, on the other hand, is comparatively well tolerated. For example, in a study of 301 patients, the discontinuation rate due to adverse effects was comparable to the placebo at 5% and 3%, respectively (Xia et al, 2007). Other studies in rTMS have reported minimal side effects led by scalp pain (35%) and local discomfort (10%) but these typically subside within a few minutes (Saini et al, 2018). The only serious side effect associated with TMS is seizure, but these are substantially rare events and the risk is less than 0.01% for each session (Cleveland Clinic, 2022). In addition to this, rTMS is considered safe and effective for pregnant and elderly patients while using either pharmacotherapy or ECT is challenging because of possible risk of adverse reactions (Somani & Kar, 2019).

Another favorable aspect of TMS is that a patient can, in fact, receive this treatment while watching television. That is to say, the procedure itself is completely non-invasive and requires no anesthesia which sets it apart distinctly from the process of ECT. In many cases, a patient will not have to go to a hospital as the process is entirely outpatient and often performed in separate TMS clinics. A TMS session requires no preparation, takes under an hour, and allows the patient to immediately go about their day afterwards without time needed for recovery (Cleveland Clinic, 2022). While this level of convenience falls short compared to taking a pill, it is marked improvement over ECT in all facets.

In spite of all of this research and these positives for TMS, perhaps its most interesting and exciting aspects are the things that nobody knows about it yet. TMS is a highly adaptable technique with "novel methods and innovations for treating depression, as well as a new clinical indication in obsessive-compulsive disorder" and other mental health areas (George, 2019). The curious thing about TMS is that there is almost no standardization or limit on what researchers will try to treat with it, and almost every study reviewed for this analysis remarked on this fact. Psychiatrists have stated that "the best way to administer [the] treatments is far from settled" and that "the protocols for maintenance boosters don't exist. Nothing has been approved by the FDA, so we devise our own protocols" (Weir, 2015). Psychiatrist Pandurangi at Virginia Commonwealth University School of Medicine noted that "when it comes to TMS, 'almost everything is a question.' What's the best frequency and intensity of the magnetic pulse? How many total treatments should patients receive, over how many days or weeks? Where on the scalp should the current be directed? Researchers are a long way from fine-tuning the technique" (Weir, 2015). Somani and Kar made a similar comment that "more research is needed in order to bring out standardized protocols of administration of rTMS covering issues like localization, frequency, intensity, number of pulses, maintenance regimen, unilateral or bilateral mode, concurrent medication, and so forth" (Somani & Kar, 2019). It is possible, and perhaps likely, that the best protocol for TMS is not currently in use and it has the potential to surpass its own current levels of efficacy and potentially even ECT, and realistically, one of these discoveries may have already happened.

Stanford Neuromodulation Therapy (SNT) is a new intensive and individualized form of TMS that holds several advantages over the typical treatment course, including significantly higher remission rates. In the first study that was conducted using this protocol nineteen of the 21 participants (90.5%) met remission criteria and neuropsychological testing showed no negative cognitive side effects (Cole et al, 2020). A follow up study was conducted the next year where 29 patients suffering from treatment-resistant depression participated in the study. In this case, after five days of treatment, 78.6% of the participants in the treatment group were no longer depressed, according to several standard methods of evaluation (Stanford Medicine, 2021). A

key differentiating factor is that the older approaches to TMS treatment took up to 6 weeks to solicit a response while the entire course of SNT treatment lasts only 5 days and all patients who achieved remission did so in that time. Furthermore, some of the already minimal physical side effects of TMS are further reduced under this protocol because it only uses an intensity of 90% of the motor threshold – the intensity of the TMS magnet needed to cause hand movement – as opposed to 120% for both traditional and deep TMS (Vogel, 2022). Given the recency of its development, SNT needs much more research behind it to validate the results of these studies and understand how it will fit into depression treatment but the results are promising to say the least. In September of 2022, the FDA approved SNT for use with treatment-resistant depression so more information about this protocol is expected in the coming years (Brain & Behavior, 2022).

Technological Momentum

The most important aspect of technological momentum to consider with these two treatments and their associated technologies is time – specifically how ECT and TMS have shifted between being technologically deterministic and socially constructed and how both phenomena have exerted their influence over time. To do this, one must take a closer look at the history of ECT whose modern reputation would betray the popularity widespread use of this treatment following its introduction to the public in 1940. For nearly two decades afterwards, ECT became extensively used around the country and, despite being other treatments being introduced in this same period, ECT thrived more than any other and "became the mainstay of biological treatments for psychiatric disorders during the 1940s and 1950s" (Payne et al, 2009). A technologically deterministic view would suggest that the most effective technology would be the dominant one and, for many years, ECT experienced this effect in a significant way, shaping mental health medicine for years.

Where technological determinism falls flat is in its assumption that this high performance would continue until a 'better' technology was produced, but technology was not the downfall of this treatment – society was. As discussed previously, media depictions created a pop culture perception of electric therapies that crippled their popularity and use to the point of near obscurity in the eyes of the public. This defeat is in spite of the fact that, in the many decades since its disgrace, medical science has failed to produce anything that could rival the procedure until relative recency. As a result, this latter half of ECT's storied history is a clear demonstration of the power of the social construction of technology (SCOT), even on the most successful and widespread technologies.

TMS, on the other hand, does not have this history. It was not created until well after the period of systemic psychiatric misuse and maltreatment and, as such, has been able to avoid any noticeable stigma associated with previous electrically-based mental health solutions. However, while it has dodged the ire of SCOT, this treatment is only now entering a period of technological determinism and has therefore failed to fully achieve technological momentum either. The defining feature of momentum is that it is highly resistant to change and of the three classes of treatments examined, this is only true of pharmaceuticals. In this case, the staying power of the drug therapies in America is a direct result of the financial and political power wielded by their creators and distributors as well as medical insurance companies.

A close look at nearly any relevant study that was examined for this work would illuminate that fact that both electrically-based treatments are almost exclusively used to counter

treatment-resistant depression. This means that neither of them, despite superior performance and significantly reduced side effects (in the case of TMS), are almost ever prescribed as the first line of defense against depression instead of pharmacotherapy. An illustration of this is one study on TMS effectiveness which noted that "patients received an average of 2.5 (\pm 2.4) antidepressant treatments of adequate dose and duration without satisfactory improvement" before ever being placed on the TMS course (Carpenter et al, 2012). One might suggest that these numbers would be expected given that TMS is a lesser-known treatment, but that suggestion would deny the reality that this system was built by design. In America, to receive insurance coverage for TMS providers require the patient to first try and fail *at least* two antidepressants and a course of psychotherapy (Bermudes, 2021). This means that the average American, who cannot afford TMS out of pocket, is financially strongarmed into using antidepressants even when TMS may be a better first option for them.

These facts become increasingly surprising for newer methods such a SNT which the FDA again only approved for treatment-resistant depression despite a remarkably short 5-day treatment course, substantial remission potential, and virtually no significant side effects (Brain & Behavior, 2022). There is even a question of whether SNT will be covered at all because of how many treatments are administered within the short timeframe. Insurance companies will have to alter their current policies before they offer this coverage for anyone. Furthermore, TMS is not alone in being artificially limited by insurance providers. In a study on the barriers to implementing ECT, authors Wilkinson et al. [2021] found that lack of physical space for the treatment posed a prominent challenge to creating and expanding ECT services. The authors suggested that this issue partially "due to low reimbursement rates of ECT compared to other procedure-based therapies and diagnostics, like colonoscopies" and that, to promote increased

availability of ECT, which has fallen significantly, insurers should increase reimbursement (Wilkinson et al, 2021). In short, insurance companies financially disincentivize medical professional from performing one of the most effective depression treatments.

The truth is that technology is not the major driving force of social and technological change – money is – and those with money will sway the balance of power away from superior technologies and treatments if it services them, even against the good of the people. That is not to say however that the monolith of medical care this is the pharmaceutical industry is immune to future developments, and it would seem likely that the future of mental health care in particular will shift toward various forms of TMS. For example, a significant drawback to the patient for both TMS and ECT is that both treatments are performed in-person at a medical facility and take around 45 minutes (Harvard Health, 2019). These logistical difficulties eliminate the option for many who do not have a facility in their area, lack transportation, or do not have the time for lengthy sessions in their day, but solutions to all of these issues are already in progress. In fact, portable household TMS devices are already in development and new TMS treatment protocols that take as little as three minutes are being studied and found to have the same effectiveness as those currently in use (Blumberger et al, 2018). These developments are encouraging for both the technology as well as mental health treatment as a whole. Given all of this, it might be appropriate to designate TMS as 'gaining momentum' but whether this future is achieved remains to be seen and will certainly be the subject of future inquiry.

Finally, for reiteration, the question posed is whether ECT or TMS should take the place of drug therapy which is currently considered the standard solution. The answer to this question is yes – for some people – but for others antidepressants will continue to be a needed and

convenient treatment. In the end, the key finding for this research is not a differential between remission rates that might cause someone to choose one treatment over another – although this was also found – but rather that, in a world with a shortage of mental healthcare, there are safe and effective treatments that are not being offered to the majority of patients in need. This is an error that must be corrected if the world hopes to combat rising mental health concerns.

Limitations and Future Research

The primary limitations of this research are scope and timing. There are a number of different technologies and treatments that, while they fit within this class of electric medicine, could not be included adequately in a report of this size. For example, vagus nerve stimulation, which is also used to counter treatment-resistance depression, had to be omitted for space reasons despite relevance to the topic. Further, for those technologies that were analyzed, such as TMS, this research comes at a time when many of the most promising new developments in the treatment have either not been discovered or they have not had the time to be researched adequately. For anyone hoping to continue this research, the best path way is to fill the gaps left in this project by diving into additional existing treatments and also staying up to date on future developments, such as the efficacy of SNT and handheld TMS, which are expected in the coming years.

Conclusion

When one analyzes remission and side effects statistics for electroconvulsive therapy, transcranial magnetic stimulation, and antidepressants, the drugs appear to be solidly in last place. However, a broader view must be taken to understand that, at its core, this issue is not one of replacement but one of access. First, with the current technology, antidepressants remain the

most accessible option for those suffering from depression. For some, the travel and time requirements of ECT and TMS will eliminate them as choices while the ease of taking a pill can still provide relief or even remission. Second, even those that are able to receive TMS and ECT, logistically speaking, will find these treatments have been 'pay-walled' behind antidepressants by pharmaceutical companies and insurance companies. These patients are thereby forced to attempt multiple rounds of the antidepressants before they can take advantage of that access. Finally, the story of global mental health care as a whole is one of inadequate access. If our society hopes to be successful in its fight against this epidemic, we must remove every possible boundary to treatment and offer every safe and effective solution to every patient. If we can accomplish these goals then the future of mental health will be brighter for everyone.

References

- Adam P. Stern, M. D. (2020, October 27). *Transcranial magnetic stimulation (TMS): Hope for stubborn depression*. Harvard Health. Retrieved November 11, 2022, from https://www.health.harvard.edu/blog/transcranial-magnetic-stimulation-for-depression-2018022313335
- Alemi, F., Min, H., Yousefi, M., Becker, L. K., Hane, C. A., Nori, V. S., & Wojtusiak, J. (2021).
 Effectiveness of common antidepressants: A post market release study. *EClinicalMedicine*, *41*, 101171. <u>https://doi.org/10.1016/j.eclinm.2021.101171</u>
- An underused option for severe depression. Harvard Health. (2019, July 1). Retrieved April 2, 2023, from https://www.health.harvard.edu/mind-and-mood/an-underused-option-for-severe-depression
- Anagha, K., Shihabudheen, P., & Uvais, N. A. (2021). Side effect profiles of selective serotonin reuptake inhibitors. *The Primary Care Companion For CNS Disorders*, 23(4). https://doi.org/10.4088/pcc.20m02747
- Balch, B. (2022, June 14). *Electricity as medicine*. AAMC. Retrieved November 11, 2022, from https://www.aamc.org/news-insights/electricity-medicine
- Bermudes, R. A. (2021). Guidance on navigating insurance plans for TMS-eligible patients. *Psychiatric News*, *56*(10). https://doi.org/10.1176/appi.pn.2021.10.36
- Blumberger, D. M., Vila-Rodriguez, F., Thorpe, K. E., Feffer, K., Noda, Y., Giacobbe, P., Knyahnytska, Y., Kennedy, S. H., Lam, R. W., Daskalakis, Z. J., & Downar, J. (2018).

Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (three-D): A randomised non-inferiority trial. *The Lancet*, *391*(10131), 1683–1692. https://doi.org/10.1016/s0140-6736(18)30295-2

- Carpenter, L. L., Janicak, P. G., Aaronson, S. T., Boyadjis, T., Brock, D. G., Cook, I. A., Dunner, D. L., Lanocha, K., Solvason, H. B., & Demitrack, M. A. (2012). Transcranial magnetic stimulation (TMS) for major depression: A multisite, naturalistic, observational study of acute treatment outcomes in clinical practice. *Depression and Anxiety*, 29(7), 587– 596. https://doi.org/10.1002/da.21969
- Cascade, E., Kalali, A. H., & Kennedy, S. H. (2009). Real-World Data on SSRI Antidepressant Side Effects. *Psychiatry (Edgmont (Pa. : Township))*, 6(2), 16–18.
- Colarossi, A. (2020, February 27). Summary and critique of technological momentum by Thomas P. Hughes. Academia.edu. Retrieved April 2, 2023, from https://www.academia.edu/1881558/Summary_and_critique_of_Technological_Momentu m_by_Thomas_P_Hughes
- Cole, E. J., Stimpson, K. H., Bentzley, B. S., Gulser, M., Cherian, K., Tischler, C., Nejad, R.,
 Pankow, H., Choi, E., Aaron, H., Espil, F. M., Pannu, J., Xiao, X., Duvio, D., Solvason, H.
 B., Hawkins, J., Guerra, A., Jo, B., Raj, K. S., ... Williams, N. R. (2020). Stanford
 accelerated intelligent neuromodulation therapy for treatment-resistant depression. *American Journal of Psychiatry*, *177*(8), 716–726.
 https://doi.org/10.1176/appi.ajp.2019.19070720

- Complete National Film Registry listing : film registry : National Film Preservation Board : programs : library of Congress. The Library of Congress. (n.d.). Retrieved March 23, 2023, from https://www.loc.gov/programs/national-film-preservationboard/film-registry/complete-national-film-registry-listing/
- *Cost-effectiveness, the QALY, and the evlyg.* ICER. (2023, February 7). Retrieved March 24, 2023, from https://icer.org/our-approach/methods-process/cost-effectiveness-the-qaly-and-the-

evlyg/#:~:text=The%20quality%2Dadjusted%20life%20year,for%20more%20than%2030%20years.

ECT (electroconvulsive therapy): What it is & side effects. Cleveland Clinic. (n.d.). Retrieved March 24, 2023, from https://my.clevelandclinic.org/health/treatments/9302-ectelectroconvulsive-therapy

Efficacy and safety of electroconvulsive therapy in depressive disorders: A systematic review and meta-analysis. (2003). *The Lancet*, *361*(9360), 799–808. https://doi.org/10.1016/s0140-6736(03)12705-5

- *Electroconvulsive therapy (ECT): Royal College of Psychiatrists*. www.rcpsych.ac.uk. (n.d.). Retrieved April 1, 2023, from https://www.rcpsych.ac.uk/mental-health/treatments-and-wellbeing/ect
- FDA clears saint rapid-acting brain stimulation approach for those suffering from resistant major depression. Brain & Behavior Research Foundation. (2022, December 9). Retrieved

March 24, 2023, from https://www.bbrfoundation.org/content/fda-clears-saint-rapid-acting-brain-stimulation-approach-those-suffering-resistant-major

- Folkerts, H. W., Michael, N., Tölle, R., Schonauer, K., Mücke, S., & Schulze-Mönking, H. (1997). Electroconvulsive therapy vs. Paroxetine in treatment-resistant depression a randomized study. *Acta Psychiatrica Scandinavica*, *96*(5), 334–342. https://doi.org/10.1111/j.1600-0447.1997.tb09926.x
- Fox, D. (2017). The shock tactics set to shake up immunology. *Nature*, *545*(7652), 20–22. https://doi.org/10.1038/545020a
- George, M. S. (2019). Whither TMS: A one-trick pony or the beginning of a neuroscientific revolution? *American Journal of Psychiatry*, 176(11), 904–910. https://doi.org/10.1176/appi.ajp.2019.19090957
- González, H. F. J., Yengo-Kahn, A., & Englot, D. J. (2019). Vagus nerve stimulation for the treatment of epilepsy. *Neurosurgery Clinics of North America*, 30(2), 219–230. https://doi.org/10.1016/j.nec.2018.12.005
- Hajak, V. L., Hajak, G., Ziegelmayer, C., Grimm, S., & Trapp, W. (2021). Risk assessment of electroconvulsive therapy in clinical routine: A 3-year analysis of life-threatening events in more than 3,000 treatment sessions. *Frontiers in Psychology*, *12*. https://doi.org/10.3389/fpsyg.2021.767915
- Lamb, D. G., Porges, E. C., Lewis, G. F., & Williamson, J. B. (2017). Non-invasive vagal nerve stimulation effects on hyperarousal and autonomic state in patients with posttraumatic

stress disorder and history of mild traumatic brain injury: Preliminary evidence. *Frontiers in Medicine*, *4*. https://doi.org/10.3389/fmed.2017.00124

- Livesey, J. (2019, January 8). *Frogs and animal electricity*. Whipple Museum. Retrieved April 2, 2023, from https://www.whipplemuseum.cam.ac.uk/explore-whipple-collections/frogs/frogs-and-animal-electricity
- Maughan, D., & Molodynski, A. (2016). An international perspective on the acceptability and sustainability of electroconvulsive therapy. *BJPsych. International*, *13*(1), 10–12. https://doi.org/10.1192/s2056474000000891
- Mayo Foundation for Medical Education and Research. (2022, October 14). Depression (major depressive disorder). Mayo Clinic. Retrieved March 23, 2023, from https://www.mayoclinic.org/diseases-conditions/depression/diagnosis-treatment/drc-20356013
- Nguyen, K.-H., & Gordon, L. G. (2015). Cost-effectiveness of repetitive transcranial magnetic stimulation versus antidepressant therapy for treatment-resistant depression. *Value in Health*, 18(5), 597–604. https://doi.org/10.1016/j.jval.2015.04.004
- Pagnin, D., de Queiroz, V., Pini, S., & Cassano, G. B. (2004). Efficacy of ECT in depression: A meta-analytic review. *The Journal of ECT*, 20(1), 13–20. https://doi.org/10.1097/00124509-200403000-00004

- Payne, N. A., & Prudic, J. (2009). Electroconvulsive therapy: Part I. A perspective on the evolution and current practice of ECT. *Journal of Psychiatric Practice*, 15(5), 346–368. https://doi.org/10.1097/01.pra.0000361277.65468.ef
- Petrides, G., Fink, M., Husain, M. M., Knapp, R. G., Rush, A. J., Mueller, M., Rummans, T. A., O'Connor, K. M., Rasmussen, K. G., Bernstein, H. J., Biggs, M., Bailine, S. H., & Kellner, C. H. (2001). ECT remission rates in psychotic versus nonpsychotic depressed patients: A report from Core. *The Journal of ECT*, *17*(4), 244–253. https://doi.org/10.1097/00124509-200112000-00003
- Pilot study suggests long covid could be linked to the effects of SARS-COV-2 on the vagus nerve. EurekAlert! (n.d.). Retrieved November 11, 2022, from https://www.eurekalert.org/news-releases/943102
- Saini, R. K., Chail, A., Bhat, P. S., Srivastava, K., & Chauhan, V. (2018). Transcranial magnetic stimulation: A review of its evolution and current applications. *Industrial Psychiatry Journal*, 27(2), 172. https://doi.org/10.4103/ipj.ipj_88_18
- Somani, A., & Kar, S. K. (2019). Efficacy of repetitive transcranial magnetic stimulation in treatment-resistant depression: The evidence thus far. *General Psychiatry*, 32(4). https://doi.org/10.1136/gpsych-2019-100074
- Stanford Medicine. (2021, October 28). Experimental depression treatment is nearly 80% effective in controlled study. News Center. Retrieved March 24, 2023, from https://med.stanford.edu/news/all-news/2021/10/depression-treatment.html

- *TMS (transcranial magnetic stimulation): What it is.* Cleveland Clinic. (n.d.). Retrieved March 24, 2023, from https://my.clevelandclinic.org/health/treatments/17827-transcranial-magnetic-stimulation-tms
- *Treating severe depression with electroconvulsive therapy*. Duke Health. Retrieved April 1, 2023, from https://www.dukehealth.org/blog/treating-severe-depression-electroconvulsive-therapy
- Tsoucalas, G., Karamanou, M., Lymperi, M., Gennimata, V., & Androutsos, G. (2014). The "torpedo" effect in medicine. *International Maritime Health*, 65(2), 65–67. https://doi.org/10.5603/imh.2014.0015
- Vogel, K. (2022, September 9). Saint depression treatment: About Stanford Accelerated intelligent neuromodulation therapy. Psych Central. Retrieved March 24, 2023, from https://psychcentral.com/depression/saint-depression-treatment#concerns
- Weir, K. (2015, February). *Can magnets cure depression?* Monitor on Psychology. Retrieved March 24, 2023, from https://www.apa.org/monitor/2015/02/magnets
- Wilkinson, S. T., Kitay, B. M., Harper, A., Rhee, T. G., Sint, K., Ghosh, A., Lopez, M. O.,
 Saenz, S., & Tsai, J. (2021). Barriers to the implementation of electroconvulsive therapy
 (ECT): Results from a nationwide survey of ECT practitioners. *Psychiatric Services*, 72(7),
 752–757. https://doi.org/10.1176/appi.ps.202000387
- World Health Organization. (n.d.). *Mental health*. World Health Organization. Retrieved March 23, 2023, from https://www.who.int/health-topics/mental-health#tab=tab_2

Xia, G., Gajwani, P., Muzina, D. J., Kemp, D. E., Gao, K., Ganocy, S. J., & Calabrese, J. R. (2007). Treatment-emergent mania in unipolar and bipolar depression: Focus on repetitive transcranial magnetic stimulation. *The International Journal of Neuropsychopharmacology*, *11*(01). https://doi.org/10.1017/s1461145707007699