INVESTIGATING STOCHASTIC RESONANCE AS A COUNTERMEASURE FOR HUMAN PERFORMANCE DECREMENT ASSOCIATED WITH SPACEFLIGHT

by

SAGE O. SHERMAN

B.S., University of Colorado Boulder, 2018

M.S., University of Colorado Boulder, 2019

A thesis proposal submitted to the

student's graduate committee in partial fulfillment

of the requirements for the degree of

Doctor of Philosophy

Ann and H.J. Smead Department of Aerospace Engineering Sciences

2023

Committee Members:

Dr. Allison P. Anderson, Chair

Dr. Torin K. Clark

Dr. David Klaus

Dr. Ronald Carter

Dr. Gary Strangman

IRB protocol #20-0419, 20-3047, and 21-0296

Sherman, Sage (Ph.D., Aerospace Engineering Sciences)

Investigating Stochastic Resonance as a Countermeasure for Human Performance Decrement Associated with Spaceflight

Thesis directed by Assistant Prof. Allsion P. Anderson

NASA's investigative team for human health and behavioral performance has deemed that the risk of adverse cognitive outcomes for future long duration space missions is high and requires mitigation. Current methods at addressing cognitive and human performance decrement may induce other negative effects or be prohibitive in deep space applications. Thus, new technologies, such as neuromodulation through non-invasive brain stimulation (NIBS), are currently countermeasures being investigated. Some of these techniques may also induce adverse cognitive outcomes or they may not integrate well into space habitat infrastructure. Therefore, this thesis investigates the use of sensory noise as a neuromodulation technique, through a phenomenon known as stochastic resonance.

Stochastic resonance occurs when noise resonates with a nonlinear signal, increasing that signal's throughput and detectability. In human experimentation, additive sensory noise has been shown to improve perception and specific elements of cognition, but it is unclear whether these effects translate to improved performance in complex, operational tasks, such as those that astronauts conduct. Thus, this thesis research explores the utility of using sensory noise, specifically white noise added to the auditory and vestibular systems, for operational contexts and how it compares to other neuromodulation techniques.

First, this research builds upon the literature that implies sensory noise can be used to improve elements of cognition. Using the Cognition Test Battery, overall cognitive performance

was assessed in subjects for seven separate cognitive domains while they did and did not receive noise stimulation. Additionally, a questionnaire was administered inquiring about subjective preference for working in noisy and quiet environments. Overall cognition was not affected by sensory noise in the broad population, but there appears to be an interaction between noise treatment and subject. When performance was correlated with preference to working in noisy environments, it was found that subjective affinity for working in noisy environments could predict whether additive noise improved cognition in a subject.

Second, this research investigated whether additive noise could be used to improve operator performance in a complex, lunar landing task. This task loaded on operational sub-dimensions related to flight, decision making, and perception identification. Again, no effects of sensory noise were found on operational performance for the broad population; however, there was a significant interaction between subject and noise treatment. Preference to working in noisy environments was not a predictor of noise susceptibility in this task though.

Third, this research explored the additive long-term effects of repetitive noise administration for an operational task to identify whether noise can improve skill acquisition. Additionally, it investigated the immediate and longitudinal effects of noise on behavioral health dimensions, such as sleep and mood. To assess this, subjects completed a lunar rover navigation task over the course of five days. In this between-subjects design, some groups received noise stimulation while completing the task while others did not. Subjective questionnaires were administered daily, before and after completing the navigation task. Learning occurred across all subjects; however, there was no significant difference in learning rate between stimulation groups. Additionally, there was no difference between groups in the behavioral health outcomes studied.

Finally, this research conducted a trade study to explore which brain stimulation technology may be the most appropriate for spaceflight given the spaceflight community's interest in using NIBS technology as a spaceflight countermeasure. This trade study was applied to five brain stimulation techniques to determine which technology was the most effective at influencing human performance and integrating with the spaceflight vehicle. Transcranial electric stimulation appears to be the most promising stimulation technique based on the trade study's criteria. Future work should identify how this technology interacts with performance in the spaceflight environment and why only certain individuals respond to sensory noise.

Dedication

This is dedicated to three individuals that were excited to see me begin this journey, but unfortunately, they passed away before it was over.

James Gustine

Robert Sherman

Steven Ator

Acknowledgements

First and foremost, I need to thank my graduate advisor, Dr. Allison Anderson. She is **the** model for excellence, perseverance, and dedication to her craft. She is an outstanding aerospace academic that strives to produce rigorous, informed, and high quality research; which she also expects her students to emulate. She continually produces meaningful work, while fostering a generous and understanding environment for her students and others. She has allowed me to explore my academic interests, encouraged me to take leadership positions, and has routinely bought the first round in celebration of my achievements. I have learned so much from Dr. Anderson professionally and personally, and I sincerely hope I can follow her example. Thank you for giving me a chance.

Next, I need to thank Dr. Torin Clark who set me on this path. I started off my research path the summer between my Sophomore and Junior years as one of Dr. Clark's first undergraduate research assistants. I worked in his lab for the rest of my undergraduate degree, which is where I conducted research with a human centrifuge on a variety of projects related to vestibular illusions and intraocular pressure. This is every young aerospace nerd's dream, and he allowed me to live it. He may be kicking himself now that I have wanted to stick around for so long. For context, I sat in on his first class lecture at CU and I later saw him be awarded tenure. Thank you for helping me find my true passion in aerospace.

Additionally, I have to thank my other three committee members: Dr. David Klaus, Dr. Ronald Carter, and Dr. Gary Strangman. They have been incredibly patient and understanding with the swings and shifts of my research. At several stages along my PhD journey, they have provided thoughtful feedback that has made me think critically about the literature, the mechanisms behind stochastic resonance, and the bigger picture of where my research applies.

Thank you for the hallway conversations, conference discussions, thoughtful questions, and taking the time to listen to me make noise about noise.

Like all complicated projects, it takes a village not an individual. I need to thank all of the graduate and undergraduate students that worked on these projects. The development, testing, and analysis of this work was not trivial, and all of these people made a substantial contribution to one or several of the Specific Aims outlined in this thesis: Dr. Young-Young Shen, Alexander (Sasha) Kryuchkov, Daniel Gutierrez-Mendoza, Anna Jonsen, Maya Greenstein, Abigail Durell, Michael Schlittenhart, Cody Watson, Quinn Lewis, and Bárbara De Figueiredo. All of these individuals have gone on to do amazing work in aerospace and have become my friends. Thank you for making it all possible.

I have to thank the Bioastronautics student community. I am blessed to work with this collection of brilliant and friendly individuals. This diverse crowd collaborates with one another to produce a thoughtful and welcoming environment. I am so thankful to say that many of my friends in this department span several generations having graduated, being in the same boat as me, or are just starting their journey. While we all work on widely different research topics, we nerd out on the same topics, laugh at the same memes, go to the same parties, and reminisce about how terrible the old building was. I want to specifically call out Dr. Jordan Dixon and Dr. Katherine Bretl for mentoring me as an undergraduate student. It was truly special for me to see you defend and I am excited to follow in your footsteps. I also want to call out Jamie Voros, we started this journey on the same project and even though we do different research now, we will graduate roughly around the same time. Thank you all for making graduate school a memorable and fun experience.

I have to thank the Mortenson Center for Global Engineering, specifically its faculty, staff, and students for helping me see the bigger picture in how my technical skills can be applied to fields outside of aerospace academia. Dr. Evan Thomas, Dr. Carlo Salvinelli, and Dr. Rita Klees have provided me opportunities and encouraged me to apply my knowledge to international development contexts, which I have found incredibly rewarding and a general reprieve from my regular aerospace work. Along these lines, I have to thank iDE Cambodia, specifically the Innovation Lab, for taking me in Summer 2022. My short time with you all was magnificent and enriching, albeit hot and sweaty. I would not trade my practicum experience for anything. Thank you for helping me see why we do the things we do.

I have to thank the College of Teaching and Learning (specifically, Dr. Preston Cumming) and select Aerospace faculty and staff (Nicole Simmons, Dr. Alexandra LeMoine, and John Mah) for encouraging me to improve my skills related to college education and improving my ability to teach complex topics to unfamiliar audiences. I also want to thank other Aerospace staff: Maggie Kolicko and Joanie Weisman for catching and fixing my countless finance mistakes, as well as, Nancy Glaze and Michaela Vandegrift for helping facilitate human research during COVID. Thank you for helping me do the things that made this possible.

I also want to thank Marissa Stephens. While I did not meet you until the end of grad school, you deserve a special mention in this section. The last six months have been crazy for me, but your never-ending support, bright outlook on life, and care for my well-being has made it a whole lot easier. I feel incredibly lucky to know you. Thank you making this last push to the finish brighter.

Finally, I need to thank the rest of my friends and family. All of your names will not fit in the three and a half pages I allocated for this section; however, I want you to know that you

deserve a call out. Since I have lived my entire life in Colorado, I can say my roots here are pretty strong. I imagine my defense will be packed with people I met during every stage of my life and that is incredibly special. At some point we have watched movies, traveled to different countries, recreated in the outdoors, shared a meal, went out on the town, walked through museums, debated politics, argued about politics, teased each other, speculated on the universe, played videogames, drank a beer, drank too many beers, laughed, cried, commiserated, pet animals, and simply existed together. At some point along this path we have had an adventure I look fondly on, an adventure that made this a little easier. While these are not entirely unique to the human experience, they are unique to me. Thank you for being there. Thank you for listening to me complain. And thank you for continually asking me, "when are you done?". Well, I'm glad to say it's today.

Table of Contents

Chapter 1: Motivation 1
1.1 Human performance 2
1.2 The Spaceflight Environment 3
1.3 Spaceflight Human Performance Decrement Countermeasures 5
1.4 Summary 7
Chapter 2: Background 8
2.1 Theories and Models behind Stochastic Resonance 8
2.1.1 Origins of Stochastic Resonance 8
2.1.2 Model Applications to Biological Systems 9
2.2 Your Brain on Sensory Noise 11
2.2.1 Cortical Influence of Noise 11
2.2.2 Deep Brain Influence of Noise 12
2.3 Stochastic Resonance Effects on Information Processing 13
2.3.1 Stochastic Resonance Perception Effects 13
2.3.2 Stochastic Resonance Cognition Effects 16
2.3.3 Extension to Complex Cognitive Functioning 18
2.3.3 Extension to Memory 18
2.3.3 Consideration of Secondary Effects resulting from Noise Stimulation 19
2.4 Conclusion 19
Chapter 3: Investigative Rationale 20
Chapter 4: Specific Aim 1 - Investigate additive noise effects on cognition. 26
4.1 Introduction 26
4.2 Methods 27
4.2.1 Independent Variables 28
4.2.2 Dependent Variables 29
4.2.3 Experimental Design 31
4.2.4 Data Analysis 32
4.3 Results 34
4.4 Discussion 39
4.5 Conclusions 42
Chapter 5: Specific Aim 2 - Evaluate the utility for noise to improve operational performance. 44

5.1 Introduction 44
5.2 Methods 45
5.2.1 Independent Variables 46
5.2.2 Lunar Landing Simulation and Dependent Variables 46
5.2.3 Experimental Design 52
5.2.5 Analysis 54
5.3 Results 56
5.4 Discussion 61
5.5 Conclusions 65
Chapter 6: Specific Aim 3 - Investigate the long-term effects of repeated noise exposure. 67
6.1 Introduction 67
6.2 Methods 67
6.2.1 Independent Variables 68
6.2.2 Dependent Variables 68
6.2.3 Simulation Task 69
6.2.4 Experimental Design 74
6.2.5 Data Analysis 75
6.3 Results 79
6.3.1 Learning Results 79
6.3.2 Behavioral Health Results 81
6.4 Discussion 85
6.5 Conclusions 89
Chapter 7: Compare the applicability of neuromodulation methods as spaceflight countermeasures for human performance decrement. 90
7.1 Introduction 90
7.2 Trade Study Criteria 91
7.3 Stochastic Resonance (SR) 95
7.4 Transcranial Electrical Stimulation (tES) 97
7.5 Transcranial Magnetic Stimulation (TMS) 100
7.6 Transcranial Photobiomodulation (tPBM) 103
7.7 Transcranial Focused Ultrasound (tFUS) 106
7.8 Discussion 109
7.9 Conclusion 114

Chapter 8: Conclusions and Final Thoughts 115
8.1 Summary 115
8.2 Other Potential Enhancement Mechanisms using Sensory Noise 115
8.3 Spaceflight Limitations and Tangential Thoughts 117
8.4 Future Work 120
References 122

\

List of Tables

Table 1. Each CTB task that subjects completed and their description 29
Table 2. Cognitive domains and brain regions associated with each CTB task 30
Table 3. 1x4 RMANOVA results for sham and noise conditions 35
Table 4. 1x3 RMANOVA results for the control conditions 36
Table 5. 1x4 RMANOVA results for the sham and noise conditions. 37
Table 6. Statistical results for linear regressions of cognitive performance improvements as a function of noisy environment preference 38
Table 7. A description of each performance metric in the lunar lander simulation. 51
Table 8. RMANOVA results for overall operator performance 57
Table 9. RMANOVA results for the flight sub-dimension and perception sub-dimension 59
Table 10. Outcome Frequency Table for the Decision-Making Metrics. 60
Table 11. Aim 3 Questionnaires and their Assessment Tools 69
Table 12. Mixed effect model results for operational learning performance 81
Table 13. Two-way ANOVA results for behavioral health effects following stimulation 82
Table 14. Two-way ANOVA results for longitudinal behavioral health effects 83
Table 15. One-way ANOVA results for the six metrics of treatment acceptability 84
Table 16. Metrics and score values to assess spaceflight efficacy of NIBS technology. 93
Table 17. Vehicle implementation score definition. 94
Table 18. Table summary of the NIBS countermeasure assessment. 110
Table 19. Table summary of the NIBS vehicle implementation information. 111
Table 20. State of NIBS for Long Duration Space Missions. 113

Table of Figures

Figure 1. The Information Processing Model ... 3
Figure 2. Visual representation of the SR dynamic model ... 9
Figure 3. Visual representation of the SR non-dynamic model. ... 10
Figure 4. Arbitrarily developed SR curve example. ... 13
Figure 5. Normalized cognition metric scores for the noise conditions and sham. ... 35
Figure 6: Normalized cognition metric scores for the control conditions ... 36
Figure 7. Efficiency scores across CTB tasks for four individual subjects ... 37
Figure 8. Linear regressions of cognitive performance improvement as a function of noisy environment preference ... 38
Figure 9. Over-the-shoulder view of the AReS lunar lander simulation ... 49
Figure 10. Visual information presented to the subject in the primary flight display ... 50
Figure 11. Main effects plot of noise treatments and map difficulty for the overall performance aggregated dataset ... 58
Figure 12. Frequency of best levels identified for nGVS and AWN ... 65
Figure 13. Rover display tools that were provided to the subject. ... 71
Figure 14. Subject point of view in the object identification task ... 73
Figure 15. Example of battery consumption and object identification ... 73
Figure 16. Experimental timeline split up into three distinct testing phases ... 75
Figure 17. Linear regression performance improvement across the five test sessions ... 80
Figure 18. Multiple comparisons in the two significantly different acceptability metrics. ... 85
Figure 19. Spider plot visualization of the SR countermeasure assessment. ... 97
Figure 20. Spider plot visualization of the tES countermeasure assessment. ... 100
Figure 21. Spider plot visualization of the TMS countermeasure assessment. ... 103
Figure 22. Spider plot visualization of the tPBM countermeasure assessment. ... 106
Figure 23. Spider plot visualization of the FUS countermeasure assessment. ... 109
Figure 24. Spider plot comparison of all NIBS technologies assessed. ... 110

Chapter 1: Motivation

Astronauts must complete a large variety of complex, operational tasks in quick succession to accomplish mission goals. Long duration exploration missions, say to the Moon or Mars, will be more complex and last for extended periods longer than current low Earth orbit spaceflight. Living and working in space requires elevated diligence, since an error could lead to damaged equipment, spacecraft, or risk the mission or crew health (Boring, 2020). Spaceflight mission paradigms have similarities to other industries such as aviation, construction, energy, transportation, and manufacturing where individuals are also engaged in complex operational tasks in high demand environments.

Understanding the risk of complex operations in these sectors can provide insight in the human error implications for spaceflight operations. The U.S. Bureau of Labor Statistics state that there were 5,333 workplace fatalities in 2019 with 2.8 per 100 workers incurring an occupational injury (*Employer-Reported Workplace Injuries and Illnesses – 2019*; *National Census of Fatal Occupational Injuries in 2019*). The American Society of Safety Engineers suggest that many workplace accidents occur as a result of human error (Petersen, 2003). The percentage of accidents due to human error vary between industries and reports, but most studies agree that accidents resulting from human error account for more than 50% of workplace accidents (Wróbel, 2021). Categories of human error include mistakes (intended action is incorrect for situation), slips (a correct action is incorrectly carried out), lapses (failure to carry out an action), or violations (an incorrect action is intentionally carried out) (Weigmann & Shappell, 1997). These categories provide a model to understand incidents of human error, where a case study found 58% of human error cases resulted from mistakes.

Thus, it is advantageous to identify and develop methods which reduce mistakes by improving human performance and offsetting decrements that result from degraded mental ability while performing complex, operational tasks. The objective of this research is to investigate stochastic resonance (SR) as one potential method.

1.1 Human performance

The study of human performance is focused on the quality of behavior execution to accomplish a task (Wickens et al., 2013). The International Civil Aviation Organization recognizes that performance capabilities and limitations are a relationship between the user's ability to interact with the equipment, procedures, and the operational environment (*Human Factors Training Manual*, 1998). One goal of engineering and applied psychology is to optimize the interaction of these four elements. One method to achieve this optimization is through cognitive engineering which focuses on enhancing the user's inherent mental capabilities (Wickens et al., 2015).

One way to frame human performance is through the information processing model, shown in Figure 1 (Wickens et al., 2015). This qualitative framework aims to explain how humans take in external sensory information, process those signals, and then apply that information to make decisions. In this framework, humans reflect upon previous knowledge and, based on current mental ability, recognize a situation and execute a decision based on what they perceive. Additionally, this feedback loop also accounts for environmental changes made by the user, which will impact future information processes. While this flexible model explains mental behavior, it remains qualitative and does not provide an accessible input-output guide to improving performance. However, since favorable response selection and execution are the end goals of enhancing performance, it follows that enhancing the informational resources at all stages leading up to decision making (i.e., by improving perception or cognition) could yield improved performance. Weigmann & Shappell (1997) posits that human error cases and types are often a failure in a user's information processing, as a result of the system, scenario, and user's performance state. They suggest 87% of pilot-casual errors fit within the information processing framework. Using this model and its framework, it is possible to understand SR's role in specifically targeting elements of the information processing model, providing a comprehensive means to evaluate improvement in human performance.

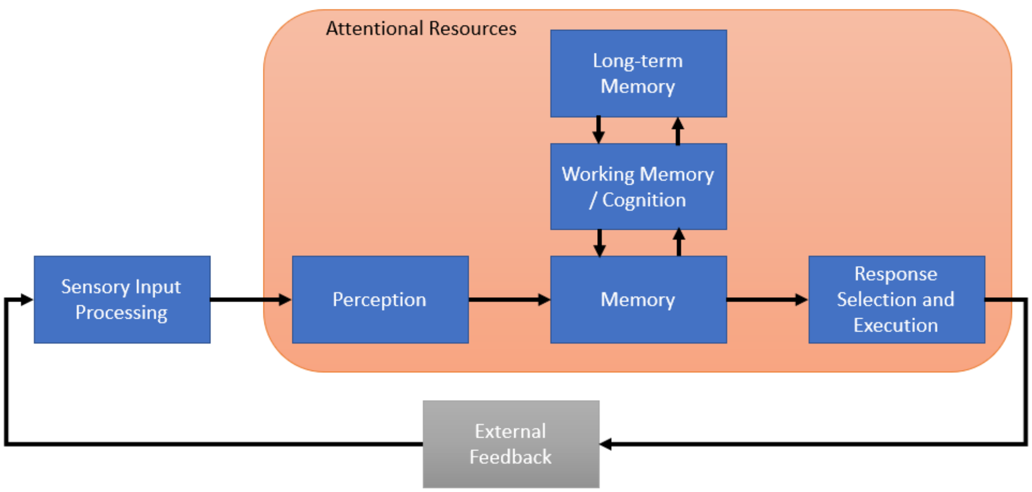


Figure 1. The Information Processing Model adapted from Wickens et al. (2015).

1.2 The Spaceflight Environment

In addition to the factors traditionally considered for understanding human performance on Earth, there are several spaceflight specific contributors that could cause decrements in human performance. Physiological hazards of spaceflight to human performance include reduced gravity and space radiation (Thirsk et al., 2009). These hazards can impact crew health and lead to physiological and neurological changes that impact mental ability and thus, human performance (Patel et al., 2020). For example, space radiation may lead to central nervous system degradation (Clément et al., 2020), and microgravity influences change in neural structure and perception (Koppelmans et al., 2016; Roy-O'Reilly et al., 2021). The spacecraft habitat further adds additional stressors to the spaceflight experience. Morphew (2001) categorizes these into physiological, psychological, psychosocial, habitability, and human factors. Many of these stressors arise from living in an isolated confined environment (ICE) with limited social options, communication, and environment diversity. Prolonged exposure to these stressors may impact the crew's emotional well-being which, in-turn, influences behavior and cognitive processes (Stangor et al. 2014; Tyng et al., 2017). ICE analogs, which mimic some of these stressors but in a terrestrial setting, have shown experimental evidence of decline in human performance over time (Bosch Bruguera et al., 2021). In addition to this, there are longitudinal concerns for operational performance and learning posed by the spaceflight environment. Astronauts must complete a large variety of complex, operational tasks in quick succession to accomplish mission goals; thus, they have to start training for these tasks upon being selected up until their mission. However, this training can be time consuming and many simulated environments fail to replicate the space environment accurately, as future space missions will impose unknowns that could necessitate learning new skills that were not included in mission design (Anglin et al., 2017). Skill decay is a concern for long-duration space missions as well (Pieters & Zaal, 2019).

While researchers have been able to investigate psychological effects of spaceflight and potential countermeasures, this knowledge is limited to flight in low Earth orbit and spaceflight analogs, which may not reflect the additional complications and uncertainties that will be presented in longer duration missions. NASA's Human Factors and Behavioral Performance (HFBP) group identified that on a deep space or planetary mission the risk of cognitive conditions requires mitigation (Slack et al., 2016). There stands a need to develop effective and standalone countermeasures that the crew could use to offset human performance decrements.

1.3 Spaceflight Human Performance Decrement Countermeasures

In spaceflight, reducing mental stress is done through prevention and intervention. Preflight, crew selection (Oluwafemi et al., 2021) and training (Howard et al., 2013) are geared toward preventing negative performance outcomes due to the stressors of space. In-flight methods of reducing stressor impact on mental health include monitoring, communication, nutrition, and psychological training (Costa et al., 2021; Moore et al., 2017; Morphew, 2020). These countermeasures are mostly preventative and fail to address acute, situational performance decrements. For example, in June of 1997, the Progress resupply vehicle collided with the Spektr module on the Mir space station as astronauts attempted to dock the vehicle to the station. While the crew participated in many of the preventative methods listed previously, the incident still occurred as a result of various factors, including degraded skills and inability to adapt to non-optimal situations (*Spektr of Failure*, 2010). Countermeasures to address real-time human performance decrements would be beneficial to crew and mission success.

Currently NASA's HFBP is investigating a variety of new intervention countermeasures that address human performance decrement, while increasing crew autonomy which is required for deep space missions. Crew self-identification and stress management systems are being developed (Rose et al., 2013). Other in-flight countermeasures to address human performance decrements which are being investigated include physiological countermeasures, such as nutrition, and psychological countermeasures, such as habitat modifications, stress training, personal relation maintenance, and entertainment access (Oluwafemi et al., 2021). These countermeasures, though, target and prevent adverse behavioral health without specifically targeting real-time cognition.

Future spaceflight countermeasures can build from research being done for human performance on Earth. Terrestrial researchers are investigating advanced medical interventions to improve information processing. Pharmaceutical stimulants, like caffeine and nicotine, can resolve factors that impact cognitive abilities, like reducing fatigue and even improve memory. These drugs, though, are addictive and have negative side effects, like anxiety (Bostrom & Sandberg, 2009; Friedman & Bui, 2017). Another performance countermeasure field being explored is neuromodulation, which refers to using a stimulus to alter nerve activity (Horn & Fox, 2020). Commonly used neuromodulation techniques include non-invasive brain stimulation (NIBS) techniques, like transcranial direct current stimulation (tDCS) or transcranial magnetic stimulation (TMS). These techniques have been shown to improved learning, working memory, and motor function (Choe et al., 2016; Reis et al., 2008). These techniques may pose a risk to user health though and their long-term use is still unknown. For example, TMS can trigger epileptic seizures and in some animal models of tDCS displayed irreversible brain injury (Bikson et al., 2016; Pereira et al., 2016). For spaceflight, these methods may be prohibited by power, volume, and the need for expert administration. Other fringe techniques being investigated include genetic modifications and brain-computer interfaces, but their use and long-term interactions are poorly understood (Bostrom & Sandberg, 2009).

Given the potential benefit of NIBS, but the limitation of existing approaches, one alternative may be SR. SR occurs when noise applied to the senses can enhance neural information transfer (Moss et al., 2004). Additive sensory noise can be applied with easy administration, requires minimal technological overhead, and may have a lower risk for adverse side effects, which would make it an advantageous method of brain stimulation in spaceflight over these alternative methods. This research investigates SR as a form of neuromodulation that may help improve information processing with little side effects and being applicable to the human spaceflight environment.

1.4 Summary

Current spaceflight techniques to address human performance decrement carefully monitor and prevent behavioral issues that can lead to adverse cognitive health and reduce human performance, but these countermeasures do not improve cognition in real-time which could have declined in spaceflight. Alternative techniques to address this, such as pharmaceuticals or NIBS, are under consideration, but pose problems resulting from side effects and challenging spaceflight hardware integration. To address these issues, a countermeasure that effectively targets human performance decrement without these downsides needs to be developed. This thesis postulates whether SR could be one such method. While SR may be a low-risk form of sensory modulation, it has yet to be investigated as a holistic countermeasure that can be applicable in the spaceflight environment. Learning how SR affects elements in the information processing model, can provide insight into the extent of which it can improve total mental ability. Additionally, this thesis also proposes a means by which SR and other neuromodulation technologies may be evaluated for spaceflight applications. The following chapter outlines current research gaps associated with SR in relation to this information processing model.

Chapter 2: Background

Stochastic resonance is a phenomenon where additive noise can improve the throughput of a signal in non-linear systems (Moss et al., 2004). Noise within this thesis refers to unstructured energy that is added to a system by external means. While additive noise has been used in digital applications, the literature suggests it may also improve biological and neural systems (McDonnell et al., 2008). If sensory noise can enhance neural functions, then SR may have the potential to influence information processing. To understand the background of this phenomenon, this chapter introduces the underlying theory of SR and its translation to human neural systems and information processing.

2.1 Theories and Models behind Stochastic Resonance

2.1.1 Origins of Stochastic Resonance

SR was originally proposed by Benzi et al. (1981) as a model for describing the reoccurrence of ice ages. The basis of the model is easily visualized as an object residing in a double well potential, with each well representing a separate settling state. A forcing function weighs one well in comparison to the other, but the current state is maintained until a perturbation from additive, random noise induces enough energy to drive the object from its resting state to the weighted state. This is known as the dynamical model of SR for bistable systems (Fig. 2). This SR model has seen applications in the fields of physics, chemistry, engineering, and biology (Gammaitoni et al., 1998).

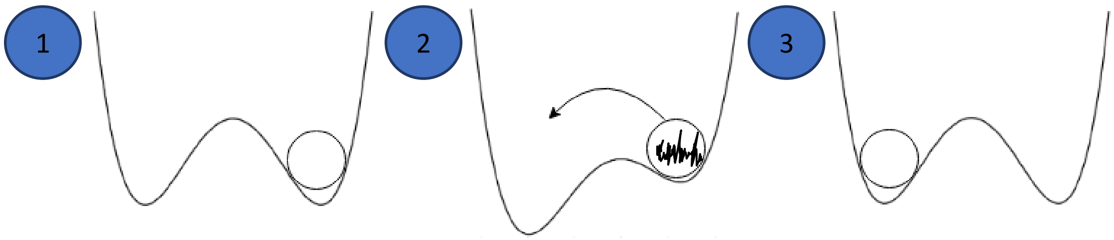


Figure 2. Visual representation of the SR dynamic model. 1: The object resides in one of two bimodal well states, right in this example. 2: Some forcing function weighs the well potential to favor one state (left) over another (right); however, the object still resides in the right well. However, some noise internal (inside the object in this image) or external to the system creates noise that induce well state change. 3: The phenomenon has successfully moved the object from one state to another and SR has occurred.

2.1.2 Model Applications to Biological Systems

Neurons encode information when their firing voltage surpasses a threshold, creating an action potential. A neuron's resting potential is a measure of stochastic energy inherent to the neuron that does not produce a recognizable signal. Therefore, neuronal assemblies can be subjected to the terms of the SR model. The two bi-modal states are suprathreshold and subthreshold firing voltages. The forcing function is an external stimulus trying to illicit a response. And the additive noise is inherent or external to the neural assembly. This is easily observed in the non-dynamical model introduced by Gingl et al. (1995). Figure 3 demonstrates this where some non-linear stimulus has a magnitude incapable of crossing over the threshold barrier. Additive noise introduces enough energy in the system to pass information above this threshold, inducing a noticeable action potential in neurons.

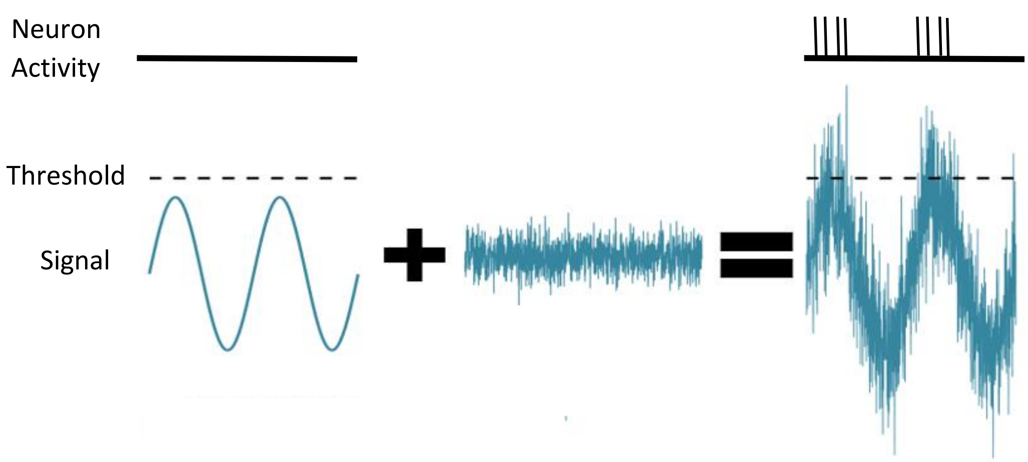


Figure 3. Visual representation of the SR non-dynamic model.

A noise of insufficient magnitude will not create enough energy to induce a noticeable action potential, and a noisy signal that is too high in magnitude can mask the underlying stimulus of interest (Moss et al., 2004). So, the magnitude of additive noise that is appropriate to create SR is dependent on its use case and stimulation method. Also, the noise must be random. Additive signals that induce attention/arousal (Lugo et al., 2008), such as a periodic signal, could be predicted (thus less energy stimulation) by the neuronal system or conflict with the information of interest, yielding none or adverse performance in the system. Thus, noise must be random and magnitude appropriate for SR induction.

It should be noted that this noise does not need to be sub-threshold sensory detection to induce benefits; this is to say, the phenomenon of supra-threshold stochastic resonance is possible (McDonnell et al., 2008). In fact, many psychophysical and cognitive based SR experiments use high noise intensities (55-80 dB SPL) to induce SR behavior (Manan et al., 2012; Othman et al., 2019; G. B. Söderlund et al., 2010). Thus, it appears that in many contexts, noise needs to be sufficiently high to induce change; however, this may not work in perceptual contexts where a high noise level could mask a signal.

2.2 Your Brain on Sensory Noise

The first experiment to confirm SR behavior in neuronal assemblies was done by Douglass et al. (1993) where they observed SR phenomena in crayfish mechanoreceptor cells. These individual neurons responded to sinusoidal stimuli at a higher frequency when white noise was added to the signal when compared to signals with no noise. These results have been replicated with rat and cricket neurons (Collins et al., 1996; Levin & Miller, 1996). The following sections summarize the literature on human investigations of the brain and SR.

2.2.1 Cortical Influence of Noise

Individual neurons exhibit SR behavior as shown in animal models, but these studies provide little insight on complex neural networks and systems, as information processing integrates signals from multiple groups of neurons in different regions. Human electroencephalography (EEG) studies suggest that external sensory noise alters activity across entire brain regions and is consistent with SR phenomenon. This is found in previous studies where global weighted coherence was observed as a factor of auditory noise level. The optimal level of noise (in both monaural and biaural auditory stimulation) induces greater coherence across the brain, whereas non-optimal levels of noise maintains or reduces coherence when compared to the zero-noise condition (Huidobro, 2020). Similar results occur when adding noise simultaneously to both auditory and visual modalities (Mendez-Balbuena et al., 2018).

EEG studies have also observed noise effects on brainwaves. Noisy Galvanic Vestibular Stimulation (nGVS) can suppress gamma waves in lateral and frontal regions, modulating neural oscillations (Kim et al., 2013). Monoptical visual noise increased neural synchrony (Kitajo et al., 2007), with lasting synchronization in theta bands with transient synchronization in the gamma bands. Some of these phase synchronizations occurred in separate areas of the brain. This is important because improved neuronal synchronization and coherence may suggest improved information transfer between those neurons (Fries, 2005). These studies suggest that additive noise may influence broad cortical function and not only individual neurons.

2.2.2 Deep Brain Influence of Noise

Since SR effects may be seen in individual neurons and the cerebral cortex, it would stand to suggest that the entire chain of perception sees some level of influence. Starting from the sensory organs, information travels through the medulla, pons, and midbrain before reaching the cortex for many perceptual channels (i.e., hearing and proprioception) (Kandel et al., 2000). Understanding the presence and impact of SR in each portion of the sensory system would provide insight into information transfer, loss, and synthesis. Unfortunately, only a few researchers have investigated noise on deep brain systems and their contribution provides little insight on neural mechanisms.

Simonotto et al. (1999) used functional magnetic resonance imaging (fMRI) scans of subjects observing visual noise in images. Total active volume increased, with most of the change occurring in the visual cortex. One limitation of this study, though, was the application of SR to the images and not actively to the biological system, implying that increased active volume might be due to improved image comprehension and saliency, as opposed to a biologically active mechanism. Othman et al. (2020) found improved right hemispheric lateralization in the superior frontal gyrus and improvements in inhibition when subjects listened to 55 dB of noise during an auditory working memory task. To my knowledge, these are the only two fMRI studies conducted investigating SR. Thus, presenting a substantial gap in the understanding of neural mechanisms behind SR in the brain.

2.3 Stochastic Resonance Effects on Information Processing

2.3.1 Stochastic Resonance Perception Effects

Intuitively, one of the first stages of information processing, perception (Wickens et al., 2015), may be subject to SR benefits. SR could enhance at-threshold or subthreshold sensory signals in accordance with the non-dynamical model (Fig. 3). However, SR benefits would occur at an optimal noise condition, where too little noise fails to alter signal detection while too much noise masks it (Voros et al., 2022). This is visualized as a u-shape function shown in Figure 4, where perceptual thresholds (or the smallest stimuli magnitude you can accurately detect) are plotted as a function of additive noise.

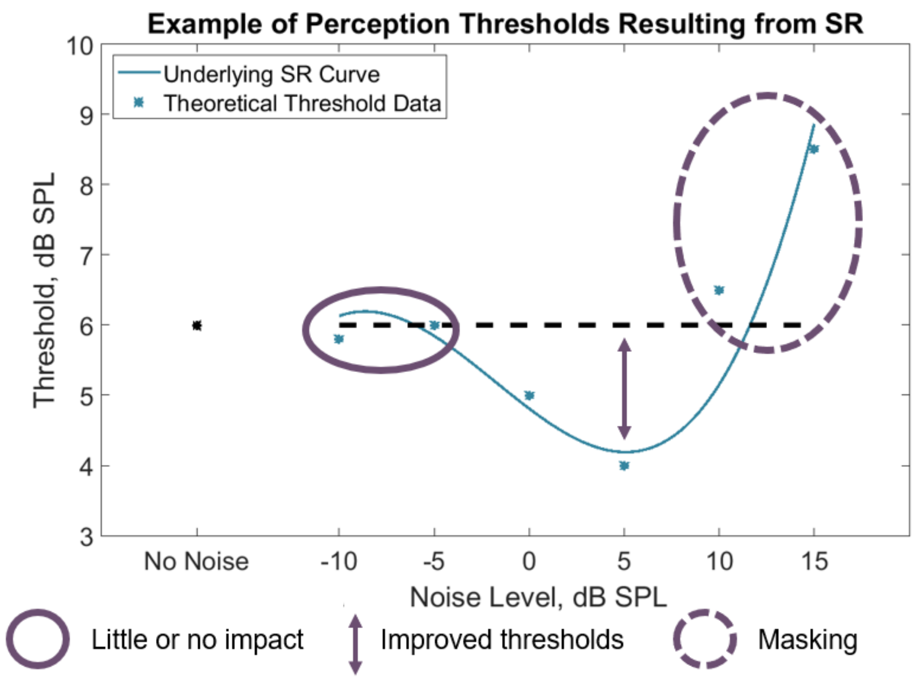


Figure 4. Arbitrarily developed SR curve example.

Note that individual differences may play a substantial role in the magnitude and location of the function’s extrema between people, making these curves challenging to detect in experimental data. Previous research in our lab utilized logistic regression to classify SR curves in simulated and experimental perceptual threshold data. This objective identifier allows for rigorous identification which was lacking in the literature (Voros et al., 2022).

Unimodal SR refers to using additive noise in one sensory modality to improve signal detection within that same modality. Human psychophysical experimentation has identified unimodal SR phenomena in multiple senses with additive noise applied externally with the signal, or additive noise applied internally to the processing system. Externally applied white noise has been shown to improve visual (Simonotto et al., 1997), auditory (Ries, 2007; Zeng et al., 2000), and tactile (Collins et al., 1997) perception thresholds. These studies also demonstrated the u-shape function with no improvement at low noise intensities and masking for higher noise intensities.

Alternatively, noise can be applied directly to sensory systems through electrical stimulation. Internally applied white noise has been shown to improve visual (van der Groen & Wenderoth., 2016), auditory (Zeng et al., 2000), and vestibular (Galvan-Garza, 2018) perception thresholds. While these unimodal results are remarkable, they make intuitive sense with the non-dynamical model of SR and provide little insight on SR's ability to enhance overall information processing; however, cross-modal perception may expand capabilities of SR in overall processing.

It has been found that certain neurons within the cortex encode more than one sensory modality (i.e., some neurons transmit information for both the visual and auditory domain) (Fuster et al., 2000). This suggests noise in one modality could increase encoding potential in these cross-modal neural assemblies; therefore, SR enhancements may be observed in a sensory modality, even if the noise is presented in a separate modality (i.e., using auditory noise to improve visual contrast detection). The first evidence of this was presented by Manjarrez et al.

(2007) where luminance detection thresholds improved with high magnitude auditory noise. In the following year, a more comprehensive study conducted by Lugo et al. (2008) showed high magnitude auditory white noise (AWN) enhanced visual (luminance and contrast), tactile, and proprioceptive perception thresholds. Recently, it has been found that nGVS can improve visual contrast detection (Voros et al., 2021) and auditory thresholds (Rise et al. 2021). These studies show the SR can be found across modalities for external and internal additive noise.

It should be noted that the u-shape function for cross-modal may deviate from the unimodal function in the following ways. Cross-modal SR improvement usually uses higher magnitude noise levels than unimodal SR to be observed. The optimal auditory noise level for unimodal improvements are near or slightly above thresholds in the absence of noise (i.e., if a 1000 Hz threshold is 10 dB, it follows that the total noise power should be just above 10 dB). In contrast, the literature shows auditory noise level for cross-modal improvements is ~70 dB (Lugo et al., 2008; Manjarrez et al., 2007). Additionally, the cross-modal SR curve, as opposed to Figure 4, may not show masking effects as high-level noise may not conflict with the signal of interest. The mechanisms are not fully understood, but subjects in previous studies that our lab had conducted did not have masking effects due to high noise for nGVS (Voros et al., 2021; Rise et al. 2021).

Cross-modal improvement may be a result of noise-induced entrainment within the central nervous system (Mori & Kai, 2002). If SR improves encoding within neural assemblies to enhance perception across different modalities, it could be postulated that additive noise could increase overall neural energy in a manner that helps higher-order mental processing. While this is a theory, this has not yet been investigated and warrants further study beyond the scope of this research.

Additionally, the literature on SR as it applies to human performance shows that the phenomenon may be influenced by individual differences. Many perception studies have suggested that some individuals are susceptible to SR enhancement, while others are not (Galvan-Garza, 2018; Ries, 2007; Voros et al., 2021). To my knowledge, there are no studies which explore the mechanisms responsible for perception performance; thus, further research is required to determine whether someone will be susceptible to SR.

2.3.2 Stochastic Resonance Cognition Effects

After perception, information processing goes through stages of long-term memory retrieval and cognition (Wickens et al., 2015). As has been discussed, since additive noise influences neural activity ranging from individual neurons to synchrony across the entire brain, as well as to enhance perception within and across modalities, it follows that cognitive abilities may be susceptible to SR effects.

Noise-enhanced sensory information could be utilized by the whole central nervous system (Hidaka et al., 2000), suggesting that SR could affect higher order information processing. In human subject experiments, background AWN (~78 dB SPL) improved verbal recall, visuo-spatial working memory, and motor response in inattentive school children (Söderlund et al., 2010; Helps et al., 2014). For a neurotypical population, AWN has been shown to improve elements of attention and visual/auditory working memory (Awada et al., 2022a; Othman et al., 2019). Cognitive SR benefits extend to modalities other than auditory though. This is supported by studies showing that nGVS improves visual working and spatial memory in healthy adults (Hilliard et al., 2019; Wilkinson et al., 2008).

Bigelow & Agrawal (2014) summarized the link between vestibular and cognitive functions, noting that visuospatial ability and attention are negatively impacted in subjects with vestibular impairments. Pineault et al. (2020) also suggested that impairments to the saccule and semi-circular canals of the vestibular system affects various aspects of cognition. It has been shown that nGVS improves vestibular self-motion perception (Galvan-Garza, 2018; Keywan et al., 2019), suggesting enhanced vestibular function. Therefore, improved vestibular function from nGVS could potentially offset cognitive decrements due to perceptual impairment. This hypothesis, though, has never been investigated.

Existing studies that suggest adding sensory noise can enhance cognition are limited as they focus on specific cognitive domains and do not investigate cognitive effects more broadly. Cognitive domains are individual cognitive processes, like working memory, which are employed when synthesizing information for decision making and behavior control (Harvey, 2019). Certain cognitive domains recruit different regions of the brain (Basner et al., 2015) and additive noise influences regional activity within the cerebral cortex (Huidobro, 2020; Mendez-Balbuena et al., 2018). This regional influence may correspond to specific cognitive domains. For example, the temporal lobe houses auditory and other multisensory association areas in addition to cognitive centers that are attributed to memory (Kandel et al., 2000); thus, surrounding regions may see neuronal influence by AWN which could affect memory. Supporting this, Kim et al. (2013) reports that nGVS leads to gamma wave suppression in the frontal region which is associated with several cognitive abilities. However, literature investigating cognitive benefits of adding sensory noise has focused on working memory and motor response, neglecting other domains, such as vigilance and visual search. This presents a substantial gap in our knowledge of sensory noise influence on overall cognition as a thorough analysis across multiple cognitive domains has yet to be investigated.

2.3.3 Extension to Complex Cognitive Functioning

Thus far, this review has focused on exploring how noise can be used to improve elements of information processing. These studies, though, focus on specific and separate information processing and microcognitive elements, such as perception detection or working memory, failing to provide insight on the utility of SR in real-world contexts.

Macrocognition refers to cognitive functioning in natural environments (Klein et al., 2003). Completing complex, mental tasks involves synthesizing many microcognitive skills to execute a relevant task, such as driving a car or landing a spacecraft. The benefits of SR have not been assessed for macrocognition, as it is potentially difficult to analyze the results of complex tasks with a great degree of sensitivity. Usher and Feingold (2000) found SR improved speed of memory retrieval for multiplication. Multiplication may be more analytical and complex than other cognitive domain assessment tasks, but this task is not operationally relevant and a weak indicator for overall performance enhancement.

2.3.3 Extension to Memory

It is postulated that being able to efficiently encode new information can help repair or restructure current knowledge (Chi, 2009). So, if SR can improve mental ability it might be able to improve learning ability as active cognitive processes may improve constructive and interactive processes. When it comes to learning as a result of noise, the literature suggests that nGVS can enhance motor control learning, specifically in spatial and locomotor tasks (Hilliard et al., 2019; Moore et al., 2015; Putman et al., 2021). AWN has been shown to improve new-word learning in adults (Angwin et al., 2017). It is unclear whether learning in these declarative memory paradigms would extend to procedural skill acquisition in a complex operational task.

This gap in the literature warrants further investigation to understand whether sensory noise can improve learning in complex tasks.

2.3.3 Consideration of Secondary Effects resulting from Noise Stimulation

A downside to current real-time human performance decrement countermeasures is that they can produce unintentional side-effects. Some neuromodulation methods have been shown to influence behavioral health. tDCS can leave long-lasting effects on cortical excitability after stimulation has occurred (Medeiros et al., 2012). TMS has been shown to reduce depression states in clinical trials (Mantovani et al., 2012). While this is a beneficial behavioral health effect, it demonstrates that there are additional side effects to these neuromodulation techniques which require further exploration. To the my knowledge, no studies were identified which investigate lasting effects of sensory noise on behavioral health (e.g., mood, stress, sleep, etc.), so it is unclear if noise can induce undesirable side effects.

2.4 Conclusion

Theoretical and neuronal models posit the mechanisms of improved signal understanding using noise through SR. These notions have been carried to psychophysical experimentation where researchers found improved perception within and across sensory modalities. As a result of noise integration in the brain, researchers have found that additive sensory noise can improve elements of higher order information processing; however, it is unclear if these improvements can be observed for complex, operational tasks. Thus, this work will investigate SR use in such tasks to postulate its utility in spaceflight.

Chapter 3: Investigative Rationale

SR may be a promising countermeasure for human performance degradation in spaceflight, however, there are several gaps in the literature. These unknowns have motivated the direction of the thesis.

- **Gap 1:** Poor understanding of SR's role in cognition.
    - While research shows additive noise may improve working memory, cognition is comprised of several domains, such as abstract reasoning and searching, that use different thought patterns. It is unclear whether additive noise can help enhance cognition broadly, both combined and in individual domains.
- **Gap 2:** Lack of research to investigate if SR can improve macrocognitive performance.
    - Prior research has shown perceptual and limited cognitive improvements due to noise; however, this fails to show whether SR improvements will translate to human performance in complex operational tasks. Macrocognitive tasks synthesize several information processing elements, but there is insufficient evidence to show that SR can help enhance such tasks.
- **Gap 3:** Lack of research exploring long term effects of longitudinal, repeated noise exposure.
    - I am not aware of any studies that explore repeatedly using noise to induce SR and its effects on long term performance and subject well-being. Longitudinal, repeated use of noise stimulation may have long term behavioral health effects or even enhance longer term information processing functions, like learning.

- **Gap 4:** Limited knowledge on its utility compared to other NIBS techniques.
    - Historically, sensory noise administration to alter human performance has been limited mostly to perception and elements of cognition. In contrast, alternative methods of NIBS have been applied to operational contexts and medical treatments. It remains unclear whether SR can be useful compared to these other techniques and which of these techniques is most applicable in a spaceflight context.

This thesis investigates SR to address these gaps with respect to the information processing model. While there are outstanding questions of noise's role in perception, the lab's prior research has shown the existence and utility of SR within that stage of information processing (Voros et al., 2022; Voros et al., 2021). Therefore, this work will focus on other blocks within the model (Fig. 1). This work will also explore noise's ability to improve overall performance and its feasibility for use in a spaceflight environment.

This research only considers sensory modalities that integrate well with, or possibly target other complications resulting from, living in a spaceflight environment. Living in microgravity imposes sensory challenges as a result of otolithic deprivation; however, several longitudinal studies have shown that humans reinterpret and adapt their understanding of orientation and spatial surroundings in spaceflight (Pathak et al., 2022). Thus, I wanted to apply noise to sensory modalities that have demonstrated the ability to influence the vestibular, motor, somatosensory, and visual systems as these central nervous system (CNS) regions are impacted and undergo sensory reweighting in spaceflight (Roy-O'Reilly et al., 2021). Directly influencing these CNS regions, nGVS has been shown to modulate spatial memory and learning in sensorimotor performance tasks (Hilliard et al., 2019; Moore et al., 2015; Putman et al., 2021).

Further, nGVS has been shown to improve postural stability and perception in vestibular and visual modalities (Galvan-Garza, 2018; Wilkinson et al., 2008; Wuehr et al., 2016). Indirectly influencing these CNS regions, AWN has been shown to improve memory encoding and learning of auditory and visual stimuli (Othman et al., 2019; Sayed Daud & Sudirman, 2023). Further, AWN may influence locomotion and perception performance in visual, tactile, and somatosensory modalities (Carey et al., 2023; Lugo et al., 2008; Manjarrez et al., 2007). These two modalities have demonstrated the ability to modulate learning and improve performance in perception and key CNS regions, lending themselves as ideal neuromodulation candidates if they also improve performance in complex, operational tasks.

Thus, I chose to investigate acoustically stimulating the auditory system using AWN and electrically stimulating the vestibular system using nGVS. Additionally, these two modalities were selected as I believed they were the least intrusive to interface design or to astronaut mobility, being ideal candidates for operating in the spaceflight environment. The literature suggests that an optimal level of noise is needed to induce SR improvements; this optimal level is subject and task dependent (Moss et al., 2004; Usher & Feingold, 2000; J. Voros et al., 2022). When applicable, this work finds the subject's best (close to optimal) AWN and nGVS noise level and evaluates performance for these levels. This work also uses AWN and nGVS simultaneously to create multi-modal stochastic resonance (MMSR) to investigate additive benefits of multi-sensory stimulation. The goal of this thesis is that:

Evaluating the role of stochastic resonance in information processing and operations will allow us to determine whether it can be an applicable spaceflight countermeasure for human performance decrement.

This thesis encompasses the following Specific Aims:

- **Specific Aim 1:** Investigate additive noise effects on overall cognition and cognitive sub-domains.
    - **Motivation:** Studies have shown SR enhancement of a limited number of cognitive domains, such as working memory, but various brain regions are associated with separate domains. Therefore, it is not known if SR can improve overall cognition or if it may influence certain cognitive domains over others. I hypothesize that AWN and nGVS will improve cognition performance when compared to no noise being used. Further, I hypothesize that their combination (MMSR) will result in additive cognition enhancement compared to AWN and nGVS alone.
    - **Summary of work:** 13 subjects completed 7 out of the 10 tasks in the "Cognition Test Battery" (Basner et al., 2015) with and without additive noise. These 7 tasks assessed distinct cognitive domains. I analyzed within-subject performance improvements in each task and overall cognitive performance between three control conditions, optimal AWN, optimal nGVS, and their combination (MMSR).
- **Specific Aim 2:** Evaluate the utility of noise to improve operational performance.
    - **Motivation:** To be a viable spaceflight countermeasure, SR needs to enhance performance in complex macrocognitive tasks. The literature has failed to investigate this, so this Aim investigates whether SR can enhance overall performance. I hypothesize that AWN and nGVS will improve operator performance in a complex task when compared to no noise being used. Further, I

hypothesize that their combination (MMSR) will result in additive operator enhancement compared to AWN and nGVS alone.

  - **Summary of work:** 16 subjects completed a lunar lander simulation with and without additive noise. This simulation comprised sub-dimensions related to flight performance, decision making, and perception identification. I analyzed within-subject performance improvements for the task overall and within each sub-dimension between a no noise sham, optimal AWN, optimal nGVS, and MMSR.

- **Specific Aim 3:** Investigate the long-term effects of longitudinal, repeated noise exposure.
  - **Motivation:** I postulate that longitudinal, repeated use of noise to induce SR could enhance long-term procedural memory retrieval in information processing. It may also have effects (either positive of negative) on behavioral health states, such as mood or stress. These results will provide insight on the acceptability of repeated exposure. I hypothesize that AWN and nGVS will improve operator learning when compared to no noise being used. Further, I hypothesize that their combination (MMSR) will result in additive learning enhancement compared to AWN and nGVS alone. Further, I hypothesize that repetitive sensory noise administration will effect behavioral health attributes.
  - **Summary of work:** Subjects completed five lunar rover driving simulations over the course of five days. Between-subject simulation performance was compared between four groups: no noise, AWN, nGVS, and MMSR using a time-longitudinal scale to observe learning enhancements. Subjects completed

questionnaires related to their perceived mood and stress to compare behavioral health states between the four groups.

- **Specific Aim 4:** Compare the applicability of certain neuromodulation methods as a spaceflight countermeasure for human performance decrement.
    - **Motivation:** The work in this thesis, thus far, has explored the ability of SR to improve higher order information processing and its potential neural mechanisms. However, there are many neuromodulation techniques, such as, tDCS and TMS that can be used to induce changes in human performance. It remains unclear which of these non-invasive neuromodulation techniques may be most applicable to spaceflight.
    - **Summary of work:** This Aim reviews the literature for several neuromodulation techniques have been investigated specifically for spaceflight. It compares several aspects of applicability such as effectiveness, side effects, integration requirements, and subjective affinity to determine which technique may currently be most applicable for usage in spaceflight.

Chapter 4: Specific Aim 1 - Investigate additive noise effects on cognition.

4.1 Introduction

This work aimed to explore the ability of enhancing broad cognitive performance using sensory noise, where cognition was evaluated using the validated Cognition Test Battery (CTB) developed by Basner et al. (2015). The CTB provides a sensitive evaluation of different cognitive domains using standardized techniques, such that when combined, the results provide a comprehensive insight on SR's influence on cognition. I hypothesized that single modality noise (AWN and nGVS) would enhance cognitive performance in human subjects when compared to performance without noise. Further, I hypothesized that stimulating both modalities simultaneously to induce multi-modal SR (MMSR) would enhance performance to a greater degree than single modality alone. This hypothesis is novel as, to my knowledge, no investigation exists evaluating the mental performance effects of compounding sensory noise across multiple modalities. To address the gap associated with improvement due to arousal, our work investigates the role of additive noise versus simple arousal stimulation in influencing cognition.

This work also begins to address Gap 4 as it investigated the degree to which subjective survey methods could identify whether subjects may be sensitive to SR cognitive performance enhancement. SR perception studies have suggested that some individuals are susceptible to SR perception improvements, while others are not (Galvan-Garza, 2018; Ries, 2007). Thus, it was expected that only some subjects may receive SR cognitive benefits. Currently, there is no way to predict *a priori* whether an individual is likely to be sensitive to SR performance improvement. Therefore, I developed a subjective questionnaire for subjects to rate how well they could maintain focus in quiet and noisy environments. I hypothesized that there would be a positive correlation between noisy environment preference and cognitive enhancement under the influence of added sensory noise.

The objectives of this Specific Aim are to:

- Assess the effects of additive sensory noise on overall cognition performance.
- Evaluate whether subjective preference can indicate cognitive SR enhancement.

Additionally, previous cognition SR studies failed to consider the potential confounding effect of arousal induced by sensory stimulation as the mechanism of cognitive improvement, as opposed to the presumed mechanism of SR. Arousal resulting from periodic visual and auditory stimuli have been shown to increase functional activity in frontal regions (Sturm & Willmes, 2001), potentially impacting cognitive abilities. Without the use of control conditions to assess the role of arousal from sensory stimulation, it is unclear whether SR is the dominant mechanism in any cognitive improvement. Thus, this work included control stimulation conditions to assess the role of stimulation arousal.

4.2 Methods

Thirteen subjects (7F/6M, range = 20-40 yrs, mean = 29.5 yrs, SD = 6.6 yrs) completed testing in the Bioastronautics Lab at the University of Colorado-Boulder. An *a priori* power analysis based on the results of Wilkinson et al. (2008) and Söderlund et al. (2010) suggested that we needed 8-12 subjects for our study design to find an effect size greater than 0.3, which was expected based on the former's findings. This research was approved by the University of Colorado-Boulder's Institutional Review Board (#20-0419) and written informed consent was obtained prior to participation. Broadband AWN was administered to subjects through ear buds (Essential Earphones HD) and a Samsung Tablet A; the auditory profiles were developed and calibrated by Creare LLC (Hanover, NH). Broadband, unipolar, zero-mean white noise was bilaterally administered to subject mastoids through the Galvanic Vestibular Oscillating Stimulator (model 0810, Soterix Medical, Woodbridge, NJ) using electrodes with a contact area of 2 cm^2. Tasks were completed using a Dell Latitude E6430 laptop, which is specifically calibrated to run the CTB, in a single walled sound booth (Whisperoom, MDL 4872).

4.2.1 Independent Variables

Six experimental conditions were investigated to assess the effects of additive noise on cognition. A sham baseline was collected. A subject-specific best level of AWN, nGVS, and MMSR were tested, as determined from an initial suite of measures, which is described further in Section 4.2.3. I hypothesized that, when compared to the sham baseline, the single modality SR conditions would improve cognitive performance and the MMSR condition would have additive benefits, causing larger improvements than single modality SR alone. I also investigated the potentially confounding effect of arousal on performance. To do so, subjects were tested with suprathreshold stimuli – an auditory pure tone signal at 55 dB and a direct current GVS (DCGVS) signal at 0.8 mV. These stimulate the sensory modalities with a non-random signal in a manner that would not induce SR but would cause arousal. Without these stimulation shams, performance changes could not be distinguished between the effects of arousal and SR. I hypothesized that these stimulation control conditions will not result in significant performance changes from sham. To summarize the following conditions were tested:

- 3 control conditions: no stimulation sham, 55 dB pure tone stimulation, and 0.8 mA DCGVS stimulation
- 3 SR conditions: Subject-specific optimal AWN, optimal nGVS, and MMSR

4.2.2 Dependent Variables

Cognitive ability performance is typically quantified in terms of speed and accuracy. However, subjects may place a heavier weight in one or the other when completing a task, making it a challenge to assess overall performance, this is known as the speed-accuracy tradeoff (Wicklegren, Wayne, 1977). The literature accounts for this through a post-hoc combination of the normalized speed and accuracy metrics, which is often referred to as efficiency (Basner et al., 2021; Scully et al., 2019). The dependent variables of accuracy, speed, and efficiency were used to assess performance in the cognitive tasks.

Seven tasks in the CTB were chosen as they are associated with distinct cognitive domains and recruit different regions in the brain, allowing us to explore cognition and its sub-domains in a manner far more comprehensively than has been found in the literature. Table 1 summarizes the seven CTB tasks subjects completed in this experiment. These seven tasks are associated with distinct cognitive domains and recruit different regions in the brain, allowing deeper exploration of cognition and its sub-domains in a manner far more comprehensively than has been found in the literature. Table 2 is a recreation of the table from Basner et al. (2015) which summarizes each task's cognitive domain and areas of the brain recruited to complete the task.

Table 1. Each CTB task that subjects completed and their description.

Task Name	**Task Description**
Digit Symbol Substitution (DSST)	A legend with corresponding numbers and symbols is presented to the subject. One of these symbols is presented to the subject and they must identify it in the legend.
Line Orientation (LOT)	Two lines are presented on the screen. One is fixed, while the other can be rotated by the subject. The subject must rotate this one to be parallel with the stationary one.

Matrix Reasoning (MRT)	Subjects are given a matrix of elements which are organized in a pattern. One of the matrix elements is absent and the subject must choose the appropriate element to put in this blank space.
Fractal 2-Back (F2B)	Subjects are presented with a sequential series of fractals, one at a time. The subject must determine if the current fractal was shown two images prior.
Motor Praxis (MPT)	Squares are presented at random locations on the screen one at a time. Subjects must click on these squares as they show up, as quick as they can. The squares decrease in size as the task goes on.
Psychomotor Vigilance (PVT)	A box is displayed to the subject. Subjects must hit the spacebar as quick as possible when a counter is displayed. They must not hit the spacebar before the counter is displayed.
Visual Object Learning (VOLT)	Subjects are shown 10 figures in a row and told to memorize them. They are then presented a secondary set of 20 figures and must determine whether they saw them in the original set of 10.

Table 2. Cognitive domains and brain regions associated with each CTB task (Basner et al., 2015)

Test	Cognitive Domains	Recruited Brain Regions
DSST	Complex scanning / visual tracking	Temporal cortex / prefrontal cortex / motor cortex
LOT	Spatial orientation	Right tempero-parietal cortex / visual cortex
MRT	Abstract reasoning	Prefrontal cortex / parietal cortex / temporal cortex
F2B	Working memory	Dorsolateral prefrontal cortex / cingulate / hippocampus
MPT	Sensory-motor speed	Sensorimotor cortex
PVT	Vigilant attention	Prefrontal cortex / motor cortex / inferior parietal and visual cortex
VOLT	Spatial learning / memory	Medial temporal cortex / hippocampus

4.2.3 Experimental Design

A within-subject experimental design was implemented. In their initial visit, subjects were trained in the standard manner on the CTB tasks by watching a 20-minute tutorial video, after which they completed two practice trials of each CTB task. Next, testing occurred across two subsequent visits, where subjects completed all testing for each specific CTB task within a single session. MRT, MPT, and PVT were tested in one session and DSST, LOT, F2B, and VOLT were tested in the other session. The order of the tasks within the test day was randomized for each of the two test days.

Recall, it is thought there is an optimal level of noise in terms of producing SR-benefits that depends on the subject, task, and sensory system (Moss et al., 2004). Thus, for each CTB task, a range of AWN and nGVS levels were assessed for each subject. Four nGVS levels ([0.2, 0.4, 0.6, and 0.8 mA]) and three AWN levels ([40, 55, and 70 dB SPL]) were tested in a randomized order, as has been done in this lab's prior work (J. L. Voros et al., 2021). Speed and accuracy were corrected to account for trial-specific differences and learning effects, using corrections from Basner et al. (2020). From this initial set of measures, the SR level yielding the best score in feedback, another measure of combined performance in the CTB, was selected as the subject-specific best (or close to subject optimal) AWN and nGVS levels.

Once the subject-specific best SR levels were identified, six experimental conditions were investigated to assess the effects of additive noise on cognition. Subject-specific best levels of AWN, nGVS, and MMSR were tested, as determined from the initial suite of measures in addition to the arousal control stimulations of suprathreshold stimuli. All conditions were presented and tested in a randomized order for the cognitive tasks within each of the two test sessions. Short breaks were provided between tests to help mitigate subject mental fatigue, but as in other studies using nGVS (Galvan-Garza, 2018; Goel et al., 2015; Inukai et al., 2018; Keywan et al., 2018, 2019; Mulavara et al., 2015; J. L. Voros et al., 2021) a more extensive break between nGVS applications was not employed, since the most rigorous studies using nGVS have not found carryover effects between nGVS stimulation levels (Keywan et al., 2020; Nooristani et al., 2019).

To address the second objective of this Specific Aim, after completing all cognitive testing, subjects completed a subjective five-point Likert scale questionnaire that asked how well they felt they could maintain focus in quiet and noisy environments. Their noisy environment preference score was defined as the difference in subject ranking between quiet and noisy environments (i.e., a negative score means the subject prefers working in quiet places and a positive score means they prefer working in noisy places). This survey can be found in Appendix A.

4.2.4 Data Analysis

A within-subjects analysis was completed for the metrics of accuracy, speed, and efficiency. Two separate analyses were done by comparing sham to the noise conditions and to the stimulation control conditions. In each analysis, performance outcomes on each of the 7 CTB tasks were collapsed into one scale to create a comprehensive cognition metric. For this comprehensive metric, data was initially adjusted by subtracting the subject's specific average across the conditions of interest in that CTB task, to account for individual differences in performance. From there, the data was standardized for the task by calculating the z-score of each measurement with respect to all measurements across subjects within that CTB task as shown in Equation 1. Z_i represents the standardized cognition metric and P_i is the raw scores of that task datapoint. M_T and σ_T were the mean and standard deviation, respectively, of all raw data in the specific task. This process has been done for CTB data in prior work (Scully et al., 2019), yielding a normalized cognition outcome.

$$Z_i = \frac{P_i - M_T}{\sigma_T} \quad (1)$$

A repeated measures ANOVA (RMANOVA) with four levels (sham, AWN, nGVS, and MMSR) was conducted to investigate the effect of noise on cognition using this normalized cognition metric. This was applied to each of the metrics of speed and accuracy. Efficiency was calculated as the mean of these two normalized metrics. A separate RMANOVA was also completed for the three control conditions (sham, tone, DCGVS) to investigate the effect of arousal on cognition. Assumptions for homogeneity and residual normality were tested to ensure that parametric statistics were appropriate. Datapoints that created semi-studentized residuals greater than three were removed as outliers. If there was an outlier in one metric, say speed, the associated datapoint was also removed from the other two metrics, accuracy and efficiency. If the F-test results from the RMANOVAs were significant, Tukey HSD multiple pairwise comparisons were used to identify which conditions were different from another. If the F-test results from the RMANOVAs were insignificant, an equivalence test was completed to indicate whether the conditions were equivalent following the methods conducted by Rusticus & Lovato (2011).

To assess noise effects on overall cognition, as per our first hypothesis, subjects were treated as a random effect in our RMANOVAs, allowing us to posit on the broad utility of additive noise across all subjects in our sample. This analysis was done for the noise conditions (sham, nGVS, AWN, and MMSR) and control conditions (sham, pure tone auditory stimulation, DC GVS). For the second hypothesis analysis, subjects were included as an interaction term along with the noise conditions, allowing us to posit on whether noise effects are different across individuals.

Additionally, for the second objective of this Aim, an exploratory analysis was conducted to see whether subjective noisy environment preference could be an indicator for individual differences in noise effects on cognition. Subjects' normalized cognition metric in the sham condition was subtracted from their normalized cognition metric in the additive noise conditions. The calculation of this metric is found in Equation 2. Linear models were fit to this entire dataset against their noisy environment preference scores.

$$\Delta Z_i = Z_{i,noise} - Z_{i,sham} \tag{2}$$

4.3 Results

For all models presented in these results, there were no observable violations of the residuals from assumptions. Figure 5 compares the normalized cognition metric scores for the noise conditions and the sham condition, for all subjects and tasks. This figure represents the difference in overall cognition, where higher scores in efficiency, accuracy, and inverted speed imply better performance. Table 3 displays the RMANOVA results with subjects included as a random effect. Contradictory to the hypothesis that additive noise would improve cognition, no significant differences were found between sham and the noise conditions for all metrics. Separate to this main comprehensive analysis, an exploratory analysis of accuracy and speed in each CTB task individually was conducted and found no significant differences. These results are found in Appendix B1 with figures and statistical findings.

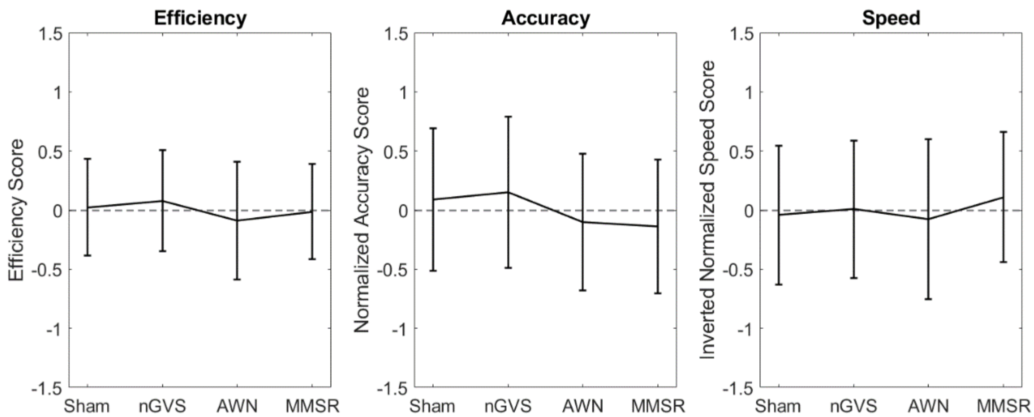


Figure 5. Scatter plots compiling normalized cognition metric scores combined across CTB tasks, for the noise conditions and sham. Error bars indicate the 95% confidence interval for score in that condition.

Table 3. 1x4 RMANOVA results for sham and noise conditions. Subjects included as a random effect.

Metric	**F(3,343)**	**P-value**	$\boldsymbol{\eta_p^2}$
Efficiency	1.08	0.357	0.009
Accuracy	2.09	0.101	0.018
Speed	0.54	0.654	0.005

Five outliers were identified and removed within this first model, out of 364 total data points. When all of the data was included in the RMANOVA, the p values increased. Thus, the conclusion that noise does not significantly affect cognition metric scores remains the same. No outliers were identified or removed in the other models presented.

To assess the effect of arousal, the same RMANOVA analysis was applied to the control conditions. These results are found in Figure 6 and Table 4. In agreement with the hypothesis that arousal stimulation alone would not impact cognition, no significant differences between the control conditions were identified.

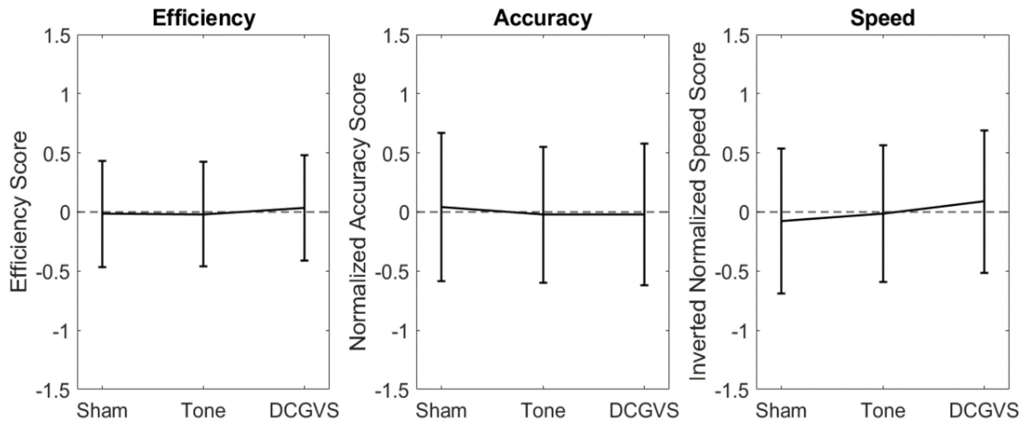


Figure 6: *Scatter plots compiling normalized cognition metric scores combined across CTB tasks for the control conditions. Error bars indicate the 95% confidence interval for score in that condition.*

Table 4. 1x3 RMANOVA results for the control conditions. Subjects included as a random effect.

Metric	F(2,258)	P-value	η_p^2
Efficiency	0.14	0.866	0.001
Accuracy	0.11	0.893	0.001
Speed	0.6	0.547	0.005

The lack of significant differences was further evaluated using a series of equivalence tests. First, leveraging the data from Wilkinson et al. (2008), a 90% equivalence interval of ± 0.793 was defined for the difference between noise conditions. When comparing the noise conditions to sham, the largest 95% confidence interval for the multiple comparison was the mean difference ± 0.263 for efficiency, while for accuracy and speed it was ± 0.369. The small confidence intervals in the data suggest that the efficiency, accuracy, and speed were all equivalent between the noise treatments and sham. The largest 95% confidence interval for the control condition multiple comparison in our data (Fig. 2) was only ± 0.348, suggesting the performance between the control conditions were equivalent.

To evaluate whether noise effects depend on subject (second hypothesis), I investigated the interaction of subject and condition. These results are presented in Table 5. In agreement with the hypothesis, significant interactions between subject and noise condition were identified for accuracy, but not speed and efficiency. This suggests that noise effects on cognition are inter-individually dependent. The efficiency results of four subjects are illustrated in Figure 7, where subject 2 appears to have cognitive benefits from applying noise, subject 5 was hindered, and subjects 8 and 10 have varied performance independent of noise. Four subjects are shown for legibility, plots containing all subjects can be found in Appendix B2.

Table 5. 1x4 RMANOVA results for the sham and noise conditions. Subjects included as an interaction term. Asterisks represent metrics that met a statistical significance below 0.05.

Metric	**F(36,312)**	**P-value**	$\boldsymbol{\eta_p^2}$
Efficiency	1.66	0.097	0.134
Accuracy*	1.58	0.023	0.154
Speed	1.07	0.364	0.110

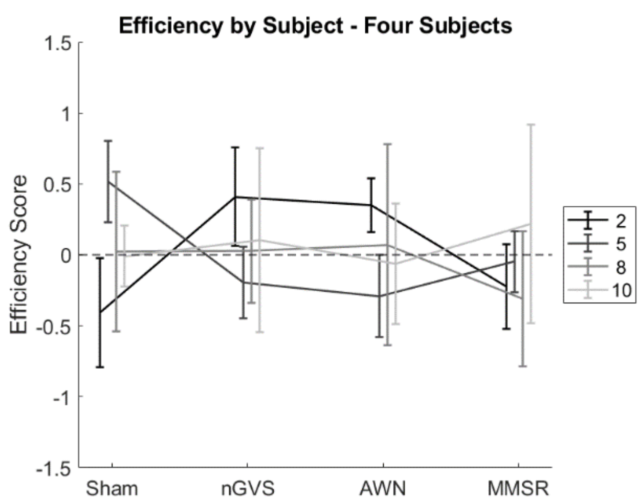


Figure 7. Scatter plots compiling efficiency scores across CTB tasks for four individual subjects for the noise conditions. Error bars indicate the 95% confidence interval for score in that condition.

Figure 8 explores the mental performance difference (normalized sham cognition metric subtracted from normalized noise cognition metric) as a function of noisy environment preference. These linear models use data from all noise conditions, independent of sensory modality, to assess trends of user susceptibility to noise given preference. The characteristics of these models are presented in Table 6. Positive slopes were identified for all three metrics (inverting speed so positive implies performance improvement). These trends, while consistent with the hypothesis, were not statistically significant for the metrics of accuracy and speed, but was statistically significant for efficiency. The slope of the regression line indicates a change in effect across the scale with an effect size of 0.44 for speed, 0.53 for accuracy, and 0.48 for efficiency.

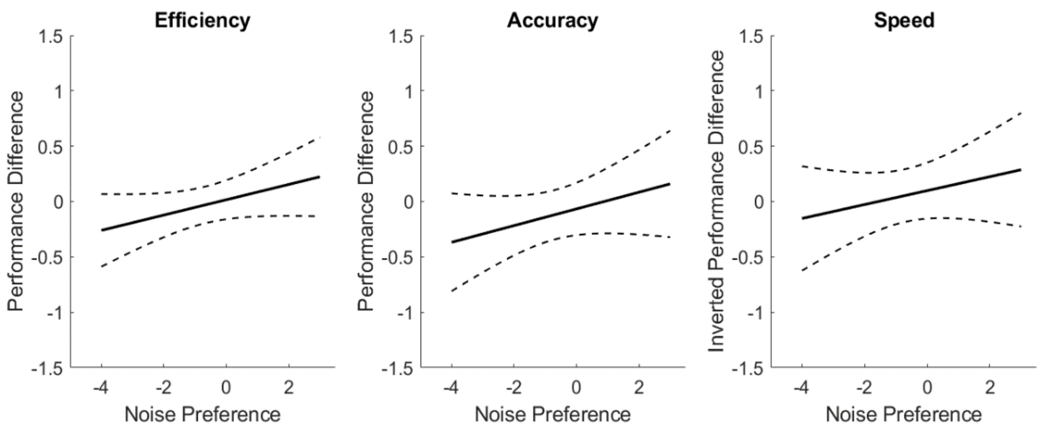


Figure 8. Linear regressions of cognitive performance improvement from sham as a function of noisy environment preference. Dashed lines indicate the 95% confidence interval of the modeled fit.

Table 6. Statistical results for linear regressions of cognitive performance improvements as a function of noisy environment preference. Models fit to all noise condition data.

Metric	Slope	P-value
Efficiency	0.069	0.048
Accuracy	0.075	0.109
Speed	0.063	0.212

4.4 Discussion

This research aimed to assess the utility of using additive sensory noise to improve overall cognition. To my knowledge, this research represents the most comprehensive assessment of the effects of SR noise on cognition, as it assessed performance across a broad range of cognitive domains. This work also incorporated an expansive set of control conditions to investigate arousal effects. This investigation was similar to cross-modality perception studies which found noise, not arousal, was the mechanism of perceptual enhancements (Lugo et al., 2008). Further, I investigated mental performance effects of compounding sensory noise across multiple modalities.

This work observed subject performance in seven tasks of the CTB while under the influence of nGVS, AWN, and MMSR. Observing performance metrics of efficiency, accuracy, and speed for the cognitive tasks in our broad population, no significant level differences were found between any of the conditions. Additive sensory stimulation, whether noisy (aimed at inducing SR), multi-modal, or control stimulations (pure tone auditory or DC GVS), had no significant effect on broad cognitive performance, neither beneficial nor degrading. Visually though, there appears to be larger performance differences between the noise conditions and sham (Fig. 1) than there were for the control conditions (Fig. 2). This may suggest that random noisy sensory stimulation influences cognition to a greater degree than non-noisy stimulation.

While previous working memory studies using nGVS were able to find significant differences with small subject numbers (Wilkinson et al., 2008), these studies, were limited in that they explored a singular aspect of cognition. While this study investigated 13 individuals, these methods comprehensively investigate seven tasks related to cognitive processing, which could allow for understanding broad effects of noise on cognition. Additionally, the repeated observations of subjects in different tasks increased the statistical power of the statistical models. A retrospective power analysis conducted on these results indicate that 12 subjects are sufficient to identify significant interaction differences, as shown in Table 5. However, based on the η^2 of the noise condition term alone (Tbl. 3) it was found that 100 subjects are needed to reach significant effect. This suggests that individual differences may be the dominant effect of SR, rather than broad cognitive benefits across all individuals. Individualized responses to sensory noise to improve cognition may be consistent with the findings of Lin (2022) and Söderlund et al. (2010) which found that only children with low attention tendencies cognitively benefitted from loud auditory white noise ($\geq$ 65 dB). On the other hand, our results contrast those of Awada et al. (2022) and Othman et al. (2019) using AWN and Wilkinson et al. (2008) using nGVS to improve working memory, both in healthy adults. It could be possible that the benefits of additive sensory noise are limited to working memory (or other specific cognitive domains) and do not yield broad cognitive benefits, as assessed here using seven tasks from the CTB. However, I conducted an exploratory RMANOVA of the adjusted scores for the fractal 2-back, a working memory task, and it still showed insignificance as well ($p > 0.3$). As such, this specific working memory task evaluation contradict findings in the literature. Referencing the exploratory analysis in Appendix B1, no significant differences were found in each of the individual tasks. It should be noted that these findings supplement mixed results within the literature when investigating the role of auditory noise in cognition for a neurotypical group. Awada et al. (2022) found evidence that certain noise levels improved aspects of attention and working memory; however, not all cognitive tests evaluated or noise levels administered yielded significant improvements from ambient noise. This could suggest that noise does not influence neurotypical individuals to the degree it influences those with attentional disorders. While these results are not promising for generally using noise to enhance cognition, they do indicate that individuals may be susceptible to benefits. Future work may move beyond inferential statistics used herein to analyze differences with Bayesian methods, which could provide further indications on the effect of noise on cognitive processes. Additionally, while these methods used the guidance of Basner et al. (2020) to correct for longitudinal effects that can stem from task learning or fatigue, it was of concern that these effects could still impact the results. Thus, I completed a regression analysis of accuracy and speed performance against number of times the task was completed to confirm this was not the case. No significant trends were found to indicate that longitudinal effects skewed the data. These results can be found in Appendix B3. Along with this sanity check, I believe the randomization procedures used made the data robust to this experimental concern.

Despite the results for the broad population, the results of the linear models on preference for working in noisy environments shows novel promise for identifying users that may effectively use sensory noise for improved cognitive performance in an SR manner. Experimental literature suggests that some individuals are perceptual SR exhibitors, while others are not influenced by additive noise (Galvan-Garza, 2018; Ries, 2007). There has not been a way to identify, a priori, whether someone is susceptible though. This work identified trends in correlating cognitive performance improvement with subjective preference for working in noisy environments. A statistically significant, positive relationship was found between the efficiency metric and noise preference. The slopes of speed and accuracy trended toward significance, showing that additive sensory noise increases accuracy and reduces speed for subjects that prefer working in noisy environments. While there remains variability in response across the seven CTB tasks, these findings indicate that for some subjects, additive noise may yield improvements in cognitive performance, via the mechanism of SR. Further, those individuals were able to self-identify as performing better in noisy settings. To my knowledge, this is the first investigation exploring a means to independently identify which individuals may be susceptible to exhibiting SR benefits. This work's brief noise preference questionnaire points toward working environment affinity as a potential indicator for finding individuals that could see cognitive enhancement from additive noise. The role of individual differences in preference towards working in noisy environments and SR exhibition, particularly in cognitive performance, warrants further investigation.

I want to note two limitations to this study. First, while the methods utilized a power analysis to guide the number of subjects we tested, thirteen is still a small sample size. This could explain the model's ability to find a significant trend for noisy environment preference in efficiency, while not being able to find significant main effects in other analyses. However, based upon the effect sizes observed, the population-wide effects of applying auditory or vestibular white noise on cognition appear quite small and may not be practically relevant. Second, I also note that the repeated application of nGVS (or AWN, DC GVS, or pure tone auditory stimulation) potentially could have long-term effects on cognition. While the literature does not indicate these carryover effects are anticipated, it also has not been rigorously evaluated, as has been done for other neuromodulation techniques (Keywan et al., 2020; Medeiros et al., 2012). Carryover effects of noise use have not been investigated for cognition prior to this dissertation, but they are further explored in Chapter 6.

4.5 Conclusions

This investigation applied a comprehensive and rigorous evaluation of using sensory noise to improve cognition using a suite of standard cognitive tests and performance comparisons with stimulation control conditions. I conclude that applying additive noise to the auditory and vestibular sensory modalities, as well as to both simultaneously, will not result in improved cognitive performance for a broad population. However, the results indicate that additive noise may have differing cognitive effects across individuals. I assessed a subjective survey's applicability to identify these individuals based on reporting of preference for working in a noisy environment and found a statistically significant, positive relationship. Thus, this type of subjective reporting may be a useful indicator, but further research into other identifying questions or techniques is needed.

This work does not appear to support the utility of using SR as a neuromodulation technique for comprehensive cognition. However, these assessments do not adequately replicate the complex operational environment that astronauts regularly encounter. Traditionally, SR has been shown to improve perception rather than cognitive capabilities in healthy individuals. Complex information processing in operational contexts could utilize these perceptual improvements; thus, Chapter 5 investigates holistic performance in a complex operational task. Additionally, this work shows that some individuals see improvements as a result of noise, and it is useful to see if this translates to operations for susceptible individuals.

The work related to this Specific Aim has been published in *Frontiers in Human Neuroscience* (Sherman et al., 2023a).

Chapter 5: Specific Aim 2 - Evaluate the utility for noise to improve operational performance.

5.1 Introduction

As it currently stands, no studies have been performed to show that SR can influence complex macrocognitive and operational processes. This is not the case for other neuromodulation techniques though. Choe et al. (2016) investigated tDCS effects for an nBack task and a flight simulator, finding improved performance and learning in both tasks, implying benefits in the microcognitive and macrocognitive domain. Further, Scheldrup et al. (2014) found improvements in multi-tasking while utilizing tDCS, suggesting improved macrocognitive performance. In addition to direct performance enhancement, tDCS has been shown to reduce perceived temporal workload in surgical simulations (Wilkinson et al., 2022). High levels of mental workload can lead to stress and performance decrements in operators (Wickens et al., 2013); thus, neuromodulation techniques that influence mental workload may indirectly impact operator performance. Given the success of other neuromodulation techniques to improve operationally relevant performance and affect workload, the absence of research on SR macrocognitive effects presents a substantial literature gap that needs to be addressed.

I aimed to fill this gap in the literature by assessing the potential for enhancing operator performance using sensory noise. I hypothesized that single modality noise (either AWN or nGVS) would enhance performance in human subjects when compared to performance without noise (sham); additionally, I hypothesized that stimulating both modalities simultaneously to induce multi-modal SR (MMSR) would have additive benefits and enhance performance to a greater degree than using a single modality alone. To assess this, subjects performed a series of lunar lander simulation tasks under sensory noise and a no noise sham. This task loads several perceptual, cognitive, and motor coordination domains, such that, the results provide comprehensive insight into the influence of noise for operational tasks.

Additionally, SR perception studies imply that perception performance enhancement is greater for at-threshold perceptual stimuli, but suprathreshold enhancement is possible (McDonnell et al., 2008; Sasaki et al., 2008). Thus, I believed that "at-threshold" operational enhancement could be a factor in noise benefit effectiveness. I hypothesized that the extent of SR performance enhancement may vary as a result of task challenge. The task design in this work allowed for task difficulty modulation and assess whether improvements are related to task difficulty. Finally, I assessed the effects of sensory noise on subjective mental workload while completing an operational task.

The objectives of this Specific Aim are to:

- Assess the effects that additive noise has on operator performance.
- Assess the effects of additive noise on mental workload.

5.2 Methods

Sixteen subjects (9F/7M), age 29 ± 7 years (range = 20-41 yrs) completed testing in the Bioastronautics Lab at the University of Colorado Boulder. An *a priori* power analysis based on the results of Scheldrup et al. (2014) suggested that 16 subjects were needed for this study design to find an effect size greater than 0.3, as Scheldrup found for tDCS. This research was approved by the University of Colorado-Boulder's Institutional Review Board (protocol #20-0347) and written informed consent was obtained prior to participation A within-subject experimental design was implemented. The independent variable of this research was the four treatments of sensory noise administered. Broadband AWN and nGVS were administered using the procedures previously described in Section 4.2.

5.2.1 Independent Variables

The independent variable in this study was the additive noise condition and included four levels. As in Specific Aim 1, a no noise sham condition, AWN, nGVS, and the combination MMSR condition were tested. I hypothesized that, when compared to no noise, the single modality noise conditions would improve overall operational performance and the MMSR condition would have additive benefits, causing larger improvements than single modality alone. I also hypothesized that additive noise would reduce perceived workload when compared to no noise. Unlike Specific Aim 1, the stimulation shams were not evaluated in this Specific Aim to reduce the effects of fatigue, given the complex nature of the task investigated and the necessity to complete all testing for the subject in a single session.

Three nGVS levels ([0.2:0.3:0.8 mA]) and three AWN levels ([40:15:70 dB SPL]) were tested in an original suite to find the subject specific best (or close to optimal) level. The best level was then retested and used for comparison.

5.2.2 Lunar Landing Simulation and Dependent Variables

The task used in this study aimed to be a representative analogue for a macrocognitive task that individuals in an operational environment may face. The simulation task was completed using the Aerospace Research Simulator (AReS), shown in Figures 9 and 10. AReS is a demonstrated, macrocognitive landing task that incorporates several cognitive processes at once (Pinedo, 2021; Zuzula et al., 2018). Figure 9 illustrates the hardware and interface of the AReS fixed-base flight simulation, while the software provides a realistic replication of lunar landing vehicle dynamics, piloting control responses, and fuel consumption. In the AReS lunar lander simulation task, subjects were presented six landing points scattered across a 2D contour map of the lunar surface. They attempted to choose the optimal landing point, considering its distance with respect to three scientific points of interest (i.e., nearest the centroid) and its potential presence within hazardous areas, such as steep slopes (Fig. 10b). The lander descended at a constant rate, continuously consuming fuel. To navigate to their designated landing zone, subjects were required to complete a tracking task on their primary flight display using a joystick by aligning the spacecraft's pitch and roll attitude (the yellow reticle) to the flight guidance cue (the magenta cue) (Fig. 10a). At a lander altitude of 250 meters (roughly 40 seconds into the task), a simulated lidar system gave the subject a new topography map which presented additional hazard information not visible initially, such as rock fields where the subject would not be able to land (bottom right panel of Figure 10b). At this point, the subject could continue to fly toward their original landing zone choice, or by pressing buttons on the joystick redesignate to a new landing site or abort the landing (allowable between 200 and 50 meters of altitude).

Novel to previous work done with AReS (Pinedo, 2021; Zuzula et al., 2018), I embedded two perception tasks. One was a tactile vibration presented to the wrist and the other was an auditory alarm presented to the cockpit via speakers. Both alarms indicated that a simulated thruster was stuck and consuming more fuel than usual. The magnitude of these perception alarms were initially low, beginning subthreshold and gradually increasing to a suprathreshold level. Subjects pressed a button on the throttle as soon as they identified either alarm, to affect a "reset" that solved their fuel leakage problem. The fuel decreased at a faster rate than usual while the alarm was active to incentivize the subjects to attend to the perception task. Each perception task occurred twice during a trial and occurred at random intervals. The timing of the four perception alarms was randomly assigned to four set times (10, 30, 50, and 80 seconds into the task) with a random time amount (between 1-10 seconds) added to each of those four set times.

Input was only accepted when the alarms were present; unsolicited presses of the button were not registered.

This task was designed to load on operational sub-dimensions of flight skill, decision making, and perception. The task's dependent variables were performance metrics that make up the task sub-dimensions found in Table 7. Each metric quantified an aspect of performance that I hypothesized may be sensitive to SR performance improvement. A description of how each metric relates to performance is also given in Table 7. Combining these sub-dimensions yields a comprehensive performance measure to capture overall operator changes caused by SR.

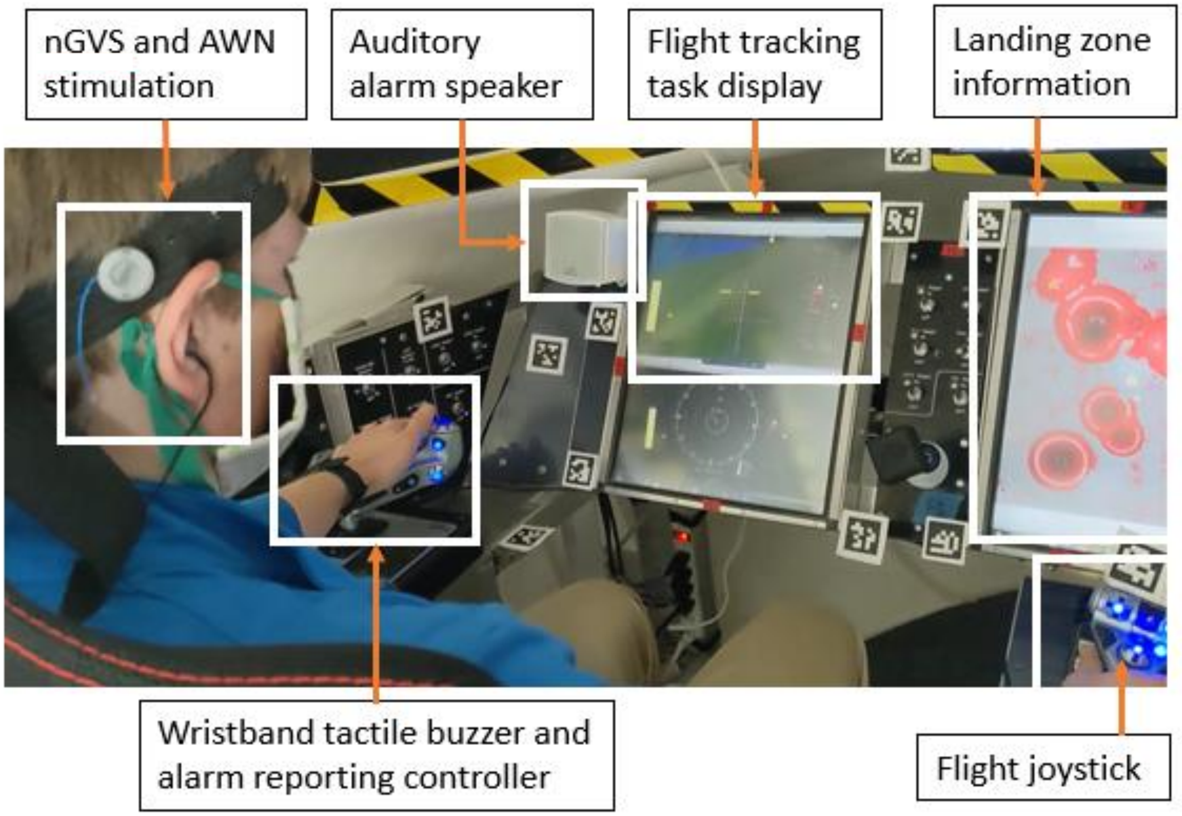


Figure 9. Over-the-shoulder view of the AReS lunar lander simulation used in this experimental paradigm. Relevant hardware and displays are highlighted in overlaid white boxes. Subjects sit stationary directly in front of the flight tracking task display with their right hand on the flight joystick which they use for the tracking task. To the right of the flight display is a map display indicating lunar topography and possible landing zone locations (i.e., landing zone information). To the left of the flight display is an external auditory speaker that intermittently presents the auditory alarm. A tactile buzzer is attached to the subject's left wrist to present the tactile alarm. The subject rests their left hand on the throttle, which they use to signal when they notice that the auditory or tactile alarm has occurred. nGVS electrodes and AWN earbuds are fixed to the subject's head in all trials, including sham where no noise was administered.

a. b.

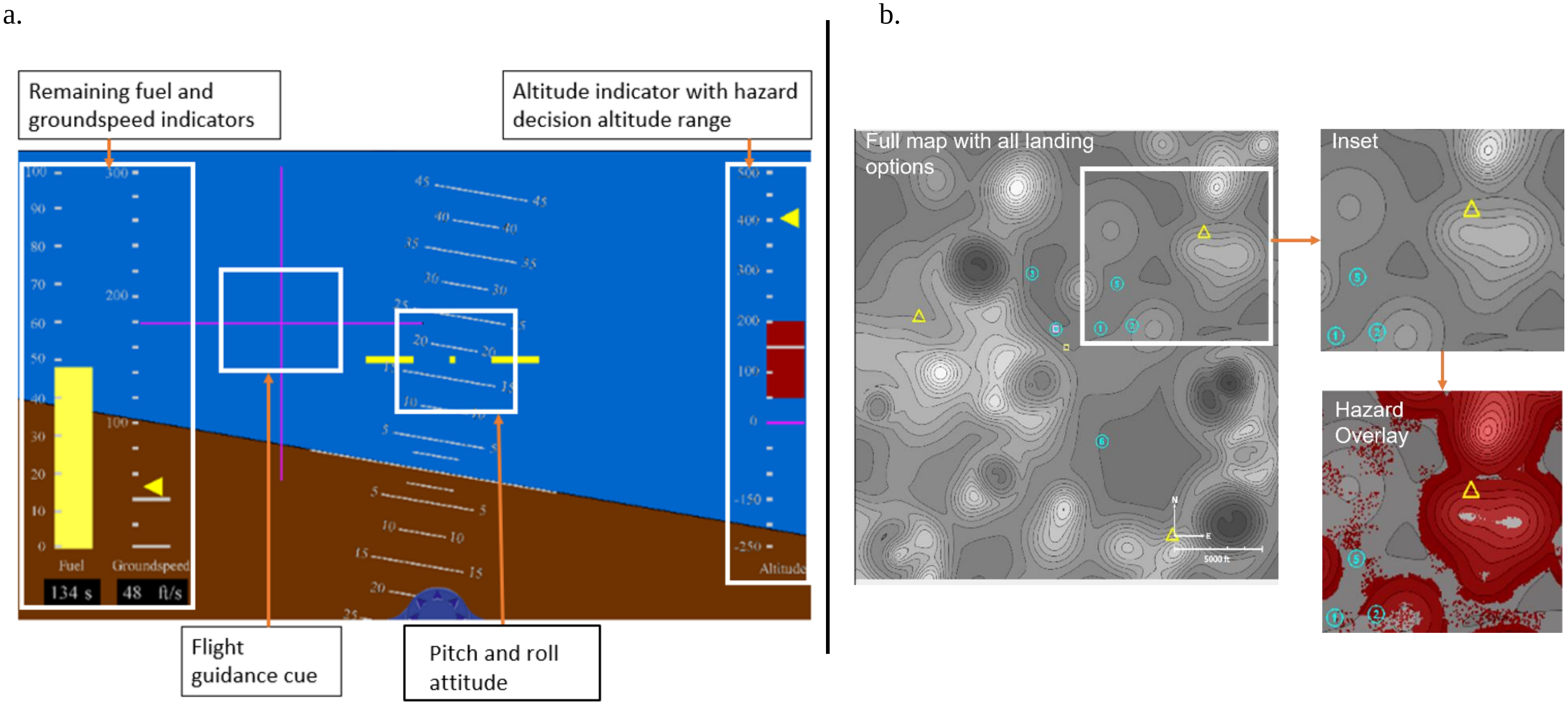


Figure 10. a) Visual information presented to the subject in the primary flight display. The panel displayed the spacecraft's pitch and roll attitude and altitude (and depiction of the hazard decision range in red), groundspeed, and fuel. The subject tracked the magenta flight guidance cue to align with the spacecraft's pitch and roll attitude as represented by the yellow reticle. b) Topography maps made available to subjects. The left was displayed to the subject at the start of the task. The yellow triangles depicted three scientific points of interest and blue circles were landing zones that subjects chose from. The top right panel is a zoomed-in inset of the map for legibility, the bottom right panel is the same display with hazard data from a simulated lidar sensor overlaid that appears once the spacecraft reaches 250 meters altitude.

Table 7. A description of each performance metric in the lunar lander simulation.

Sub-dimension	Performance Metric	Metric Description	Metric Justification
Flight	Root mean square distance (RMS) [deg]	The root mean square (RMS) distance error of the yellow reticle from the magenta cue over the simulation duration	The ability for subjects to track the lander's attitude with the guidance system. Better performance corresponds to a reduction in RMS error.
	Joystick Input (Stick)	The percentage of time the subject spent giving an input to (i.e., deflecting) the joystick during the simulation	A measure of efficiency, the simulated lander has an attitude hold. If subjects overuse the joystick when it is not necessary, they are spending more fuel.
	Smooth Flying (Smooth)	The number of times the subject crosses over the magenta cue in pitch and roll as they track with the reticle	A measure of excessive control. A flyer that overshoots the magenta cue spends more fuel correcting for their mistake, better flying results in less overcorrecting.
Decision Making	Landing Zone (LZ)	A ranked score based on the combination of initial and post-hazard display landing zone choices	Some landing zones are better choices than others in terms of their distance to scientific points and their presence in hazards. Re-selecting a better landing zone based upon lidar-updated hazard information was rewarded.
	Crash, Abort, or Land (CAL)	A ranked score based on whether the subject landed, crashed, or aborted when it was or was not possible to land	Based on their landing zone selections and flight performance subjects may need to make trade-offs for safety or landing success.
Perception Identification	Tactile [sec]	The time it takes for subjects to detect and report each of the two tactile alarms	A quicker reaction time to press the alarm button results in less fuel loss, suggesting enhanced perceptual performance.
	Auditory [sec]	The time it takes for subjects to detect and report each of the two auditory alarms	A quicker reaction time to press the alarm button results in less fuel loss, suggesting enhanced perceptual performance.

As hypothesized, I also investigated whether operational enhancement due to SR may be dependent upon task difficulty. For example, performance on an easy task may be insensitive to adding sensory noise. Thus, three levels of task difficulty (easy, medium, or hard) were tested as determined by the layout of hazards, points of scientific interest, and potential landing zones on the landing maps, a description of which is found in Appendix C1.

5.2.3 Experimental Design

A within-subject experimental design was implemented in a single session, where subjects completed simulation testing in all conditions. After enrollment, subjects watched a 15-minute tutorial video to orient them to the lunar landing task. They then completed a minimum of nine practice trials of the task, or until they felt comfortable with the controls, displays, and goals. This was done to ensure they had fully learned how to operate the simulation and understood all dimensions of the task. Further, a test operator assessed the subject's basic competency level with the task before proceeding.

On a separate test day (within one week of their initial visit), subjects completed 34 trials of the task. Each trial contained a unique map with differing terrain (and thus hazards) and landing points from the other trials. There were two phases to the experimental trials on test day. The first phase identified the subject-specific optimal noise levels in AWN and nGVS for testing in the second phase, as will be described in the next paragraph. In the second phase, we investigated our main hypotheses for task performance and subjective workload using our four sensory noise treatments (AWN, nGVS, MMSR, and sham).

There is an optimal level of noise to induce SR that depends on subject, task, and sensory system (Moss et al., 2004). This has been demonstrated in studies evaluating noise enhancement of sensory perception within and across modalities (Galvan-Garza, 2018; Ries, 2007; Voros et al., 2021). It was believed this would be the case for cognitive performance enhancement; thus, an initial suite of three nGVS levels (0.2, 0.5, and 0.8 mA) and three AWN levels (40, 55, and 70 dB SPL) were tested in a randomized order, as has been done in the previous Specific Aim. Subjects completed three trials for each level, resulting in 18 total trials in this first phase to identify the subject-specific best noise level. Raw performance in each metric was fractionally ranked across the 18 trials and assessed. In order to identify each subject's best noise level, broad task performance was quantified (Eqn. 3), from this initial set of trials. This metric is the sum of each individual metric captured and equally weighted among the three sub-dimensions of flight performance, decision making, and perception.

$$P_{Total} = \frac{1}{3} * (P_{RMS} + P_{Stick} + P_{Smooth}) + \frac{1}{2} * (P_{LZ} + P_{CAL}) + \frac{1}{2} * (P_{Tactile} + P_{Auditory}) \quad (3)$$

The SR noise level that yielded the best performance described by Equation 3 was selected as the subject-specific best (experimentally close to optimal) AWN and nGVS levels. The performance value calculated in Equation 3 was not used for any further analysis beyond identifying these best noise levels.

Once the subject-specific best SR levels were obtained in the first phase, subject-specific best levels of AWN, nGVS, and MMSR were tested across 16 additional unique trials (four trials per treatment) in the second phase. Within each treatment, four trials were administered based on the map difficulty (one easy, two medium, and one hard map) in a randomized order. After each treatment was tested, mental workload was captured using a modified Bedford workload scale (Kintz et al., 2022; Roscoe & Ellis, 1990). This allowed us to assess average subjective workload independent of map difficulty. All sensory noise treatments were presented in a randomized order. Data from these 16 trials were retained for analysis.

After completing all trials, subjects completed a subjective five-point Likert scale questionnaire that asked how well they could maintain focus in quiet and noisy environments. Their noisy environment preference score was defined as the difference in their ranking between quiet and noisy environments (i.e., a negative score means the subject prefers working in quiet places and a positive score means they prefer working in noisy places). This survey can be found in Appendix A.

5.2.5 Analysis

A within-subjects analysis was completed to evaluate operator performance differences due to sensory noise treatments. Each of the performance metrics described in Table 7 have different measurement units, making them difficult to combine into a composite performance score. Thus, ranking was used. For each metric, the raw performance values in each of the 16 trials was fractionally ranked for each subject (e.g., when assessing performance for RMS distance, each of the subject's 16 trials were ordered and ranked from best to worst). This allowed us to compile ranked data across metrics to assess overall operator performance and per sub-dimension by isolating the sub-dimension metrics of flight, decision making, and perception.

Upon visualization, the sub-dimension of decision making yielded substantial violations of normality assumptions for residuals. This is due to the skewed nature of the nominal and ordinal data collected for the decision-making metrics. Specifically, across all subjects 89% of trials were landed successfully and in 66% of trials subjects identified the optimal landing zone (LZ) in their first selection (this increased to 70% by their second selection). Therefore, it was determined that this sub-dimension was not sensitive enough to observe deviations in performance based upon nonparametric rankings, so data related to this sub-dimension was removed from overall operator performance analysis. Thus, I conducted a separate χ^2 goodness of fit analysis to observe differences between treatments in each separate decision-making sub-dimension metric (CAL and LZ). Sub-dimensions of flight and perception were analyzed as no observable assumption violations were present. This suggests that a parametric statistical analysis for this data was appropriate and retained for overall operator performance analysis.

For overall operator performance analysis, and the sub-dimensions of flight and perception, a repeated measures Analysis of Variance (RMANOVA) was conducted between noise treatments on the fractional ranked values. Fixed main effects included in the model were noise treatment, from which the main hypothesis was investigated, and map difficulty. Additionally, the interaction of noise treatment with subject was included since only some subjects may exhibit performance changes with SR. An interaction between noise treatment and map difficulty was included to test whether the effect of sensory noise on performance was influenced by task difficulty. Assumptions for homogeneity and residual normality were tested to ensure that parametric statistics were appropriate. If the F-test results from the RMANOVAs were significant, Tukey HSD multiple pairwise comparisons were used to identify which treatments were different from one another.

A non-parametric Friedman test was used to assess mental workload from Bedford scale data, as the data is ordinal in nature. I also applied an RMANOVA to the Bedford scale data for completeness, using the same factors as described for the fractionally ranked performance data.

Additionally, similar to Specific Aim 1, I aimed to see whether a subject's noisy environment preference indicated operator performance sensitivity to the noise treatments. Within individual metrics, performance was averaged across the four maps, resulting in one value per noise treatment per subject. From there, performance in the sham treatment was subtracted from their performance in each sensory noise treatment. This data resulted in 240 outcomes (16 subjects x 3 baseline-adjusted sensory noise conditions x 5 metrics in Table 7 = 240 outcomes). Linear regression models were fit to this entire performance dataset against subjects' noisy environment preference scores, to identify if subjects with a preference for noisy environments benefited more from SR.

5.3 Results

The AWN and nGVS noise levels presented in these results are the subject best noise levels which were derived from pre-trial performance evaluation across all metrics (Eqn. 1). Visualizations of this pre-trial performance data for each subject are given in Appendix C2 and C3. Table 8 displays the RMANOVA results that correspond to overall operator performance (flight and perception sub-dimensions combined). Contrary to the main hypothesis, no significant differences were found for noise treatment alone. However, consistent with the secondary hypothesis, a significant interaction between subject and noise treatment was identified. A main effect of map difficulty was also identified for this compiled dataset. A multiple comparisons analysis for the main effects of map difficulty on overall performance found that performance in "easy" maps (mean (M)=0.10 +/- standard deviation 0.26) was significantly better than "medium" (M=-0.01 +/- 0.23) and "hard" maps (M=-0.05 +/- 0.24) ($p<0.001$) and performance in "medium" maps was significantly better than "hard" maps ($p=0.041$). Contrary to the secondary hypothesis, no significant interaction effects were identified between noise treatment and map difficulty. These results are visualized in Figure 11a.

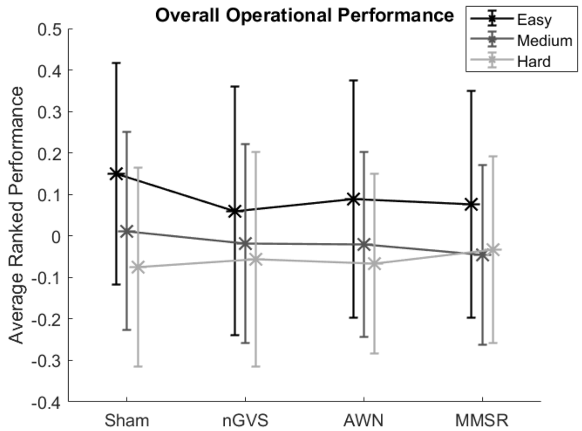
Table 8. RMANOVA results for overall operator performance. Asterisks represent metrics that met a statistical significance below 0.05.

Factor	**F (dof)**	**p-value**	η_p^2
Noise Treatment	0.069 (3, 1279)	0.61	0.003
Map Difficulty	35.28 (2, 1279)	<0.005*	0.055
Noise Treatment x Subject	2.13 (45, 1279)	<0.005*	0.073
Noise Treatment x Map Difficulty	1.29 (6, 1279)	0.26	0.006

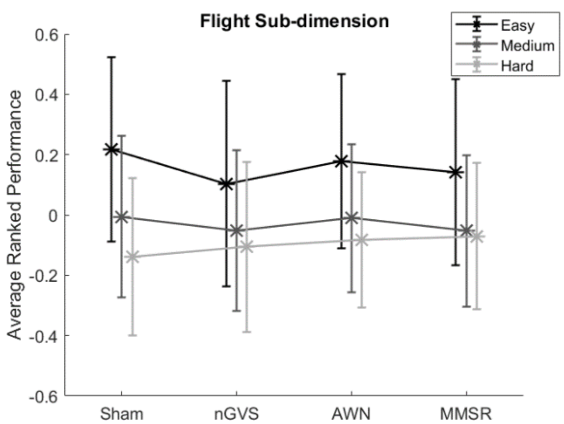
Table 9 displays the RMANOVA results that correspond to the sub-dimensions of flight and perception. For the flight sub-dimension, there was a significant main effect of map difficulty, as well as a significant interaction between noise treatment and subject. A multiple comparisons analysis for the main effects of map difficulty on flight data found that performance in “easy” maps (M=0.17 +/- 0.3) was significantly better than “medium” (M=-0.02 +/- 0.25) and “hard” maps (M=-0.09 +/- 0.25) (p<0.001) and performance in “medium” maps was significantly better than “hard” maps (p=.008). Contrary to the secondary hypothesis, no significant effects were identified for the noise treatments or the interaction of noise treatment and map difficulty. These results are visualized in Figure 11b.

For the perception sub-dimension, there was a significant main effect of noise treatment and a significant interaction between treatment and subject. A multiple comparisons analysis for the main effects of treatment on the perception data found that performance in the AWN treatment (M=-0.04 +/- 0.22) was significantly lower (i.e., worse) than in the sham treatment (M=0.04 +/- 0.17). No other significantly different comparisons were identified. As might be expected, map difficulty had no effect on the perception task. These results are visualized in Figure 11c. Note that no significant interactions between noise treatment and map difficulty were identified for the sub-dimension (Tbl. 9) performance evaluations.

11a.



11b.



11c.

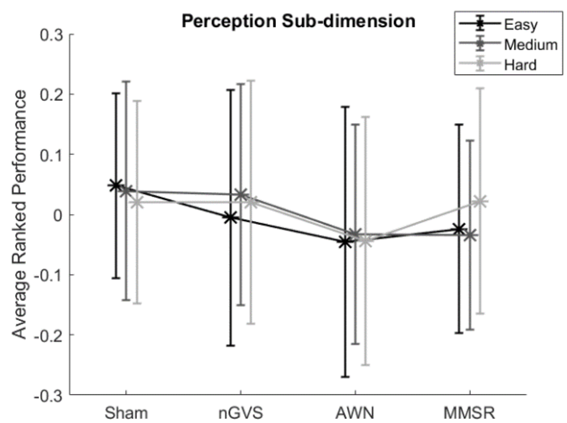


Figure 11. a) Main effects plot of noise treatments and map difficulty for the overall performance aggregated dataset. The three sensory noise treatments were applied at subject-specific best levels determined in the first phase of testing. Higher ranks correspond to better performance. Error bars represent the standard deviation. b) Main effects plots of noise treatment and map difficulty for the flight sub-dimension, error bars represent the standard deviation. c) Main effects plot of noise treatment and map difficulty for the perception sub-dimension, error bars represent the standard deviation.

Table 9. RMANOVA results for the flight sub-dimension and perception sub-dimension. Asterisks represent metrics that met a statistical significance below 0.05.

	Flight			**Perception**		
Factor	**F (dof)**	**p-value**	$\boldsymbol{\eta_p^2}$	**F (dof)**	**p-value**	$\boldsymbol{\eta_p^2}$
Noise Treatment	0.53 (3, 767)	0.67	0.005	2.75 (3,511)	0.049*	0.026
Map Difficulty	43.3 (2, 767)	<0.005*	0.130	0.14 (2,511)	0.87	0.001
Noise Treatment x Subject	2.49 (45, 767)	<0.005*	0.136	1.62 (45,511)	0.008*	0.138
Noise Treatment x Map Difficulty	0.97 (6, 767)	0.44	0.008	0.58 (6,511)	0.75	0.008

For the sub-dimension of decision making, a separate analytical approach was applied. The frequency of the nominal outcomes is presented in Table 10. A χ^2 goodness of fit test was applied to each decision-making metric presented in Table 10. When assessing the CAL metric, due to the low frequency of aborts or crashes, these outcomes had to be combined to meet the assumption for sufficiently sized expected frequencies. Thus, the statistical test was applied to the outcomes of "land" and "not-land". For the CAL metric, the resulting test statistic was $\chi^2(3) = 4.17$. For the landing zone selection metric, the resulting test statistics were $\chi^2(3) = 0.63$ for the choice before hazards were displayed and $\chi^2(3) = 1.84$ for the choice after hazards were displayed. Thus, contrary to the main hypothesis, no significant effects were identified between the noise treatments when it came to our decision-making metrics.

Table 10. Outcome Frequency Table for the Decision-Making Metrics.

	Crash – Abort – Land Metric			
Outcome	**Sham**	**nGVS**	**AWN**	**MMSR**
Land	53	57	60	58
Abort	5	5	3	6
Crash	6	2	1	0
	Optimal Landing Zone Selection (Prior to Hazard Appearance)			
Outcome	**Sham**	**nGVS**	**AWN**	**MMSR**
Selects OLZ	43	43	44	40
Fails to select OLZ	21	21	20	24
	Optimal Landing Zone Selection (After Hazard Appearance)			
Outcome	**Sham**	**nGVS**	**AWN**	**MMSR**
Selects OLZ	41	47	47	44
Fails to select OLZ	23	17	17	20

A non-parametric Friedman analysis was used to assess the Bedford workload scale data. Contrary to my hypothesis, the results showed no significant main effects of noise treatment (p=0.21). For completeness, an RMANOVA test was also performed since it may have more power, but the ordinal data technically violates the model's assumptions, however it yielded the same conclusion (p=0.84).

Additionally, a linear regression was fit between subject performance difference for the aggregated dataset across all noise treatments and the subject's noisy environment preference as was done in Specific Aim 1. Contrary to my hypothesis and those results, I did not find a significant correlation between noisy environment preference and operator performance relative to sham (p=0.57).

5.4 Discussion

This research aimed to assess the utility of using additive sensory noise to improve operator performance. To my knowledge, this is the first assessment of SR for macrocognitive tasks. This was done by having subjects complete a complex lunar landing task, requiring participants to make decisions, actively track moving stimuli, and vigilantly identify perceptual alarms under sensory noise aimed to induce SR.

By observing performance across sub-dimensions of flight and perception, I intended to identify what attributes of operations that sensory noise may influence. No main effect of noise treatment on performance in the flight task was found, but noise had a significant main effect in the perceptual task; however, based upon our pairwise comparison, this significant difference results from AWN masking the auditory alarm, reducing auditory detection relative to the sham treatment. While certain levels of additive AWN are shown to reduce auditory thresholds and enhance perception (Moss et al., 2004), these intensity levels are often low, in contrast to higher levels inducing masking behavior (Ries, 2007). However, the auditory noise levels needed to induce SR across sensory modalities (e.g., in visual perception) and enhance cognitive functions are sufficiently suprathreshold (Lugo et al., 2008; Söderlund et al., 2010). This is a relevant concern when it comes to implementing auditory white noise treatments in operational environments (i.e., the high level of AWN necessary to induce cross-modal SR may produce decrements in auditory perception via masking).

Interestingly though, the interaction results reflect findings in other SR literature. Note that Specific Aim 1 found that applying AWN or nGVS had no effect on overall cognition for the broad population. However, subjects that self-reported preferring to work in noisy environments received cognitive enhancement from additive sensory noise. Building upon that work, the noisy environment preference questionnaire was included in this study to further investigate this notion. While a significant interaction was identified between subject and noise treatment, no correlations were identified between noise preference and performance changes. This could result from the low number of noise preference scores identified in this study's population. In this Specific Aim, subject answers created only four separate noise preference bins, but in the previous Aim, eight bins were identified. While the interaction results of this Aim suggest that individual differences may be a dominant factor in whether SR improves operator performance, the noise preference questionnaire may not be a useful indicator in this context.

Map difficulty was identified as a main effect in influencing flight skill, but not perception. This may be expected, as map difficulty modifies the simulation's optimal flight pattern and trajectory, without changing aspects of the perception task (auditory and tactile detection response times). I hypothesized that there may be an interaction between sensory noise treatment and map difficulty, as SR effects might be more pronounced at certain levels of task difficulty. Yet, the results did not find a significant interaction between treatment and difficulty in the overall or sub-dimension performance analyses to support this hypothesis. While SR has been shown to improve suprathreshold performance in sensory systems (McDonnell, M. D. et al., 2008; Sasaki et al., 2008), it is classically believed to modulate threshold, or at-limit, capabilities; therefore, by varying task difficulty we could capture whether improvements are only observed near subject limits. It is possible that this task was not challenging enough for our subjects to achieve this at-limit improvement, as subjects, on average, successfully landed 89% of the trials (95% for hard maps, 86.7% for medium maps, and 87.5% for easy maps). This appears consistent with our average subjectively-reported mental workload, as the reported average was 3.2 with a 1.1 standard deviation which suggests the task was always "satisfactory" or "tolerable".

While a null finding can't prove there is no effect, this is the first evidence supporting that both nGVS and AWN do not enhance multiple aspects of operational performance. Like any study, it could be that there is an effect and this study was just not sufficiently well powered to identify it. First, this investigation consisted of sixteen subjects as guided by an *a priori* power analysis. While I mention that the task may not have been sensitive enough to find performance differences, it is entirely possible that the effect size is small enough such that a greater number of subjects is needed to increase power and identify significant changes. Small effect sizes can result from large measurement variability. It was noted that older subjects had greater challenges adjusting to pitch inversion, finding task more challenging than younger subjects, which could result in larger measurement variability. Originally, to avoid this, some subjects were given a longer training session than others. An exploratory analysis found that age had no significant effect on operational performance despite these reported challenges ($p>0.9$), so age may not be a result of variability. Note that I report effect sizes to enable future meta-analyses. Second, it could be that our specific lunar landing task is not susceptible to SR effects, while other operational tasks may be. This is a first investigation and motivates future work. However, the lack of evidence across multiple sub-domains of the complex task, does not support benefits in other complex tasks. Third, other SR work has concluded that different levels of sensory noise are optimal for different individuals and tasks, but many cognition-based SR studies investigate a single noise level across all participants. To try to address this an initial suite of tests at three different sensory noise levels were rigorously tested (0.2, 0.5, and 0.8 mA for nGVS and 40, 55, and 70 dB SPL for AWN) to identify the subject-specific best levels. The frequency of best levels identified are shown in Figure 12. It is possible that this procedure was inadequate at identifying a level of sensory noise that was beneficial for each individual, either because the suite was not inclusive of the optimal levels for most subjects (e.g., a subject's optimal nGVS level was 1 mA and our suite only extended up to 0.8 mA) or because the suite was not fine enough (e.g., optimal was 0.65 mA and we only tested at 0.5 and 0.8 mA, neither of which yielded much benefit). However, this suite was selected based upon levels at which SR benefits had previously been observed (Galvan-Garza, 2018; Helps et al., 2014), have been used in Specific Aim 1, and reasonably traded off the time required to do the initial suite (and associated subject learning/fatigue/boredom). Figure 12 motivates that levels with increased sensitivity around 0.5 mA nGVS and 55 dB SPL AWN levels should be further explored. Additionally, the results found in Appendix C2 and C3 motivate that it is possible that some noise levels may be more appropriate for specific sub-dimensions within subjects (e.g., 40 dB SPL may be best for perception detection, but 70 dB is best for flight). This can pose operational challenges in identifying noise levels that are comprehensive in performance improvement.

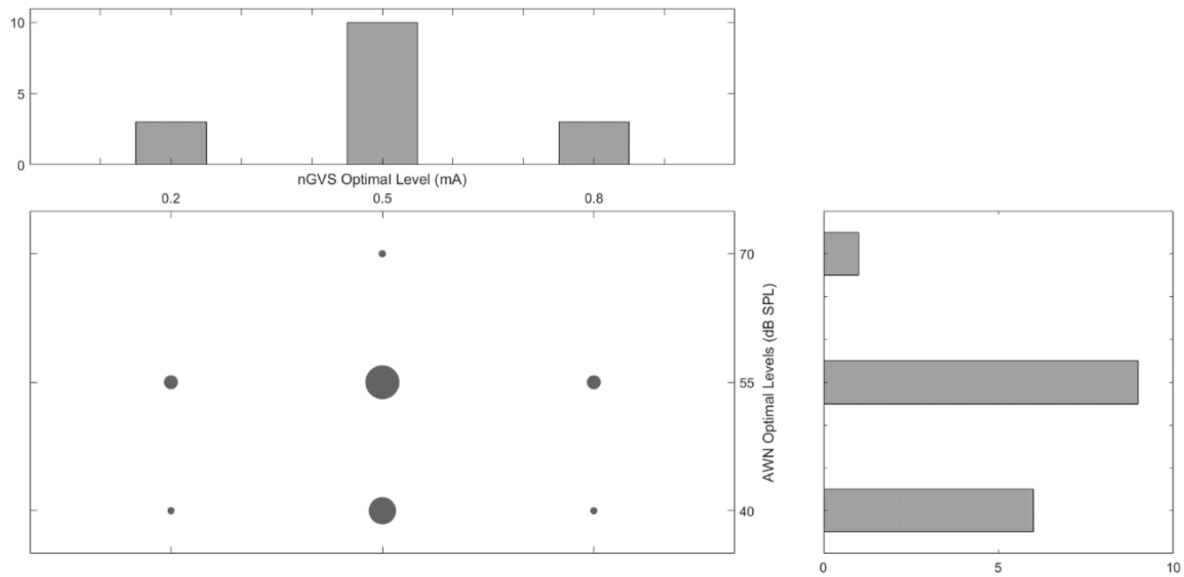


Figure 12. Scatter bubble plot with marginal histograms showing the frequency of best levels identified for nGVS (x-axis) and AWN (y-axis) across our subject pool. Larger bubbles indicate a higher frequency of that combination. Note that the best levels in each sensory modalities were the central levels tested.

While the literature shows that SR may help enhance perception and aspects of cognition, this study did not find that it has a substantial influence on operator performance for the broad population. This work, however, is the most comprehensive assessment of sensory noise effects on operator performance in a complex task to date. As such, for complex aerospace applications similar to the one investigated in this study it may not be a critical operationally relevant countermeasure. Nonetheless, since neither nGVS or AWN did seem to affect some individuals, but was not related to an individual's noise preference, future work should explore these individual differences in SR susceptibility for operator performance.

5.5 Conclusions

This investigation evaluates the utility of applying sensory noise to improve performance in a macro-cognitive task. I conclude that applying additive noise to auditory and vestibular modalities will not result in improved operator performance or reduced perceived mental workload for the broad population. However, similar to other SR investigations and Specific Aim 1, I found that specific individuals may be affected by additive noise. Considering these results, and the literature on SR for perception, it may be that sensory noise effects are useful for specific use cases (improving perception) or specific individuals. It is important to understand the lasting impacts of repetitive noise stimulation, because if stimulation has harmful carryover secondary effects or is deemed unacceptable, the negatives effects caused by stimulation may outweigh the benefits.

The work related to this Specific Aim has been accepted for publication in *Aerospace Medicine and Human Performance* (Sherman et al., 2023c).

Chapter 6: Specific Aim 3 - Investigate the long-term effects of repeated noise exposure.

6.1 Introduction

As mentioned in Chapter 1, there are longitudinal concerns to operational performance and skill retention imposed by long-duration spaceflight. Thus, there remains a need for enhanced training techniques for on-ground and in-flight environments enabling quick skill acquisition to offset these concerns. Other forms of neuromodulation may have long-term effects on information processing. tDCS and TMS have been shown to improve learning and memory in complex tasks (Clark et al., 2012; Manuel & Schnider, 2016; Reis et al., 2008a). However, they have also been shown to have lasting impacts on neuronal excitability and behavioral health (Mantovani et al., 2012; Medeiros et al., 2012). The literature has failed to investigate if additive sensory noise affects learning in a complex task or has secondary effects on behavioral health. Considering the behavioral effects that other neuromodulation techniques have on neuronal excitability and behavioral health outcomes, it would be beneficial to know whether sensory noise induces effects that are not beneficial for spaceflight operators. Thus, this work investigates the effects that repetitive administration of sensory noise has on operational learning and behavioral health.

The objectives of this Specific Aim are to:

- Assess the effects that additive noise has on skill acquisition.
- Evaluate the secondary effects of repeated SR use on behavioral health and acceptability.

6.2 Methods

Twenty-four subjects (12F/12M, age 26 +/- 10 years, range = 18-55 yrs) completed testing in the Bioastronautics Lab at the University of Colorado Boulder. This research was approved by the University's Institutional Review Board (protocol #21-0296) and written informed consent was obtained prior to participation. Broadband AWN and nGVS were administered using the procedures previously described in Section 4.2. Subjects were given a unique SR equipment combination which administers either sham or a noise profile. The virtual reality (VR) rover macrocognitive task was completed using the Lunar Rover Simulation (LRS).

6.2.1 Independent Variables

The independent variable (IV) in this study was the additive noise condition which included four levels. As in Specific Aims 1 and 2, a no noise sham condition, AWN, nGVS, and the combination MMSR condition were tested. I hypothesized that the single modality groups will enhance task performance over time more quickly when compared to the no noise group, and the MMSR group will have access to additive benefits, causing larger longitudinal improvements than single modality alone. As opposed to Aims 1 and 2, this research uses a cohort-based AWN and nGVS level, rather than the subject-specific optimal level. Identifying the subject-specific optimal level would mitigate the ability to assess learning, as the optimal level of noise is subject and task dependent. The noise levels chosen for AWN and nGVS were the mode optimal noise levels from Specific Aims 1 and 2. The four IV levels were no stimulation sham, 55 dB SPL AWN, 0.5 mA nGVS, and MMSR (55 dB + 0.5 mA).

6.2.2 Dependent Variables

The LRS experimental paradigm is a macrocognitive task which loads on two subtasks designed to quantify performance elements that could be captured over multiple sessions. The first subtask observes path optimization, and the second subtask loaded on object identification. Path optimization performance was characterized as the amount of total power a subject consumed navigating to destinations, while object identification was assessed as the number of correct object identifications minus incorrect ones.

Behavioral health metrics related to mood, stress, and sleep were collected over the course of the experiment to analyze behavioral health effects of repeated noise exposure. An additional subjective metric of SR acceptability was also collected. Deviations of these metrics from baseline were observed between groups. Table 11 details the assessment tools that are being used to assess these behavioral health effects.

Table 11. Aim 3 Questionnaires and their Assessment Tools

Questionnaire	**Metric**	**Assessment Tool**	**Reference**
Daily Questionnaire	Stress	Stress in General (SIG)	Fuller et al., 2003
	Mood	Profile of Mood States – Short Form (POMS-SF)	Terry et al., 2003
	Sleep	Consensus Sleep Diary (CSD)	Carney et al., 2012
Pre-task Questionnaire	Stress	Short Stress State Questionnaire (SSSQ)	Helton, 2004
Post-task Questionnaire	Stress	SSSQ	Helton, 2004
	Mood	POMS-SF	Terry et al., 2003
	Acceptability	SR Acceptability Questionnaire (SRAQ)	In house

6.2.3 Simulation Task

The Lunar Rover Simulation (LRS) is a complex, operational task that allows for the assessment of learning through daily use. Subjects interacted with the LRS using an HTC Vive Pro head mounted display to view the lunar landscape and a Logitech X-52 Pro HOTAS joystick to operate the rover. The LRS environment was developed and modified in Unity pulling existing assets from another lunar rover simulation the broader lab group developed (McGuire, S et al., 2018). This simulation was designed to feature aspects of the lunar environment such as: realistic terrain, varied crater sizes, representative lunar lighting and lunar gravity. The LRS was comprised of two operational sub-tasks: path optimization and object identification.

For the path optimization subtask, subjects navigated their rover to several waypoint target destinations along the lunar surface with the goal of minimizing their battery consumption between each waypoint. Power consumption used the specific energy rate equations defined by Carr (2001), where the total power was the sum of the power consumed while moving on a level plane or slope, and a constant power drain (Eqn. 4).

$$W_{Total} = W_{level} + W_{slope} + P_e \tag{4}$$

Battery power consumption was a factor of speed, slope angle, and time (either driving or remaining still, due to constant power drain) across the total distance traveled. Subjects had to learn to weigh each of these factors in optimizing their navigation paths. Subjects were given a variety of tools to help them plan a power-efficient traverse. The first was a 2D topographical contour map of the lunar environment which displayed the waypoint they were navigating to using a blue animated marker with their current location being represented with a magenta circle (see Fig. 13, top middle). Subjects could use this tool to plan their traverse trajectory through terrain to optimize power consumption, but they could not move the vehicle while the map was open. Subjects had autonomy on when they looked at and put away the map (selected by button press on the joystick). Subjects were also given a vehicle dashboard which displayed active state information on current power consumption, battery remaining, torque, vehicle speed, and body-centered heading. Figure 13 shows the map and dashboard presented to subjects.

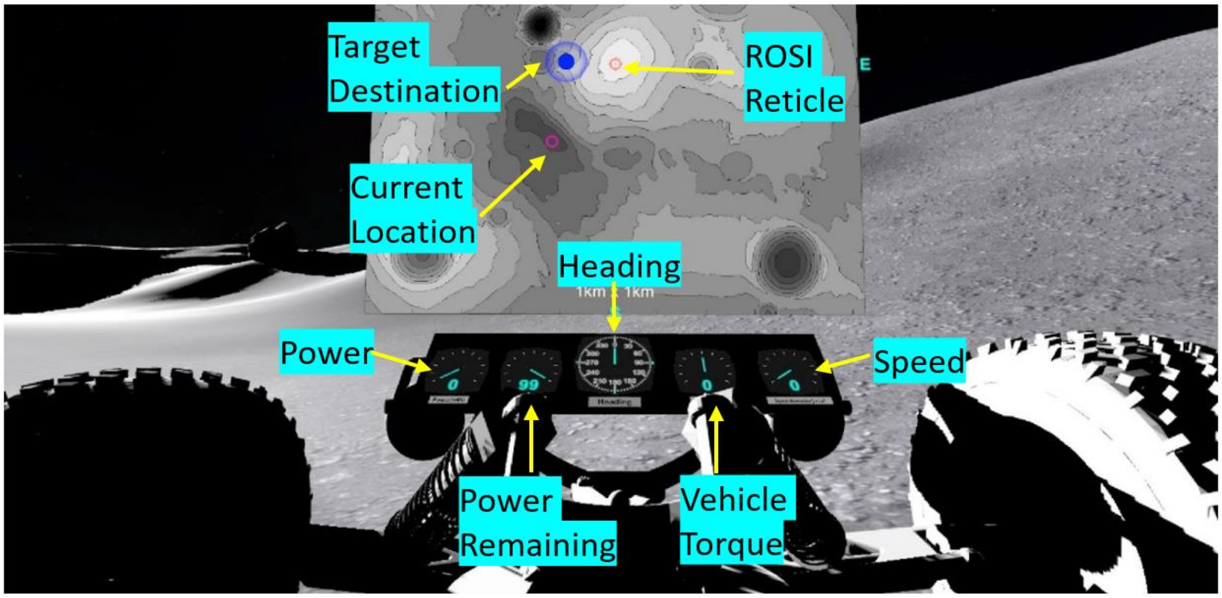


Figure 13. Rover display tools that were provided to the subject. Subjects could pull up a geo-fixed 2-D topographical map of the landscape (shown in this example, top middle), where their location was represented as a magenta circle and the destination waypoint was a blue animated marker. Additional dashboard elements that were continuously available to subjects included current power consumption, battery remaining, torque, vehicle speed, and body-centered heading. A red reticle could be moved along the topographical map for subjects to tag Rock of Scientific Interest (ROSI) locations.

Along with the animated blue marker on the 2D map, subjects knew they had reached their target destination via a stationary 3D robotic rover on the lunar terrain. Once subjects reached their target destination, a new waypoint was presented on the map and their battery was recharged. Each simulation had five waypoints which created a loop (Fig. 15a); therefore, subjects end where they started. Their starting position in the loop was randomized, but all subjects experienced the same waypoint target destinations. If subjects placed their rover in an unrecoverable position (e.g., overturned in the bottom of a steep crater) or they ran out of battery, the current waypoint trial was considered an "incomplete" and they were teleported to their current target waypoint, which prompted the next traverse.

For the object identification subtask, subjects were required to tag Rocks of Scientific Interest (ROSIs). Several rocks littered the lunar landscape, some of these rocks blended in with the environment and were ubiquitous (dummies); however, the ROSIs were black in color and contrasted the landscape (Fig. 14). Subjects were instructed to be vigilant and tag only ROSIs (and not dummy rocks) during their traverses. Subjects tagged ROSI locations via the 2D contour map, moving the red reticle to their perceived ROSI location and laying down a marker (Fig. 13). All rock locations were randomized *a priori* and placed in the terrain during development, ensuring all subjects experienced the same rock placements. Based on map design, subjects were expected to see 2-3 ROSIs for each waypoint trial. One LRS trial session took ~20 minutes to complete across the five waypoints. A unique lunar terrain was given for each test day, such that strategies, skills, and techniques could be learned, but the exact layouts of the lunar terrain and map was not transferrable.

Figure 15 visualizes an example result of one subject's operational performance in a map. Figure 15a represents their performance in the path optimization subtask with power consumption along a traverse being color coded. Figure 15b visualizes their rock tag placements in contrast to the actual ROSI locations.

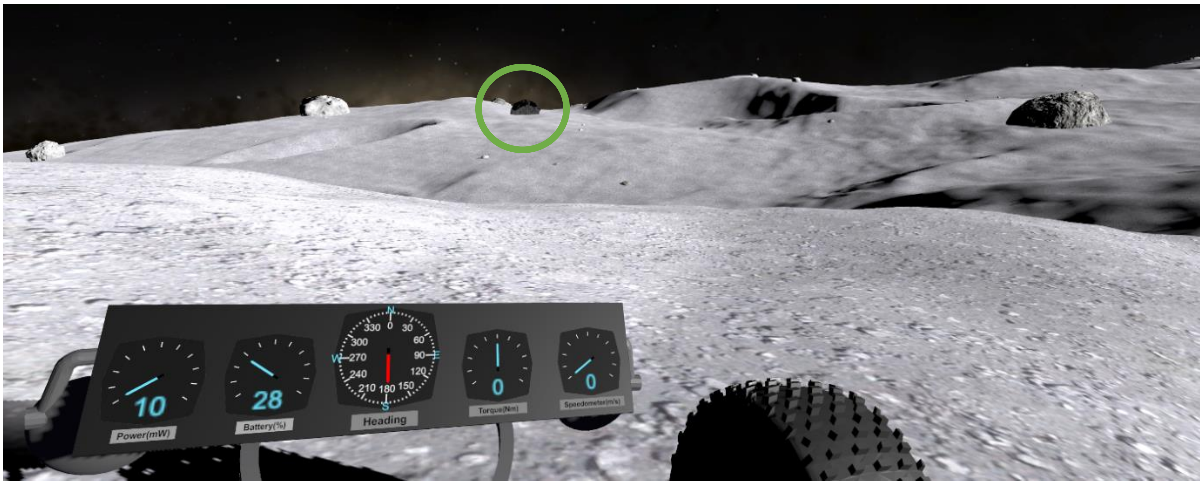


Figure 14. Subject point of view in the object identification task. Upon finding a black rock of scientific interest (ROSI, circled in green for the reader), subjects would direct the 2-D map's red crosshair on their perceived ROSI location and confirm or "tag" its location.

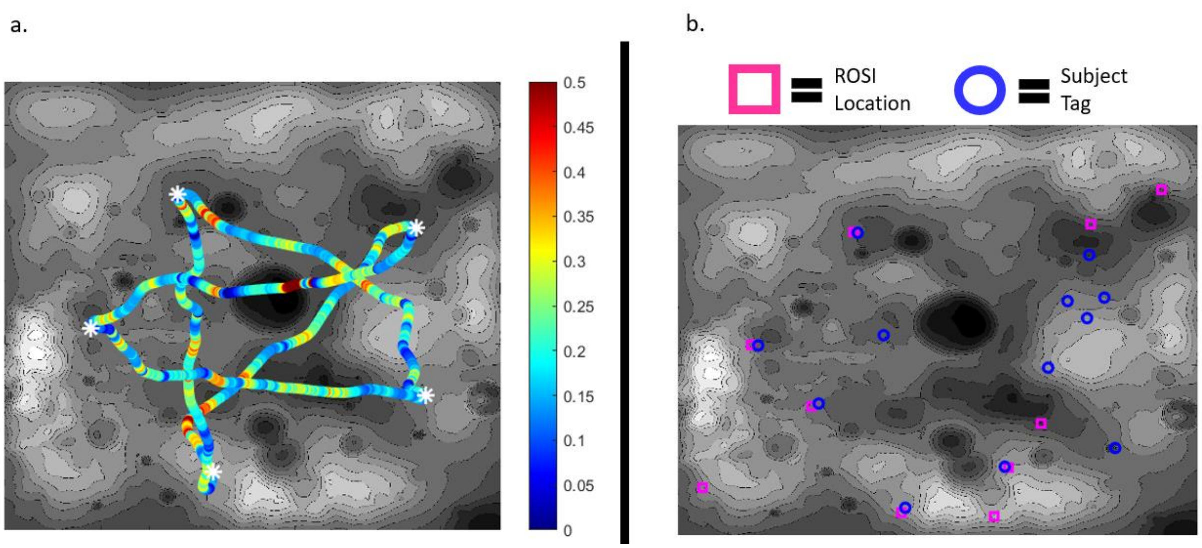


Figure 15. a) Example of subject battery consumption along traverses in the path optimization subtask. White asterisks represent the waypoint locations. Low battery consumption (Watts) is represented by blue in the spectrum and high battery consumption is represented by red. b) Example of subject object identification. Actual ROSI locations are marked in magenta, while subject reported rock tags are marked in blue. In this example, five of the rock tags correspond to ROSI locations but seven do not (i.e., incorrectly identifying a dummy rock as being a ROSI), while five ROSIs were left untagged.

6.2.4 Experimental Design

A between-subject longitudinal experimental design was implemented to evaluate the lasting operational and behavioral health effects of repeated noise exposure. Four groups (n=6 in each group, 3F/3M) were assigned a noise stimulation treatment that was used for the duration of the experiment. Subjects were assigned to treatments using a covariate randomization technique to ensure equal sex grouping in each treatment. These treatments included a no noise sham (3F/3M, age 25.3 ± 6.1 years, range = 21-34), AWN with an intensity of 55 dB SPL (3F/3M, age 27 ± 11.5 years, range = 20-50), nGVS with an intensity of 0.5 mA (3F/3M, age 22.2 ± 5.1 years, range = 18-32), and the combination of the AWN and nGVS treatments, termed multi-modal SR (MMSR) (3F/3M, age 30.5 ± 16 years, range = 19-55). These noise levels (55 dB SPL and 0.5 mA) were selected as previous work in Specific Aims 1 and 2 showed they near optimal in terms of inducing SR for a majority of subjects tested. In the sham treatment, no sensory noise was administered, but subjects were equipped with electrodes and earbuds. Subjects in all treatment groups were fit with AWN and nGVS hardware, independent of whether they actually received sensory noise stimulation.

In their initial visit, subjects watched an 8-minute tutorial video to orient them to the lunar rover simulation environment. They then completed one run of the simulation to become familiar with the motives and controls of the simulation. This was done under the guidance of a test operator, which helped explain the rules of the simulation, while avoiding telling them how to do well in the simulation or giving them an opportunity to practice and thus reduce the ability to assess learning.

For this time-longitudinal experiment, all subjects followed a strict, eleven-day timeline, which is displayed in Figure 16. This 11-day timeline is comprised of three phases. Phase 1 served as a three-day baseline assessment of behavioral health prior to any treatment stimulation being applied. Phase 2 was the five-day simulation testing period where subjects completed lunar rover simulations under the influence of one of the noise treatments. Phase 3 was a post treatment stimulation assessment that allowed for identification of after-effects as a result of repetitive treatment stimulation. Across all eleven days, an online daily questionnaire was completed in the morning. In addition, subjects completed a questionnaire before and after simulation testing in phase 2.

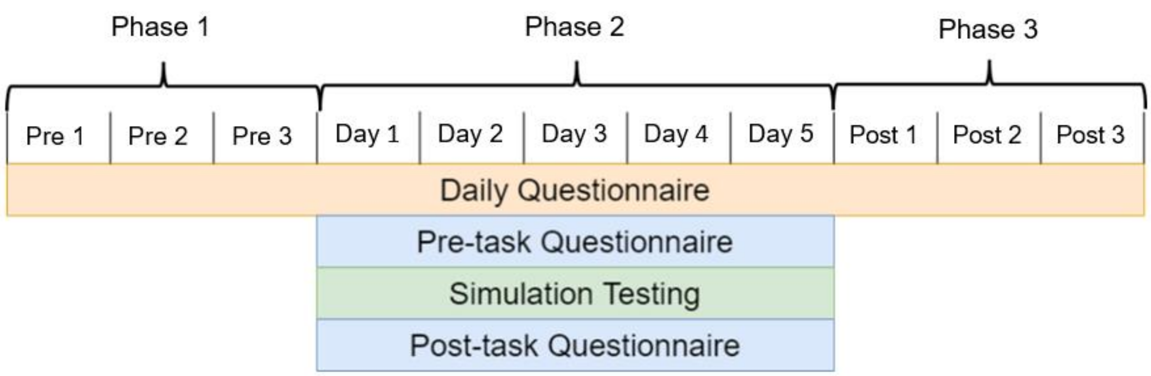


Figure 16. Experimental timeline split up into three distinct testing phases. The first phase is a three-day behavioral health metric collection period to serve as a baseline. The second phase consists of five days of simulation testing under treatment stimulation. The third phase is a three-day collection period to observe after-effects of treatment stimulation.

6.2.5 Data Analysis

In summary, analysis approaches differed between operational learning performance and behavioral health effects. Learning was assessed as changes in operational performance over the five-day testing phase (Phase 2), whereas, group behavioral health differences were considered across all phases (Fig. 16). Several Analysis of Variance (ANOVA) models were applied to analyze the effect of the noise treatments. Assumptions for homogeneity and residual normality were tested to ensure that parametric statistics were appropriate. If the omnibus F-test results from the ANOVAs were significant, Tukey HSD multiple pairwise comparisons were used to identify which treatments were different from one another.

6.2.5.1 Learning Analysis

Performance scores in a traverse for the path optimization subtask was defined as the "battery needed" to reach the desired waypoint. If a subject reached the waypoint, this was simply the amount of battery consumed since the start of the traverse. If a subject failed to reach the waypoint as a result of an "incomplete", the battery needed term was calculated as 100 (the total amount of battery allotted) plus the battery that would be used to traverse the distance remaining to waypoint (at full speed with no sloped terrain). While this additional term may not accurately reflect subject driving behavior, it prevents the performance ceiling effects of incomplete traverses (if they all remain at 100) and weighs incomplete traverses that made it closer to the waypoint target more favorably than those further away. The performance (P) used in the statistical model (Eqn. 6) for each day was the summation of the five "battery needed" traverse scores for the single LRS divided by five (i.e., a value of 100 corresponded to the full battery consumed on each of the 5 traverses, while lower values corresponded to better performance since less battery was consumed, and higher values were the result of some incomplete traverses and thus worse performance).

Performance scores in the object identification subtask relied on the total number of correct ROSI identifications on a given map. This was done by identifying which rock (ROSI or dummy) was closest to the user's tagged location. Correct identifications (c) were selected if a ROSI was the closest rock to this tagged location and incorrect identifications (i) were marked if a dummy rock was closest. Identification scores (ID_P) for a given map were calculated using Equation 5 to reward correct tags and penalize incorrect tags. This was standardized by dividing the result by 10, as there were only 10 ROSIs in each map. The performance (P) used in the statistical model (Eqn. 6) for each day was this ID_P score.

$$ID_P = (c - i)/10 \quad (5)$$

To observe between subject differences in path optimization or object identification performance (P), a mixed effects model was utilized with day (D) was a continuous covariate. Map (M, as a categorical variable) was also included as a covariate to capture variations simply due to the difficulty of the map. A fixed effect of noise treatment (NT) was included to evaluate whether treatment influenced operational performance independent of learning. Finally, to assess differences in learning between the four groups, an interaction term between treatment and day was included in the model. The interaction accounts for the slope of performance improvement between treatment groups. The final analytical model for the two operational subtasks is given in Equation 6.

$$P \sim NT + M + D + NT * D \quad (6)$$

6.2.5.2 Behavioral Health Analysis

Following the guidance of previous studies that validated the assessment tools from Table 1, quantifiable metrics of behavioral health were defined. Stress and mood were considered when assessing immediate behavioral health effects from noise stimulation. For mood, the total mood disturbance (TMD) metric was calculated by adding the raw score responses of tension, depression, anger, fatigue, and confusion and then subtracting the vigor score (Terry et al., 2003); thus, lower scores indicate more stable mood profiles. Stress metrics of engagement, distress, and worry were calculated by adding the raw score response of the questions associated with that metric (Helton, 2004). This Aim cared about deviations in behavioral health after task completion and stimulation; thus, the final metric scores being statistically assessed were the behavioral health metric post testing minus the behavioral health metric pre-testing.

Following this objective, I wanted to know whether repeated noise exposure over time impacted immediate behavioral health (B); thus, behavioral health metrics were observed across the five days. A two-way ANOVA was used to observe between group differences in mood and stress. For this, categorical variables of treatment, day, and their interaction were used, allowing for changes in behavioral health state to be understood. The final analytical model used for these behavioral health states is given in Equation 7.

$$B \sim NT + D + NT * D \tag{7}$$

Expanding on this, I wanted to evaluate longitudinal behavioral health effects, seeing whether repetitive noise administration affected behavioral health in the long term (during or afterwards). With respect to the daily questionnaires which loaded questions related to mood, strain, and sleep, I completed two-way ANOVAs to assess differences between the three testing phases (Fig. 16). This allowed me to evaluate whether the treatments impacted behavioral health during and after the stimulation testing period, which could suggest long-term after-effects. The categorical testing phases (TP) assessed were the three days prior to testing, the five days of testing, and the three days after testing. Categorical variables of treatment, test phase, and their interaction were used, allowing changes in behavioral health state across these three test phases to be understood. Longitudinal behavioral health measures were standardized by subtracting the average in each subject's baseline measures. The means were calculated for each test phase in each subject and compared to reduce the weighting of the second test phase (as there were two more measures in this period compared to the three measures collected in the other periods). The final analytical model used for these behavioral health states is given in Equation 8.

$$B \sim NT + TP + NT * TP \tag{8}$$

Finally, based on the structure of the acceptability questionnaire (Appx. D1), raw scores at the conclusion of stimulation were assessed in each of the six questions. A one-way ANOVA was used to evaluate general acceptability of the stimulation treatments.

6.3 Results

The results are presented in terms of, first, the operational performance improvement (i.e., learning effects) and, second, the behavioral health impacts.

6.3.1 Learning Results

These results explore learning through changes in operational performance over time in the path optimization and object identification subtasks. Overall needed battery consumption was the metric of performance in path optimization and ID performance (Eqn. 5) was the metric for rock identification. Figure 17 shows the rates of operational performance change in these metrics for all subjects (Fig. 17a & Fig. 17b) and by treatment group (Fig. 17b & Fig. 17d). Table 12 shows the results of the statistical tests produced by Equation 6. Significant effects of day were identified in each learning subtask (indicating learning across all subjects); however, the interaction effects were not significant (indicating no difference in learning between treatment groups).

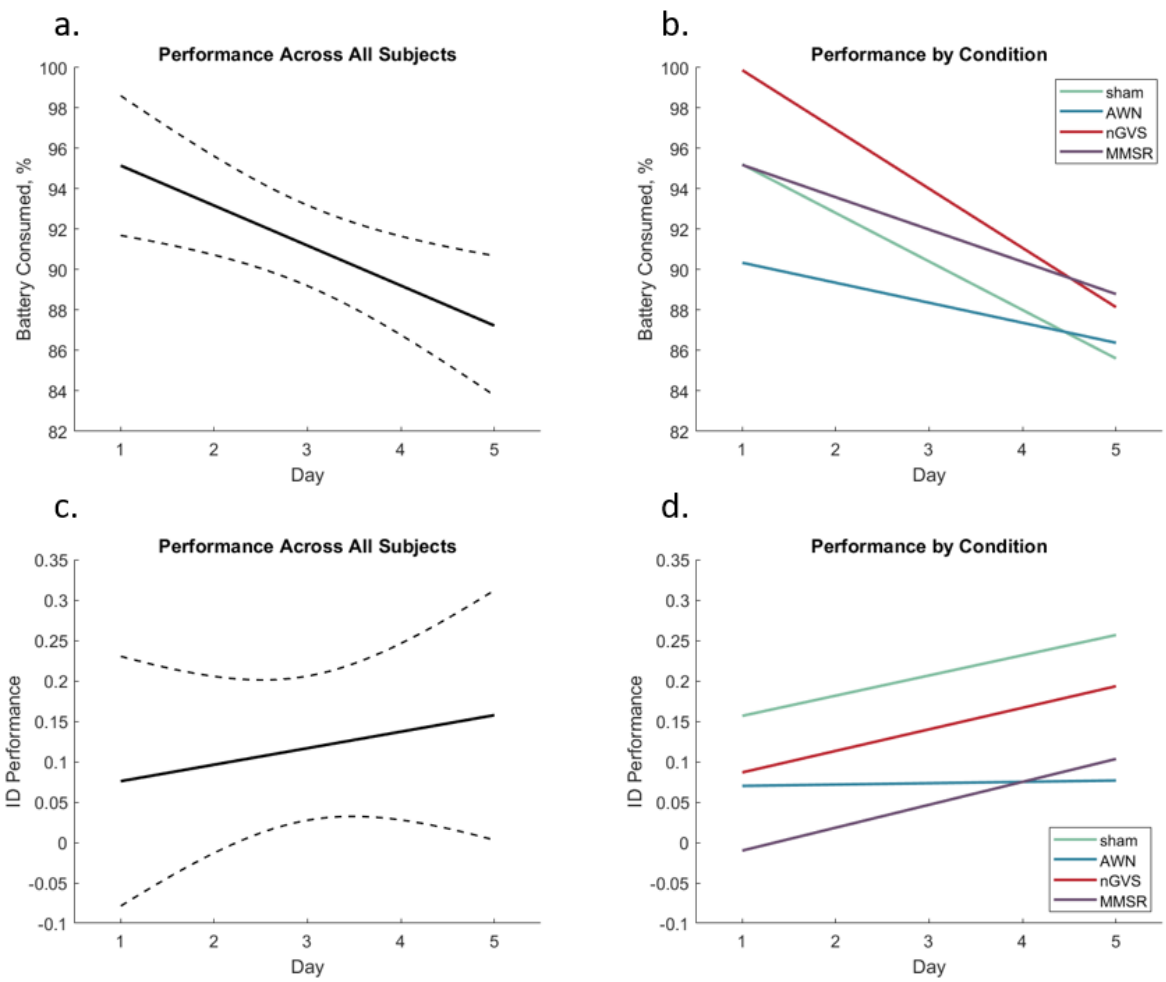


Figure 17. a) Linear regression of path optimization performance improvement across the five test sessions for all subjects. Dashed lines indicate the 95% confidence interval of the modeled fit. b) Linear regressions of path optimization performance improvement across the five test sessions for each treatment group. c) Linear regression of object identification performance improvement across the five test sessions for all subjects. Dashed lines indicate the 95% confidence interval of the modeled fit. d) Linear regressions of object identification performance improvement across the five test sessions for each treatment group.

Table 12. Mixed effect model results for operational learning performance, for each operational sub-task of path optimization and object identification. Asterisks represent metrics that met a statistical significance below α=0.05.

	Path Optimization			**Object Identification**		
Factor	**F (dof)**	**p-value**	η_p^2	**F (dof)**	**p-value**	η_p^2
Noise Treatment	1.74 (3, 108)	0.16	0.046	0.23 (3, 108)	0.87	0.006
Map	0.94 (4, 108)	0.44	0.034	5.98 (4, 108)	<0.005*	0.181
Day	13.98 (1, 108)	<0.005*	0.115	3.86 (1, 108)	0.05*	0.035
Noise Treatment*Day	0.66 (3, 108)	0.58	0.018	0.15 (3, 108)	0.93	0.004

For the path optimization task, since map appeared to not be a statistically significant factor in the model, I followed up with a simplified model without the map factor to add extra statistical power to the other factors considered. However, this removal did not induce significance in the other factors (p > 0.19). This was not applied to the object identification data as map was a significant factor. This technique was not applied to the behavioral health data as it was important to assess the factor effects of treatment and day to identify time longitudinal changes in behavioral health. Contrary to the main hypothesis, improvements in learning were not observed for the noise stimulation treatments, for either path optimization or objective identification performance. Further visualizations of these results, separated by group with representative variance, can be found in Appendix D2.

6.3.2 Behavioral Health Results

Immediate behavioral health results

Considering tDCS has immediate lasting effects on neuronal excitability (Medeiros et al., 2012), I wanted to identify immediate differences in behavioral health among the groups. Thus, the differences in mood and stress were explored prior to and after completing the task with treatment stimulation. Table 13 show the statistical test results given by Equation 7. Visualizations of these results can be found in Appendix D3.

Table 13. Two-way ANOVA results for behavioral health effects following stimulation, split between mood and the three metrics of stress. Asterisks represent metrics that met a statistical significance below 0.05.

	TMD			**Engagement**		
Factor	**F (dof)**	**p-value**	η_p^2	**F (dof)**	**p-value**	η_p^2
Noise Treatment	2.23 (3, 100)	0.09	0.063	1.6 (3, 100)	0.19	0.046
Day	0.4 (4, 100)	0.81	0.016	0.84 (4, 100)	0.5	0.033
Noise Treatment*Day	1.22 (12, 100)	0.28	0.128	2.1 (12, 100)	0.02*	0.202
	Distress			**Worry**		
Factor	**F (dof)**	**p-value**	η_p^2	**F (dof)**	**p-value**	η_p^2
Noise Treatment	1 (3, 100)	0.39	0.029	0.5 (3, 100)	0.68	0.015
Day	0.73 (4, 100)	0.57	0.029	0.5 (4, 100)	0.74	0.02
Noise Treatment*Day	1.42 (12, 100)	0.17	0.145	1.42 (12, 100)	0.17	0.146

A significant interaction between noise treatment and day was identified for the stress metric of engagement; however, no other factors were significant. Contrary to my hypothesis, it appears there are no strongly influential effects of stimulation on immediate behavioral health.

Longitudinal behavioral health results

Considering TMS has lasting effects on behavioral health, I wanted to observe differences in behavioral health between the three phases; pre-testing baseline, testing with stimulation, and post-testing aftereffects. Table 14 shows the statistical test results given by Equation 8. Visualizations of these results can be found in Appendix D4.

Table 14. Two-way ANOVA results for longitudinal behavioral health effects between treatments, split by mood, strain (three metrics), and sleep (three metrics).

	TMD			Relaxed and Calm		
Factor	**F (dof)**	**p-value**	η_p^2	**F (dof)**	**p-value**	η_p^2
Noise Treatment	0.02 (3, 60)	0.99	0.001	1.51 (3, 60)	0.22	0.07
Period	0 (2, 60)	0.99	<0.001	0.49 (2, 60)	0.61	0.016
Noise Treatment*Period	0.19 (6, 60)	0.98	0.019	0.48 (6, 60)	0.82	0.046
	Comfort and Smooth			**Pushed and Stressed**		
Factor	**F (dof)**	**p-value**	η_p^2	**F (dof)**	**p-value**	η_p^2
Noise Treatment	2.65 (3, 60)	0.06	0.117	1.09 (3, 60)	0.36	0.052
Period	2.18 (2, 60)	0.12	0.068	0.2 (2, 60)	0.82	0.007
Noise Treatment*Period	0.88 (6, 60)	0.51	0.081	0.77 (6, 60)	0.6	0.071
	Total Sleep			**Sleep Quality**		
Factor	**F (dof)**	**p-value**	η_p^2	**F (dof)**	**p-value**	η_p^2
Noise Treatment	0.89 (3, 60)	0.45	0.042	1.38 (3, 60)	0.26	0.064
Period	0.21 (2, 60)	0.81	0.007	0.01 (2, 60)	0.99	<0.001
Noise Treatment*Period	0.52 (6, 60)	0.79	0.049	0.42 (6, 60)	0.86	0.041
	Feeling Refreshed					
Factor	**F (dof)**	**p-value**	η_p^2			
Noise Treatment	5.16 (3, 60)	<0.005*	0.205			
Period	1.13 (2, 60)	0.33	0.036			
Noise Treatment*Period	1.34 (6, 60)	0.24	0.118			

A significant effect of noise treatment was identified for the sleep metric of "feeling refreshed"; however, no other factors were significant. Multiple comparisons showed that the AWN treatment group was significantly more refreshed than the sham group ($p < 0.005$). Contrary to my hypothesis, it appears there are no strongly influential effects of stimulation on longitudinal behavioral health since only this difference was identified.

Acceptability Results

I developed an acceptability questionnaire (Appx. D1) to assess differences in stimulation acceptability between treatment groups. Table 15 shows the statistical test results for the resulting one-way ANOVAs. Visualizations of these results can be found in Appendix D5.

Table 15. One-way ANOVA results for the six metrics of treatment acceptability. Asterisks represent metrics that met a statistical significance below α=0.05.

Metric	F (dof)	p-value	η_p^2
Felt the equipment did not inhibit performance	2.43 (3,116)	0.07	0.059
Felt that the AWN was comfortable	5.55 (3,116)	<0.005*	0.126
Felt that the nGVS was comfortable	0.93 (3,116)	0.43	0.023
Felt that they were able to maintain focus	2.31 (3,116)	0.08	0.056
Found the treatment stimulation was distracting	5.07 (3,116)	<0.005*	0.116
Found the treatment stimulation fatigued them	2.52 (3,116)	0.06	0.061

A significant effect of noise treatment was identified for the acceptability metrics of "AWN was comfortable" and "stimulation was distracting". No other acceptability questionnaire metrics were significant. For the first significant metric, a multiple comparison analysis showed that the MMSR treatment group believed the AWN stimulation was significantly more comfortable than the sham group ($p < 0.005$). For the second significant metric, a multiple comparison analysis showed that the nGVS treatment group believed the nGVS stimulation was significantly more distracting than the sham group ($p = 0.006$) and the MMSR group ($p = 0.04$). These results are visualized in Figure 18. Independent of these two metrics, it appears that sensory noise stimulation is generally deemed to be acceptable between the treatment groups.

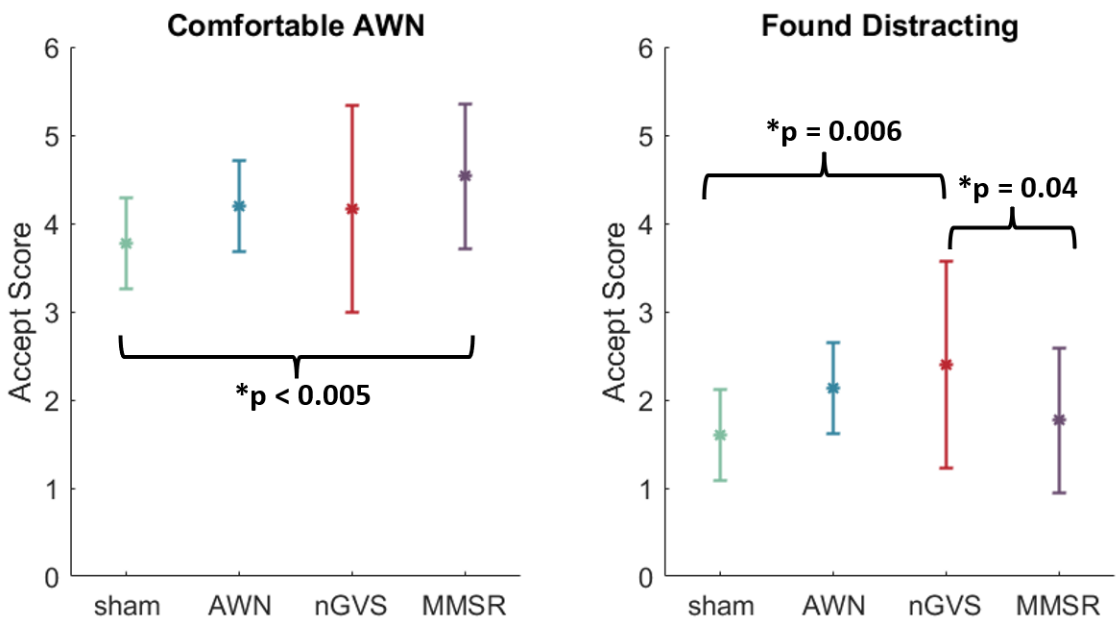


Figure 18. Multiple comparisons in the two significantly different acceptability metrics. Error bars indicate the standard deviation of the data point. Brackets indicate the treatments that were identified to be different from one another.

6.4 Discussion

This Specific Aim investigated for the first time the effects of repetitive sensory noise stimulation on operational learning, as well as its long-term effects on behavioral health. This was done by having subjects complete a lunar rover simulation once daily, for five days, under treatment stimulation. While subjects broadly performed better in the operational task across days, there were no differences in the rate of task improvement between groups (ie. no differences in learning). Prior, post, and during this period, subjective questionnaires related to behavioral health metrics of mood, stress, and sleep were collected. No significant differences in behavioral health or acceptability were found between treatment groups except in a few specific metrics.

Previous sensory noise literature related to memory found that nGVS can improve spatial memory and AWN can improve auditory working memory (Hilliard et al., 2019; Othman et al., 2019); however, the study presented here was not able to find significance. Focusing on the study conducted by Hilliard et al. (2019), subjects completed a within-subject cross-over design with a virtual spatial memory task under the influence of nGVS stimulation (tailored to 80% of their sensation threshold) in one of two sessions that were separated by two weeks. During testing subjects were tasked to explore a virtual arena, learn the location of objects, and then mark their location when they were removed. They completed three of these runs. This study found improved accuracy of object location across the learning run. It should be noted that Hilliard et al. (2019) tested more subjects than ours, but we want to call into question the use of nGVS for declarative vs. non-declarative memory formation, where procedural memory tasks are non-declarative in nature (Brem et al., 2013). The task completed in this study was procedural, whereas Hilliard et al. (2019) object location task can be argued as declarative. It is possible that the memory formation paradigm that SR targets is semantic and declarative in nature, but further investigations into procedural memory formation paradigms.

The closest procedural paradigm similar to the experiment presented here was found for alternative forms of neuromodulation which had observed that neural stimulation from tDCS applied to the right dorsolateral prefrontal cortex can lead to improved learning rates in complex operational tasks as opposed to receiving no stimulation (Choe et al., 2016). Choe et al. (2016) investigated operational learning in an aviation landing simulation across four days. In this task subjects aimed to replicate a landing that was similar to an autopilot demonstration that was presented to them before their simulation began. To do this, subjects used instrumentation cues during the autopilot demonstration to guide their landing. For the simulation paradigm I investigated, this type of replication scenario was not represented, as the task was a self-guided learning paradigm. Results compiled across all subjects suggest that performance in operational task significantly improved across all subjects over time, but there was no difference between stimulation treatments and sham. This indicates the lunar rover simulation paradigm could still capture effects of learning, but the results could imply that additive sensory noise is not an appropriate neuromodulation technique for learning enhancement within this group or that the noise treatment produces sufficiently low effect sizes that this experiment is not sensitive to. Yet, it is entirely possible that I assessed the incorrect learning task mode to demonstrate SR improvements as the tDCS study referenced in this paper used a replication paradigm.

However, it is useful to assess whether sensory noise has secondary effects to behavioral health which would undermine the usage of sensory noise in these specific use cases or individuals. Alternative neuromodulation techniques, specifically tDCS and TMS, have been shown to create immediate, lasting effects on neuronal excitability and long-term behavioral health (Mantovani et al., 2012; Medeiros et al., 2012). A suitable neuromodulation technique for repeated administration would not negatively affect behavioral health, especially on a long-duration space mission. Since sensory noise effects on behavioral health have not been observed in the literature, I aimed to address this gap. Behavioral health questionnaires following stimulation and testing allowed for assessment of immediate behavioral impacts. The longitudinal daily collection of behavioral health questionnaires related to mood, strain, and sleep allowed for assessment of sensory noise effects on general behavioral health and potential aftereffects. In general, these results do not suggest that sensory noise impacts behavioral health. While a null result cannot be proven, the effect sizes related to most of the metrics suggest that an extremely high subject number would be needed to identify significant differences. For example, a retrospective power analysis for immediate mood changes with a $\eta_p^2 = 0.063$ (Tbl. 13) showed that 104 subjects are required to identify treatment group differences. With such a small effect size from these validated and sensitive questionnaires, I feel confident that many of the measures related to behavioral health would not result in meaningful impacts from sensory noise stimulation. Inferring from these results and the findings which suggest noise stimulation is generally acceptable (Tbl. 15), I believe that repetitive administration of AWN and nGVS has no effects on behavioral health and is generally acceptable for repeated use in situations and individuals that necessitate its usage.

There are two limitations to this study that are worth noting. First, previous research conducted in this thesis and literature for perceptual SR have identified that there is a subject and task specific optimal noise level to induce performance enhancement (Ries, 2007; Voros et al., 2021). Since this task is a learning paradigm, there was no efficient way of identifying a subject's specific optimal noise level. I tried to navigate this problem by choosing the noise levels that were most commonly represented as near optimal in previous Specific Aim investigations, which I believed would produce potential SR effects for a majority of participants in this study. However, it is possible that these levels would not induce SR benefits in terms of improved learning for some or many of our subjects, but that had we applied different levels (or individualized levels) SR benefits may have been observed. Second, the subject number per group (n=6) is relatively low. That being said, I have included effect sizes for future research and meta-analyses. The effect sizes related to operational learning are sufficiently low enough for the interaction terms (Tbl. 12) that a few more subjects within each treatment group would probably not yield significant changes. However, this low subject number may explain significant differences in certain ordinal measures. For example, sham subjects believed the AWN stimulation was more uncomfortable than the MMSR group which did receive AWN stimulation (as well as nGVS); the AWN treatment group was not significantly different from either. While is possible that the simultaneous application of nGVS and AWN caused the experience of AWN to be more comfortable, it could suggest that this result is a false positive. Greater sensitivity in the acceptability questionnaire or greater subject numbers may have prevented this result. However, the significant acceptability result of nGVS being more distracting than sham follows with preconceived notions.

6.5 Conclusions

This investigation evaluates the long-term effects of repetitive sensory noise administration on operational learning and behavioral health. I conclude that applying AWN and nGVS repeatedly does not affect the rate of learning of an operational task for a neurotypical population. Additionally, there appears to be no effects of sensory noise exposure on behavioral health, either immediately or on a longitudinal timescale. I also found that AWN and nGVS stimulation is perceived to be acceptable by subjects. Thus, repeated sensory noise exposure to elicit SR in specific use cases or individuals may be utilized with little side effects.

These results for acceptability and behavioral health suggest that additive sensory noise stimulation may be safe and acceptable for repetitive use (given that noise stimulation is given in a non-harmful intensity, such as <80 dB SPL). Thus, for broad specific use cases and individuals that would benefit from noise, it may be used with minimal adverse effects. This is promising for astronauts and aerospace operators as they can use the stimulation technique over and over without expecting detrimental effects which may occur with other forms of neuromodulation.

The work related to this Specific Aim has been published in *Frontiers in Neuroscience* (Sherman et al., 2023b).

Chapter 7: Compare the applicability of neuromodulation methods as spaceflight countermeasures for human performance decrement.

7.1 Introduction

Non-invasive brain stimulation (NIBS) is a class of neuromodulation that stimulates neural processes using real-time external influences (Polanía et al., 2018). Invasive and pharmacological techniques of neuromodulation can target neural behavior, but often with side-effects (Bostrom & Sandberg, 2009; Friedman & Bui, 2017), so NIBS may be a suitable alternative as careful administration produces effects that are safe, reversible, and target neural circuits directly (Luigjes et al., 2019). The work of this thesis thus far has focused on SR as a form of NIBS. Specific Aims 1-3 of this thesis have not demonstrated promise in using SR as a technique to improve human performance in complex operations. However, there are a host of other NIBS techniques that could be promising alternatives for future application in spaceflight to affect operational performance and long-term health. Thus, the focus of this Aim is to conduct a trade study that considers and compares five NIBS techniques. This Aim assesses the utility of each technology using an assessment methodology that is aligned with the motivations that this thesis uses to evaluate SR. Further, the methodology considers which NIBS technique is most applicable to current spaceflight. The NIBS technologies evaluated include SR, transcranial electrical stimulation (tES), transcranial magnetic stimulation (TMS), transcranial photobiomodulation (PBM), and transcranial focused ultrasound (tFUS). There may be other NIBS techniques to induce neuromodulation, but to my knowledge these non-invasive techniques are relatively mature in our understanding of the mechanisms that induce neural change and have all been tested with human populations. All technology under consideration have a technology readiness level of four or more, following the definitions by NASA (Mankins, 1995).

7.2 Trade Study Criteria

Appropriate spaceflight countermeasures must effectively mitigate the physiological and psychological effects of spaceflight, while creating minimal intrusion to astronaut's daily life and space habitat. Thus, I developed criterion to assess the trade space of novel countermeasure technologies related to human mental performance. This evaluation models the framework developed by (Rollock, 2023) to assess emergent technologies. It loads upon three variables related to human performance effects and three variables related to astronaut life and the spaceflight habitat. From there it defines a value hierarchy in each variable to score the ability of each technology in meeting this variable.

Building upon the work throughout this thesis, the three performance variables are as follows:

- ***Demonstrated information processing influence (IPI):*** Much of the motivation in this thesis is to reduce human error in spaceflight operators. Many human error incidents are tied to deficits in aspects of the information processing model (Weigmann & Shappell, 1997). Thus, this variable assesses the number of elements the NIBS technology has been shown to influence in the information processing model including: sensory processing, perception, working memory / cognition, long-term memory, and attention.
- ***Operational performance effectiveness (OPE):*** When evaluating SR for human performance, this thesis targeted broad cognitive and operational performance effects; additionally, it focused on procedural skill acquisition. Since these evaluations load on complex, holistic macrocognition, this variable targets how certain NIBS influence these complex processes.

- ***Long-term health effects (LHE):*** Given the nature of long duration spaceflight, NIBS technology that induces adverse side effects may not be acceptable for repeated use. However, many NIBS technologies are being considered as clinical treatments for adverse mental health conditions. An added benefit to some NIBS technology may be its ability to improve behavioral health affect; thus, this variable was included to assess these indirect performance benefits.

Considering aspects of the spaceflight environment and astronaut livelihood, the three habitat variables are as follows:

- ***Safety and risk (SAR):*** Medical treatments can often have undesirable adverse side-effects (Benyamin et al., 2008). These effects could impact intervention utility should they exceed perceived benefits and harm the crew. Leveraging consensus and medical agency use, this variable weighs the safety of NIBS devices considered in this chapter. This variable assumes the equipment is used as intended.
- ***Crew time and scheduling (CTS):*** Astronauts have strict schedules that are usually parsed down to increments as short as five minutes (Wen, 2020). Thus, a useful countermeasure would minimize the amount of time its usage detracts from set schedules. This variable accounts for time that NIBS equipment setup and usage strictly takes away from other astronaut abilities; thus, if the equipment can be used while completing other tasks, only donning and doffing time is considered.
- ***Vehicle Implementation Requirements (VIR):*** Spaceflight hardware must be developed in consideration around limited mass, volume, and power requirements to properly integrate with launch vehicles and the spaceflight habitat. This variable combines values

related to these design considerations (Tbl. 17) to create one combined score which considers spaceflight hardware needs.

The hierarchy of values within the variables are defined in Table 16, where the vehicle implementation requirements are defined in Table 17.

Table 16. Metrics and score values to assess spaceflight efficacy of NIBS technology.

Variable	**Value**	**Score**
Demonstrated Information Processing Influence (IPI)	One model element influenced	0
	Two model elements influenced	1
	Three model elements influenced	2
	Four model elements influenced	3
	Five model elements influenced	4
Operational Performance Effectiveness (OPE)	Negative or no effects to cognitive or operational performance	0
	Improvements in specific cognitive elements	1
	Demonstrated improvements in overall cognition and declarative memory	2
	Demonstrated improvements in operational performance	3
	Demonstrated improvements in operational skill acquisition	4
Long-term health effects (LHE)	Negative or undesired effects to mental health and behavior	0
	No demonstrated lasting effects on mental health	1
	Demonstrated positive effects to aspects of behavioral health	2
	Systematic reviews point to positive effects to aspects of behavioral health	3
	Meta-analyses support ability to offset negative behavioral health states	4
Safety and risk (SAR)	Safety not investigated or severe adverse effects reported	0
	Only minor adverse effects reported in original research studies	1
	Only minor adverse effects reported in systematic reviews	2
	Only minor adverse effects proven in meta-analyses	3
	FDA Classification 2 & minor side effects proven in meta-analyses	4
Crew time and scheduling (CTS)	Administration detracts 60+ minutes from astronaut schedules	0
	Administration detracts 30-60 minutes from astronaut schedules	1
	Administration detracts 15-30 minutes from astronaut schedules	2
	Application detracts 5-15 minutes from astronaut schedules	3
	Application detracts <5 minutes from astronaut schedules	4
Vehicle Implementation Requirements (VIR)	Combined implementation score of 0	0
	Combined implementation score of 1-2	1
	Combined implementation score of 3	2
	Combined implementation score of 4-5	3
	Combined implementation score of 6	4
	Max:	24

Table 17. Vehicle implementation score definition.

Score	**Mass**	**Volume**	**Power**
0	> 25 kg	> 7.2 ft^3	Requires > 500 W
1	10-25 kg	1.8 – 7.2 ft^3	Requires 100 – 500 W
2	< 10 kg	< 1.8 ft^3	Requires < 100 W

Google scholar was used to search for studies related to human performance variables and criteria listed above. Keywords included the NIBS technology and terms that related to the variable of interest. For the variable of IPI keywords such as; “sensory processing”, “perception”, “cognition”, “long-term memory”, and “attention” were used. For the variable of OPE keywords such as; “learning”, “operations”, “simulation task”, “creativity”, and “skill acquisition” were applied. And for the variable of LHE keywords such as; “therapy”, “mental health”, “clinical”, and “mood” were applied. To the extent possible, the methodology in this Specific Aim uses systematic reviews and meta-analyses rather than singular studies and narrative reviews in several scoring metrics, positively weighing expert consensus on the abilities of a certain NIBS technology to target aspects of performance. Assessments also focused on studies and reviews that involve human subjects rather than animal studies (however a couple studies referred to for tFUS were conducted on non-human primates).

To investigate variables related to livelihood and vehicle implementation, information was collected in the following ways. To determine SAR scoring, systematic reviews related to “adverse effects” were searched for along with potential regulation citations in FDA classifications (fda.gov). CTS scoring was assessed while reviewing how NIBS were applied in the reviews related to human performance variables. VIR scoring was the combination of technologies meeting criteria defined for mass, volume, and power (Tbl. 17). The values in Table 17 were determined using resource utilization guidelines found in a NASA research solicitation for exploration technology demonstrations on the International Space Station (announcement

NNJ13ZBG001N). Specific NIBS equipment models that were selected for evaluation appeared to have a compact form factor for that NIBS technique and had available technical specifications listed online.

Spider plot figures were created for each NIBS technique assessed to visualize which variables the technology supported greater. Each axis corresponds to a different variable. Variables with scores toward the center of the plot are lower than variables scored to the outside. Variables in this polar type plot were grouped together, such that variables toward the northeast of the plot correspond to human performance and variables toward the southwest correspond to astronaut livelihood and vehicle implementation. For example, spider plots that with greater shading toward the northeast than southwest may have large potential in improving human performance, but low applicability in aerospace vehicles.

The following sections discuss and evaluate the NIBS technology being considered against the criteria listed in Tables 16 and 17. A discussion follows to compare the technology and future work that is needed; additionally, it posits which method may be the most appropriate spaceflight countermeasure in its current state.

7.3 Stochastic Resonance (SR)

SR will be the first NIBS technology reviewed in this trade study. As previously mentioned, SR as a NIBS technique uses an optimal level of sensory noise to induce changes in neural behavior. In the absence of systemic reviews in the literature, the background of this thesis and the work presented in Specific Aims 1, 2, and 3 will be used to inform this assessment. In human performance, SR has been shown to influence the five information processing model blocks considered including sensory processing (Collins et al., 1996; Huidobro, 2020; Simonotto et al., 1999), perception (Galvan-Garza, 2018; Lugo et al., 2008; Voros et al., 2021), elements of cognition (Awada et al., 2022; Söderlund et al., 2010; Wilkinson et al., 2008), long-term declarative memory (Hilliard et al., 2019; Putman et al., 2021; Sayed Daud & Sudirman, 2023), and attention (Hosseinabadi et al., 2021; Lin, 2022). This yields a score of 4 in the IPI variable.

Recall that much of the motivational background in this thesis identified that SR could improve performance in the information processing model. However, it was unclear whether these piecemeal findings would translate to operational performance. Thus, Specific Aims 1-3 evaluated noise effects on comprehensive cognition, operational performance, and procedural skill development. Since these novel investigations presented null findings there is no evidence that noise is very effective in operations. Therefore, SR scores a 2 in the OPE variable. Finally, the work presented in Specific Aim 3 found no effects of noise on immediate or longitudinal behavioral health, which results in an LHE score of 1.

Next this assessment considers the variables related to astronaut livelihood. The FDA has no classification for noise stimulation in medical treatments or devices; however, I was not able to identify in my work in Specific Aim 3 or the literature any severe side-effects of sensory noise stimulation when used appropriately. Across the work in this thesis there was only one incidence of a subject being removed due to adverse effects, where nGVS caused an uncomfortable skin lesion (specifically a rash) at the stimulation site. Even narrative reviews describe the inadequacy of studies to report adverse effects as a results of nGVS (Stefani et al., 2020). Note, there are many sensory modalities to administer noise to. While I discuss adverse risk effects for nGVS (no adverse effects were found for AWN in this thesis work), other risks may exist for noise administered to other modalities. Considering these results, SR receives an SAR score of 1 based on the criteria of this assessment. One substantial benefit of noise stimulation is that it is quick to apply and does not require operators to abstain from their tasks during stimulation. SR interfaces well with astronaut schedules and scores a 4 in CTS as it results in minimal time interruptions. Finally, I used a conservative approach toward vehicle implementation and assessed the Soterix device used for nGVS (the most cumbersome of the two SR devices) in Specific Aims 1-3. This device is 0.5 kg, 0.075 ft^3, and needs two 9V batteries as a power source; thus, SR scores a 4 in vehicle implementation. Figure 19 visualizes the results of the SR NIBS assessment, which resulted in a total score of 16.

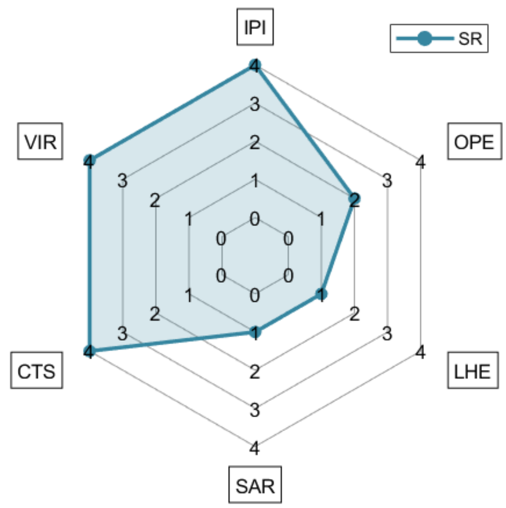


Figure 19. Spider plot visualization of the SR countermeasure assessment.

7.4 Transcranial Electrical Stimulation (tES)

tES techniques apply low magnitude electrical current (<3 mA) to the scalp to induce changes in neuronal excitability. These current signals include direct current pulses (transcranial direct current stimulation, tDCS), sinusoidal waveforms (transcranial alternating current stimulation, tACS), or random noise profiles (transcranial random noise stimulation, tRNS). The associated NIBS mechanism is believed to be that stimulation affects the spontaneous firing rate of neurons by altering their membrane potentials, which in turn modulates the neural activation burden of a task (Yavari et al., 2018). Regional current can be configured to be either anodal (up-regulation) or cathodal (down-regulation). Anodal stimulation depolarizes neurons and increases the probability of action potentials occurring, whereas cathodal stimulation hyperpolarizes the neurons, reducing the probability of action potentials (Thair et al., 2017). The use of anodal or cathodal stimulation may depend on the application being used, but I found most researchers apply anodal tES. Stimulation for a specific task or goal can be applied online (i.e., during) or offline (i.e., before) suggesting that tES influences on neuronal excitability are both concurrent and have associated with lasting post-stimulation effects (Medeiros et al., 2012; Thair et al., 2017; Yavari et al., 2018). While some researchers suggest that tRNS waveforms are the most effective tES signal to induce cortical excitability (Inukai et al., 2016), tDCS signal appears most often in the literature and will be the focus of review. It should be noted that these studies often apply anodal tDCS to the dorsolateral prefrontal cortex (DLPFC) and the primary motor cortex (M1). This is important as tDCS impacts regions that are functionally connected to the region being stimulated, which may have implications for spatial targeting when applying tES (Yavari et al., 2018).

tDCS for aging individuals find that a majority of studies report performance improvements in a variety of motor tasks ranging from finger tapping to postural control (Summers et al., 2016). Additionally, tDCS improves object perception in young and healthy adults (Lavezzi et al., 2022). These findings imply that tDCS can affect sensory processing and perception. Meta-analyses into cognition performance for aging, healthy, and clinical populations agree that tDCS positively influences aspects of working memory, decision making, attention, recognition, and language production (Berryhill & Martin, 2018; Reis et al., 2008b;

Summers et al., 2016). These results suggest that tDCS can effectively influence the entire information processing model, resulting in an IPI score of 4.

In comparison to SR, tDCS effects on complex operational performance and skill acquisition have been more thoroughly investigated. As previously mentioned, Choe et al. (2016) applied tDCS to subjects conducting a flight landing simulation and found that tDCS positively influences variance in complex skill acquisition and affects the learning rate in working memory. Tangential studies found that tDCS can enhance skill acquisition of medical students in surgical task learning (Ciechanski et al., 2017, 2018) and planning ability in the Tower of London task (Dockery et al., 2009). These investigations show promise for tDCS influencing operations and procedural learning, resulting in an OPE score of 4.

Finally, tDCS implications for long-term health appear to be rather expansive. Reviews and meta-analyses confirm that tDCS can reduce symptoms and improve the mood of individuals experiencing depression, attention-deficit disorder, anxiety, addiction, and schizophrenia (Ekhtiari et al., 2019; Gallop et al., 2023; Razza et al., 2021). Additional reviews extend the influence of tDCS further to identify studies where tDCS improves social cognition, influencing social functioning, affective reactions, and morality (Sellaro et al., 2016). This may be useful for team dynamics in a spaceflight environment. Considering the plethora of findings supporting the beneficial effects of tDCS for behavioral health, this results in an LHE score of 4.

The FDA has no classification for electrical stimulation in medical treatments or devices. However, meta-analyses and reviews of tDCS report incidences of minor adverse effects. These effects include itching, tingling, discomfort, headache, and skin lesions of stimulation sites (Bikson et al., 2016; Brunoni et al., 2011). Considering these results, tES receives an SAR score of 3 based on the criteria of this assessment. One substantial benefit of tES is that it does not require operators to abstain from their tasks during stimulation; however, placement of stimulation electrodes is more specific to adequately target neural sites. As such, its application could be particular and time consuming thus, while tES is fairly accommodating to astronaut schedules, it receives a score of 3 in CTS. Finally, I selected to assess the tES 1x1 device developed by Soterix (Woodbridge, NJ). This device is 0.5 kg, 0.075 ft^3, and needs two 9V batteries as a power source; thus, tES scores a 4 in vehicle implementation. Figure 20 visualizes the results of the tES NIBS assessment, which resulted in a total score of 22.

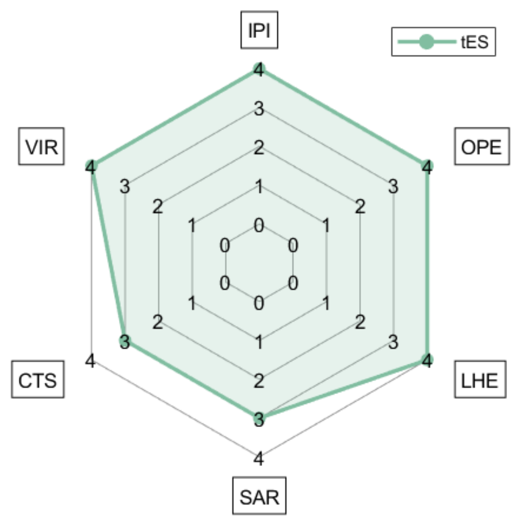


Figure 20. Spider plot visualization of the tES countermeasure assessment.

7.5 Transcranial Magnetic Stimulation (TMS)

TMS techniques use a powerful magnetic coil to induce high-intensity, short-lasting electromagnetic pulses to briefly depolarize a nerve membrane and initiate an action potential. As such, TMS needs to be placed orthogonal to brain regions that researchers wish to target, considering that the spatial focus of stimulation is narrow (Hallett, 2007; Nollet et al., 2003). TMS pulse administration can be presented in singular, paired, repetitive, or patterned fashions, where pulses are no longer than 100 μs in duration (Romanella et al., 2020). Similar to tES, the frequency that TMS pulses are applied can excite (<1 Hz) or inhibit (>5 Hz) neuronal activity and can be presented in an online or offline fashion, depending on the task (Hallett, 2007). Additionally, TMS must be configured to target the DLPFC or M1 to induce cognitive and motor changes. A stark difference between tES and TMS is that TMS directly induces an action potential and tES increases the likelihood of an action potential occurring (Yavari et al., 2018). This notion allows researchers to evaluate TMS effects through evoked potentials or peripheral responses (e.g., stimulating the motor cortex may cause a muscle twitch), rather than subjective performance changes in a task (Hallett, 2007; Nollet et al., 2003). Thus, researchers can have confidence that they are stimulating spatially dependent regions of interest. These evoked potentials can also be used to supplement shortcomings of neuroimaging methods with low spatial resolution, such as electroencephalography (EEG) (Hallett, 2007). Thus, in addition to being a NIBS technology, TMS can be used for neuroimaging applications and understanding motor response effects, which may be able to improve health diagnosing capabilities in spaceflight.

As mentioned, TMS is capable of directly influencing the motor cortex and motor performance (Hallett, 2007; Reis et al., 2008b); however, it can also affect and improve visual perception and discrimination (Ruzzoli et al., 2010; Waterston & Pack, 2010). This indicates TMS can induce changes in sensory processing and perception. Further, Luber & Lisanby (2014) conducted a systemic analysis in healthy and ill individuals for cognitive and perceptive tasks, identifying 61 publication suggesting that TMS can improve aspects of memory, learning, judgement, attention, and sensory thresholds. Similar reviews and investigations on performance for patients with depression and/or Parkinson’s have also shown cognitive improvements

(Myczkowski et al., 2012; Serafini et al., 2015; Trung et al., 2019). Together, these reviews imply that TMS can effectively target all aspects of information processing, resulting in an IPI score of 4.

While TMS can influence information processing, I was not able to find studies that applied this technique in complex operational tasks or procedural skill acquisition. Considering the plethora of studies that point toward the variety of cognitive and memory elements that TMS can influence (Luber & Lisanby, 2014; Reis et al., 2008b), improvements in overall cognition and declarative memory have been demonstrated. Thus, TMS receives an OPE score of 2.

Within the literature, a major promise of TMS is its ability to be used as a treatment for severe adverse mental health conditions and negative emotional affect. Longitudinal TMS has been shown to reduce symptoms for patients with treatment resistant depression, postpartum depression, post-traumatic stress disorder, epilepsy, autism spectrum disorder, bipolar disorder, and schizophrenia (Cole et al., 2015; Gold et al., 2019; Karsen et al., 2014; Myczkowski et al., 2012; Oberman et al., 2016; Pereira et al., 2016b; Serafini et al., 2015). Similar to tDCS, TMS has also been shown to affect cognitive processes that are related to emotion regulation (Lantrip et al., 2017). TMS appears to be a substantially useful tool for long term mental health and receives an LHE score of 4.

The FDA has given a classification for TMS medical treatments for adverse mental health. Meta-analyses and reviews of TMS report incidences of minor adverse effects. These effects include dizziness, discomfort, and headaches (Karsen et al., 2014; Pereira et al., 2016b); interestingly, these two meta-analyses both report a singular incidence of an unexplainable seizure. Considering the criteria of this assessment, TMS receives a SAR score of 4. One potential downside of current TMS is the restriction of stationary equipment and specificity of site location. TMS coil placement interfaces have been developed for microgravity, but the command interface is still not portable (Badran et al., 2020). This hardware may necessitate offline stimulation which would impede astronauts' ability to move around to complete tasks. Offline stimulation can range anywhere from a few minutes to 30 minutes based on the stimulation procedure (Van Rooij et al., 2023). As such, TMS is not accommodating to astronaut schedules and receives a score of 1 in CTS. Finally, I selected to assess the PowerMAG Lab 30 TMS device developed by MAG and More (Munich, Germany). This device is 38 kg, 2.7 ft^3, and needs 800 W to power to the coil; thus, TMS scores a 1 in vehicle implementation. Figure 21 visualizes the results of the TMS NIBS assessment, which resulted in a total score of 16.

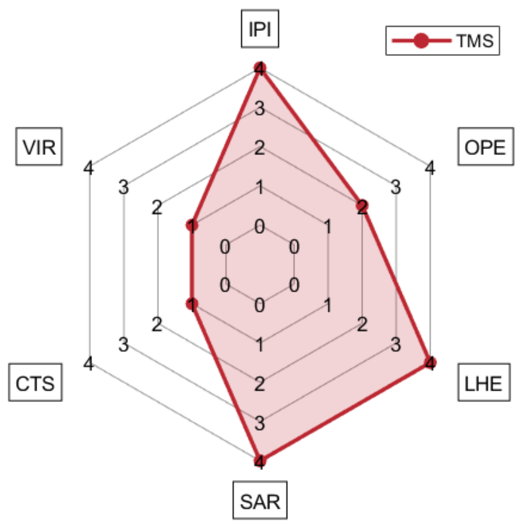


Figure 21. Spider plot visualization of the TMS countermeasure assessment.

7.6 Transcranial Photobiomodulation (tPBM)

This NIBS mechanism does not influence neuronal action potentials in the way that TMS and tES do, rather tPBM stimulates cellular metabolic processes using light of a specific wavelength. In the 1960s, NASA engineers pioneered investigations using LEDs to enhance healing processes in spaceflight to increase osteoblast proliferation for bone loss (Nhut & Nam, 2010; Whelan, 2000). Since then, PBM has been investigated as a NIBS technology. Specific to neural cells, red and near infrared light stimulates the mitochondrial respiratory chain which increases adenosine triphosphate (ATP) synthesis in neuronal tissue. Additional potential mechanisms in which PBM may affect the brain are by increasing cerebral blood flow, stem cell proliferation, and stimulating cell properties that are anti-inflammatory, anti-apoptotic, and anti-oxidant (Dompe et al., 2020; Salehpour et al., 2018). Further, neuroimaging studies suggest that focal stimulation using PBM can illicit global changes in neuronal excitability and functional connectivity (Dole et al., 2023), which has implications for spatial placement. PBM administration can either be continuous or pulsed, but there is consensus that stimulation duration must be at least 10 minutes for the tissue to respond (Dompe et al., 2020). A notable obstacle in the effectiveness of tPBM applications is light penetration to the brain, as outward layers, including the scalp and skull, absorb and scatter light. It is estimated the 5-12% of the light administered through transcranial means reach the cerebral cortex (Dompe et al., 2020). Approaches to this problem include intracranial and intranasal applications; however, intracranial usage is considered invasive, so only transcranial and intranasal applications are considered in this review.

I was unable to find evidence that tPBM improves sensory processing as it relates to information processing (i.e., perceptual sensitivity may not be improved); however, studies suggest that PBM can reduce the perception of pain in patients (Caccianiga et al., 2023). While tPBM has not been shown to influence sensory perception, meta-analyses suggest that it is useful in improving cognitive performance related to attention, memory, learning, executive functioning, and fluency in healthy and unhealthy populations (Chan et al., 2021; Gutiérrez-

Menéndez et al., 2020; T. Lee et al., 2023; Salehpour et al., 2019). Note that these authors clarify that the optimal wavelength to target cognitive enhancement is 1064 nm. Since tPBM can influence three elements of information processing, it scores a 2 in the IPI metric.

Similar to SR and TMS, I was unable to find applications of tPBM while subjects performed a complex operational task or acquired skills. Considering the consensus that tPBM can improve a variety of cognitive elements and memory in young and elderly populations (Chan et al., 2021; Salehpour et al., 2019), tPBM receives a score of 2 in OPE.

Since tPBM may stimulate neuronal cell properties that improve their health and longevity (eg., anti-inflammatory), there may be promise that tPBM can promote long-term mental health. In fact, many of the reviews referenced in this section explored the effects of tPBM for neurological diseases; however, the reviews only report a limited number of investigations for each neurological disease discussed. These investigations suggest that tPBM can influence patients with mild cognitive impairment, Parkinson's, traumatic brain injuries, depression, insomnia, and anxiety to some degree (Lee et al., 2023; Salehpour et al., 2020). These authors also clarify that the optimal wavelength to target neuronal disorders is 810 nm. Since these effects are demonstrated in systematic reviews rather than meta-analyses, tPBM receives an LHE score of 3.

The FDA has no classification for photobiomodulation in medical treatments or devices. However, systematic reviews report incidences of minor adverse effects when used correctly; these effects include headaches (Gutiérrez-Menéndez et al., 2020). Additionally, the literature recommends that subjects where eye protection while using tPBM. Considering these results, tPBM receives a SAR score of 2 based on the criteria of this assessment. One substantial benefit of tPBM is that it does not require operators to abstain from their tasks during stimulation;

additionally, many tPBM interfaces are as easy to apply as putting on a helmet. As such, PBM is accommodating to astronaut schedules and receives a score of 4 in CTS. Finally, I selected to assess the Neuro 3 tPBM device developed by Vielight (Toronto, ON). This device is 0.5 kg, 1 ft^3, and needs 10 W as a power source; thus, tPBM scores a 4 in vehicle implementation. Figure 22 visualizes the results of the tPBM NIBS assessment, which resulted in a total score of 17.

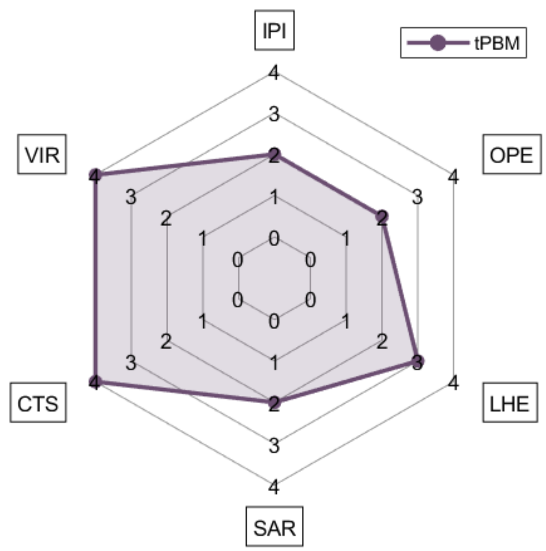


Figure 22. Spider plot visualization of the tPBM countermeasure assessment.

7.7 Transcranial Focused Ultrasound (tFUS)

tFUS is the least studied form of NIBS in this review; however, current research into this emerging technology shows promise. Traditional ultrasound uses acoustic pressure waves (average frequency of 2.5 MHz and short wavelength of 6mm) to image physiological structures beneath the skin (Yoo, 2018). However, ultrasound technology can be highly focused to produce higher-intensity sound pressure waves that can be used for applications other than imaging. For example, high-intensity ultrasound can be used to ablate tissue in localized areas and has seen applications in removing tumors and kidney stones (Bystritsky et al., 2011; Harper et al., 2013). However, low-intensity ultrasound can be used to produce sonification, or mechanical pressure waves that propagate through neuronal tissue and stimulate the brain. Potential stimulation mechanisms include modulation of the blood-oxygen-level-dependent (BOLD) response, inducing cavitation in the neuronal tissue, deformation of neuronal cell membranes, and manipulation of glial cells via mechanoreceptors (Bystritsky et al., 2011; Sarica et al., 2022; Yoo, 2018). tFUS has incredible spatial sensitivity though, which allows for exact stimulation targeting. Sonification requires pulse stimulation with frequencies ranging from 200-700 kHz, although no consensus on stimulation duration is found in the literature (Yoo, 2018).

Since this technology is in its infancy, many human studies focus on investigating mechanisms and neural effects of tFUS, without having subjects complete tasks. Thus, many investigations I found were limited to neuroimaging. I was able to identify one study has shown that tFUS can modify perceived tactile sensations of the hand when applied to the somatosensory cortices (Lee et al., 2016) and one study that suggested Alzheimer's patients saw improvements in cognitive state post stimulation as determined by a neuropsychological battery (Beisteiner et al., 2020). Studies conducted on non-human primates have shown tFUS alters motion stimulus recognition and cognitive behavior (Downs et al., 2017; Munoz et al., 2022). A lack of literature suggests that tFUS can influence sensory processing, perception, and certain cognitive elements (no evidence for attention or long-term memory was found); thus, tFUS receives an IPI score of 2. I was not able to find any tFUS studies related to complex operational performance and skill acquisition. This and a lack of variety in elements of demonstrated cognitive performance improvement suggest that tFUS receives an OPE score of 1. Aside from cognitive changes, Beisteiner et al. (2020) found no effects of tFUS on mood and I was unable to find instances of other behavioral health metrics investigated in a tFUS study, which results in a score of 1 for LHE.

Next this assessment considers the variables related to astronaut livelihood. The FDA has no classification for focused ultrasound for brain stimulation. However, one systematic review reported incidences of minor adverse effects when used correctly; these effects include headaches, scalp heating, neck pain, muscle twitches, and anxiety (Sarica et al., 2022). Additionally, while no negative effects related to opening the blood brain barrier using tFUS have been reported in studies with human subjects, Bowary & Greenberg (2018) speculate that this could promote unsafe entry of foreign materials. Additionally, if a malfunction caused the FUS intensity to increase, the resulting heat could harm neural tissue. These severe outcomes have not been reported in human studies though, so following the criteria of the assessment, tFUS receives a SAR score of 2. This hardware may require offline stimulation which would impede astronauts' ability to move around to complete tasks. Referring to the stimulation procedure of Beisteiner et al. (2020), offline stimulation is just over six minutes. Setup time and offline stimulation may take roughly 15 minutes, so tFUS receives a score of 3 in CTS. Finally, I selected to assess the CTX-250 FUS device developed by NeuroFUS (Bothell, WA). This device is 4 kg, 0.45 ft^3, and needs 620 W as a power source; thus, tFUS scores a 3 in vehicle implementation. Figure 23 visualizes the results of the tFUS NIBS assessment, which resulted in a total score of 12.

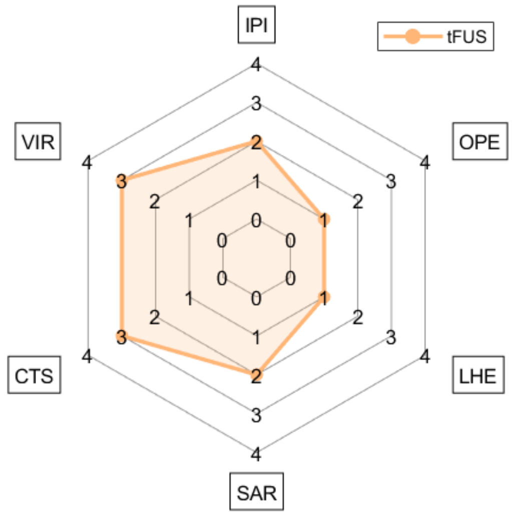


Figure 23. Spider plot visualization of the FUS countermeasure assessment.

7.8 Discussion

In this Specific Aim, five NIBS technologies were considered as potential human performance decrement countermeasures. An assessment methodology was applied to define scoring for six variables; three of which related to human performance and three of which related to astronaut livelihood. A literature search provided insight into the current knowledge of the capabilities of these NIBS methods and what score they should receive in these variables. A summary of these results is found in Table 18 and Figure 24. Based on the criteria defined *a priori* to this review, tES meets most of the requirements to be operationally effective and accommodate the unique challenges of living in a space habitat. The plethora of work that supports tES impact on information processing and operational performance is substantial. When assessed using this trade study methodology, tES should be selected as a human performance decrement countermeasure if only one were to be used.

Table 18. Table summary of the NIBS countermeasure assessment.

NIBS	IPI	OPE	LHE	SAR	CTS	VIR	Total
SR	4	2	1	1	4	4	16
tES	4	4	4	3	3	4	22
TMS	4	2	4	4	1	1	16
PBM	2	2	3	2	4	4	17
tFUS	2	1	1	2	3	3	12

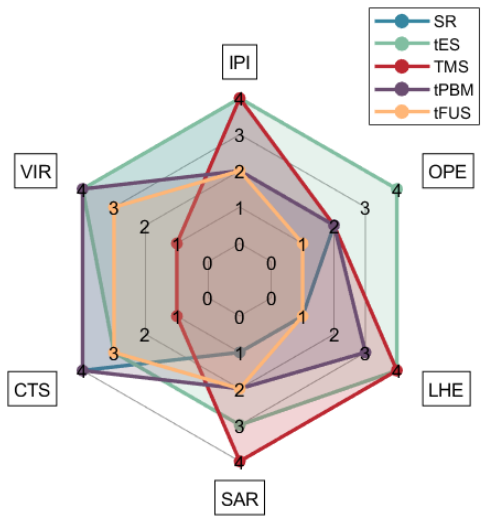


Figure 24. Spider plot comparison of all NIBS technologies assessed.

A limitation of this trade study that should be noted is that the scoring criteria relies solely on significant findings and the frequency of these findings for variables related to human performance while neglecting the effect size on performance. This is important to consider because some systemic reviews and meta-analyses suggest that TMS is more affective at targeting adverse mental health than tES (Hyde et al., 2022; Stilling et al., 2019; Torres et al., 2013). However, TMS does not implement well with spaceflight vehicles and may require offline administration. In comparison to other NIBS techniques, TMS substantially scores lower in vehicle implementation, a comparison of this burden can be observed in Table 19 which summarizes the mass, volume, and power requirements of each NIBS method. Further, this analysis may be limited by nascency of a given technology, rather than negative findings. I counteracted this limitation by bounding the TRL level. Future work may investigate certain dimensions of a NIBS where a dearth of literature was found.

Table 19. Table summary of the NIBS vehicle implementation information.

NIBS Method	**Mass (kg)**	**Volume (ft^3)**	**Power**
SR	0.5	0.075	Two 9V batteries
tES	0.5	0.075	Two 9V batteries
TMS	38	2.7	800 W
PBM	0.5	1	10 W
tFUS	4	0.45	620 W

Additionally, this trade study points out that many of these NIBS techniques can also be used for alternate purposes. For example, the high spatial resolution of TMS and tFUS make them ideal candidates to supplement neuroimaging techniques and can be useful for improving diagnoses. High intensity FUS can be used for in-flight surgeries, or as noninvasive treatments to ablate tissue. PBM could be used to promote cellular repair in other physiological systems that see degradation due to spaceflight. None of these technologies, though, have been investigated in space for the primary use of brain stimulation, nor to investigate these potential secondary uses. In-space investigations would be critical to ensure viability of any technology on-orbit. Each NIBS method has advantages and disadvantages; however, further work can implement technologies and strategies to increase their effectiveness. Table 18 summarizes these main points that were identified in this trade study. It should be noted that this list is not exhaustive and limited to this review.

Finally, the use of NIBS technology for spaceflight have been considered by medical researchers around the world. In fact, Romanella et al. (2020) explores using tDCS and TMS as human performance spaceflight countermeasure. This review outlines the potential of tDCS and TMS to target decrements in motor and cognitive behavior, as well as, provides a theoretical framework in what an in-flight stimulation regiment could be. This group went further and modeled how TMS optimization and regimens for spaceflight would be inter-individually dependent and regiments should be designed with this in mind (Romanella et al., 2023). Their work opens the conversation for NIBS to be used in spaceflight; however, it is not critical about the unknowns and limitations of the NIBS technologies they selected. First, TMS requirements currently place a burden on the spaceflight vehicle. The infrastructure needed to power the coil per pulse is relatively large and exceeds the criteria put forth by current ISS solicitations. The weight and volume requirements of TMS are rather large when compared to other methods as well. Second, their work fails mention potential mechanism impacts of spaceflight on TMS. Badran et al. (2020) shows that motor evoked potential thresholds decrease in parabolic flights compared to ground-based thresholds. The researchers mention that an upward displacement of the brain in microgravity may increase TMS sensitivity as the brain is physically closer to the magnetic coil. This may reduce researchers' abilities to translate ground-based findings to determine spaceflight applications. I posit that CNS morphology changes as a result of spaceflight (Roy-O'Reilly et al., 2021) may cause interactions with any NIBS technology; thus, additional investigations are needed in orbital and sub-orbital flight before they can be relied on in long-duration missions.

Table 20. State of NIBS for Long Duration Space Missions.

NIBS	Advantages	Disadvantages	Future Work
SR	• Evidence of influencing information processing. • Can be used online. • Has little to no side effects. • Quick to use and easy to administer. • Implements with spaceflight vehicles well.	• No evidence of improving operational performance and/or skill acquisition. • Has not demonstrated positive influence on behavioral health. • Has no medical classification by the FDA.	• Need to understand what information processing tasks related to spaceflight SR may be useful for. • Greater understanding as to why only some individuals see benefits from using noise.
tES	• Evidence of influencing information processing. • Evidence of improving operational performance and/or skill acquisition. • Evidence of promoting behavioral health and offsetting adverse disorders. • Can be used online and offline. • Has little to no side effects. • Quick to use and easy to administer. • Implements with spaceflight vehicles well.	• May have less utility in treating severe adverse mental health conditions than TMS. • Has no medical classification by the FDA.	• Better understanding into how low spatial resolution benefits or detracts from its utility. • Detailed investigation into administration procedure and tasking with specific tES waveforms.
TMS	• Evidence of influencing information processing. • Strong evidence of promoting behavioral health and offsetting adverse disorders. • Has little to no side effects. • Has medical classification from the FDA. • Has high spatial resolution. • Can be used to support neuroimaging.	• No evidence of improving operational performance and/or skill acquisition. • May need to be used offline. • Does not accommodate crew schedules well. • Does not implement with the spaceflight habitat well.	• Development into TMS systems that are smaller and require less power. • Investigate its role in operational performance and skill acquisition. • Improving our ability to diagnose adverse health conditions that necessitate TMS. • Designing a personalized TMS regimen that works with astronaut schedules.

tPTB	• Evidence of influencing cognitive tasks. • Evidence of promoting behavioral health. • Has little to no side effects. • Quick to use and easy to administer. • Implements with spaceflight vehicles well.	• No evidence of improving operational performance and/or skill acquisition. • May have less utility in treating severe adverse mental health conditions than alternatives. • Has no medical classification by the FDA.	• Investigate its role in operational performance and skill acquisition. • Improving our ability to use technology for other physiological injuries. • Develop solutions to increase amount of light inflicted on the brain.
tFUS	• Preliminary evidence of influencing information processing. • Appears to have little to no side effects. • Has high spatial resolution. • Can be used to support neuroimaging.	• Little knowledge into the utility of FUS for cognition, operations, and skill acquisition. • Must be used offline. • Has no medical classification by the FDA. • Power needs do not implement well with spaceflight vehicles.	• More, detailed knowledge into how FUS impacts information processing, operations, and skill acquisition is needed.

7.9 Conclusion

A trade study was conducted against five NIBS techniques to identify which one is most applicable for use in a spaceflight environment. The study loaded on three variables related to human performance which aligned with the focus of this thesis; the other three variables related to astronaut livelihood and the vehicle environment. A short review of each method and justification in how they scored against these variables was given. Based on the methodological assessment applied to these NIBS technologies, tES currently stands out as the best countermeasure to affect human performance. However, further work is needed to account for shortcomings in NIBS applications and to understand how these technologies interact with the spaceflight environment.

Chapter 8: Conclusions and Final Thoughts

8.1 Summary

This thesis explored the potential of neuromodulation, specifically through brain stimulation, to improve human performance as a countermeasure for spaceflight. SR as one such solution was further explored because of its perceived safety to use and ability to integrate well with spaceflight vehicles. Specific Aims 1-3 investigated the extent to which SR can be useful for tasks that require complex cognitive reasoning and skill acquisition. Ultimately, these rigorous investigations found no evidence that additive sensory noise can improve comprehensive cognitive or operational performance for the broad population; however, sensory noise effects in these paradigms appear to have different effects across individuals. Building off these findings, Specific Aim 4 conducted a trade study into NIBS techniques to identify which technology may be the most promising for operational performance and use in spaceflight. This trade study suggests that tES is currently the most promising NIBS candidate for this application. While SR (as compared to tES) as a human performance decrement countermeasure appears to be underwhelming for the broad population, open questions remain on whether it is still useful in specific use cases, such as enhancing perception, or for specific individuals.

8.2 Other Potential Enhancement Mechanisms using Sensory Noise

The work presented in Specific Aims 1 and 2 suggests that sensory noise effects may be inter-individually driven, where some subjects receive cognitive enhancement from sensory noise and others do not. SR is classically believed to alter neuronal firing rates and enhance signal detection, which may imply that everyone should be susceptible if this mechanism still holds true for cognition. However, this was not observed for the broad population and people who were helped or hindered by noise were able to *a priori* determine this through a subjective questionnaire (Appx. A). These results could suggest that another mechanism, separate from stochastic resonance, is contributing to cognitive enhancement.

Söderlund & Sikström (2008) have proposed that sensory noise enhancement for cognitive abilities could result from the moderate brain arousal (MBA) theory, which suggests that external noise may influence dopaminergic signaling in individuals with lower levels of background extracellular dopamine. This theory points out that catecholaminergic signaling is either tonic (stimulus independent background firing) or phasic (stimulus driven firing), where some people have higher levels of tonic signaling than phasic (and vice versa). Söderlund & Sikström posit that individuals with higher levels of tonic signaling (internal signaling noise) suppress phasic responses, but those with lower levels of tonic signaling may utilize phasic activity (external signaling noise). Thus, sensory noise may influence dopamine release and mental ability in individuals with low levels of tonic signaling. In other research, AWN has been shown to modulate neural activity in two midbrain regions associated with dopamine release, the substantia nigra and ventral tegmental area (Rausch et al., 2014). This experiment helps confirm that external noise can influence dopaminergic signaling, which, in turn, could affect cognition. The MBA theory may provide insight into how some individuals are susceptible to SR while others are not.

One way to assess this theory is to test a population known to have lower levels of tonic signaling. Individuals with ADHD appear to have a disbalance in catecholaminergic signaling (Aboitiz et al., 2014), which results in lower tonic dopamine levels. Thus, individuals with ADHD may see benefits from external noise to a greater than neurotypical groups. Human experimental research on children appears to support this in cognitive testing where children with ADHD had better attention and cognitive performance when loud auditory noise was playing compared to normal attentive children (Chen et al., 2022; Lin, 2022; Söderlund et al., 2010). These results imply that noise can improve elements of information processing in individuals with ADHD. Yet, ADHD can be considered a spectrum disorder, with varying symptoms between individuals (Heidbreder, 2015); thus, the magnitude of noise effects could be inter-individually driven which has not been thoroughly explored. Future work could explore the extent to which differences in tonic signaling facilitate the cognitive effects of additive sensory noise.

Additionally, the work in this thesis may guide future research objectives within the field of SR. The results and visualizations of Specific Aims 1-3 do not indicate that there is a greater effect of using MMSR compared to single modality SR; thus, to better understand the neural mechanisms in performance enhancement due to noise, future work may want to focus on singular modality applications. While this work has not indicated useful cognitive benefits for a broad population, the literature has suggested that it is useful at impacting perception in a broad population. There are many perceptual alterations in spaceflight as a result of sensory reweighting (Pathak et al., 2022), and these alterations could affect planetary operations once astronauts reach their destination. Sensory noise to influence perception may have implications for these perceptual alterations and may be a potential countermeasure that mitigate their damaging effects.

8.3 Spaceflight Limitations and Tangential Thoughts

The spaceflight environment can induce background auditory noise, stemming from hardware such as fans, that can have implications for administering AWN. The average continuous sound pressure level of the International Space Station (ISS) is about 60 dB SPL (Allen & Denham, 2011). While this level is considered to be similar in intensity to a normal conversation, the studies in this work were conducted in a sound reducing booth (Specific Aim

1) or in lab environments with minimal background noise (Specific Aims 2 and 3). The reduced environmental noise levels in these studies do not represent those that astronauts experience. While AWN levels in the literature are considered to be high in magnitude for cross-modality perception and cognition improvement (~70 dB SPL), the mode optimal noise levels found in Specific Aims 1 and 2 were usually lower (~55 dB SPL). Thus, the background noise levels in spaceflight could interfere and reduce the effectiveness of SR noise signals used to improve operational performance. Additionally, if AWN were used for specific use cases, such as improving auditory perception performance, the noise signals would be masked by background noise levels and render the treatment ineffective.

It is difficult to speculate on how nGVS results from an Earth gravity environment translate to similar performance in spaceflight, as microgravity induces otolithic deprivation which results in sensory reweighting, especially in the vestibular system (Pathak et al., 2022). This could cause an interaction that changes the effects of GVS stimulation in spaceflight. While Lajoie et al. (2021) provide an in-depth review on the potential promise of nGVS for spaceflight human performance and vestibular enhancement, the interaction effects of nGVS with the microgravity-affected vestibular system are still unknown as no spaceflight studies using GVS have occurred to date. As previously noted, microgravity altered TMS motor behavior compared to on-ground results (Badran et al., 2020). These unknown interaction effects caused by the spaceflight environment may have implications for any NIBS method used as a countermeasure.

Finally, this work aimed to apply SR for enhancing cognitive processes that would, in turn, improve operational performance; however, it is unclear whether cognitive decline requires mitigation. NASA's HFBP group suggests that the impact of adverse cognitive and behavioral conditions for missions that are one year or longer requires mitigation to reduce operational and long-term health risks (Slack et al., 2016). Yet the risks posed by reductions in cognition are relatively unknown. Strangman et al. (2014) reviewed spaceflight effects on cognitive functioning across relevant studies and found inconclusive evidence on whether cognitive deficits occur in long-duration low Earth orbit missions. This review notes that there is a mismatch between subjective and empirical reports, where crew members report cognitive decrements, but task performance is not impacted by these perceived declines. Studies conducted in isolated, confined environment (ICE) analogs, such as Antarctica stations, also convey mixed results with varied impairments in cognitive performance. Small sample sizes, individual variability and robustness, limited mission durations (< 1 year), and limited physiological spaceflight effects in ICE analogs may be such reasons for observing these mixed results (Strangman et al., 2014). This could suggest that cognitive countermeasures may not be necessary for operations in the current spaceflight mission profile and greater focus should be applied to mitigating adverse behavioral conditions, since evidence gathered from observations and projected risk of mood disorders in spaceflight is more pervasive (Slack et al., 2016). Since this review, improved techniques to assess cognitive state in spaceflight have been created and are in current use (Basner et al., 2015). Research is ongoing, but NASA's twin study found reductions in cognitive speed and accuracy in their spaceflight subject during Scott Kelly's one year mission (Garrett-Bakelman et al., 2019). Long-duration deep space missions could also lead to greater morphological and radiative destructive changes in the central nervous system which may lead to large cognitive and behavioral decline (Roy-O'Reilly et al., 2021). These greater neurological changes could imply the potential of cognitive decline in future long duration spaceflight despite previous spaceflight investigations. These neurological changes could have compelling future implications. Considering these implications, active countermeasures with low effect sizes, such as SR investigated in this thesis, may be inefficient in substantially enhancing cognition such that it offsets future cognitive declines resulting from an altered nervous system.

8.4 Future Work

Each chapter of this thesis outlines limitations and potential avenues for future work specific to that research Aim; however, I wanted to summarize what I deem to be the most important next steps.

First, it remains unclear how long duration missions in deep space will fully impact human CNS. The morphological and radiative changes could create neurological issues that are too severe to be addressed with NIBS alone. Thus, other countermeasures that promote CNS health and prevent adverse physiological outcomes need to be understood and integrated in future spaceflight mission architecture.

Second, there are many NIBS techniques that can be used for spaceflight, but each may be more suitable for different applications. For example, tES can be used to enhance online functioning while completing an operational task and TMS can be used for more effective offline treatment of adverse mental states. A standard procedure for when astronauts would use each technology would be necessary before implementation in a space vehicle. Additionally, further research is required to know how the spaceflight environment interacts with these technologies and whether the beneficial results found on Earth translate to this context.

Third, SR may be promising for specific use cases and individuals, but it is unclear how to determine what and who benefits from this additive sensory noise. Future work should investigate the potential mechanism of moderate brain arousal to determine how noise may improve cognition in certain individuals, from the *a priori* identification and tailoring of noise treatments can be provided to some astronauts and operators. As commercial spaceflight gains traction, nontraditional populations will have access to spaceflight. Thus, if an astronaut with attention deficit disorder can utilize SR or technologies that are ineffective to traditional astronaut populations, the technology should be accessible to them. Future countermeasures should strive to support more diverse groups other than the healthiest of individuals, which have traditionally been the only population considered space worthy until now.

References

Aboitiz, F., OssandÃn, T., Zamorano, F., Palma, B., & Carrasco, X. (2014). Irrelevant stimulus processing in ADHD: Catecholamine dynamics and attentional networks. *Frontiers in Psychology*, *5*. https://doi.org/10.3389/fpsyg.2014.00183

Allen, C., & Denham, S. (2011). International Space Station Acoustics—A Status Report. *41st International Conference on Environmental Systems*. 41st International Conference on Environmental Systems, Portland, Oregon. https://doi.org/10.2514/6.2011-5128

Anglin, K. M., Anania, E., Disher, T. J., & Kring, J. P. (2017). Developing skills: A training method for long-duration exploration missions. *2017 IEEE Aerospace Conference*, 1–7. https://doi.org/10.1109/AERO.2017.7943602

Angwin, A. J., Wilson, W. J., Arnott, W. L., Signorini, A., Barry, R. J., & Copland, D. A. (2017). White noise enhances new-word learning in healthy adults. *Scientific Reports*, *7*(1), 13045. https://doi.org/10.1038/s41598-017-13383-3

Awada, M., Becerik-Gerber, B., Lucas, G., & Roll, S. (2022). Cognitive performance, creativity and stress levels of neurotypical young adults under different white noise levels. *Scientific Reports*, *12*(1), 14566. https://doi.org/10.1038/s41598-022-18862-w

Badran, B. W., Caulfield, K. A., Cox, C., Lopez, J. W., Borckardt, J. J., DeVries, W. H., Summers, P., Kerns, S., Hanlon, C. A., McTeague, L. M., George, M. S., & Roberts, D. R. (2020). Brain stimulation in zero gravity: Transcranial magnetic stimulation (TMS) motor threshold decreases during zero gravity induced by parabolic flight. *Npj Microgravity*, *6*(1), 26. https://doi.org/10.1038/s41526-020-00116-6

Basner, M., Dinges, D. F., Howard, K., Moore, T. M., Gur, R. C., Mühl, C., & Stahn, A. C. (2021). Continuous and Intermittent Artificial Gravity as a Countermeasure to the Cognitive Effects of 60 Days of Head-Down Tilt Bed Rest. *Frontiers in Physiology*, *12*, 643854. https://doi.org/10.3389/fphys.2021.643854

Basner, M., Hermosillo, E., Nasrini, J., Saxena, S., Dinges, D. F., Moore, T. M., & Gur, R. C. (2020). Cognition test battery: Adjusting for practice and stimulus set effects for varying administration intervals in high performing individuals. *Journal of Clinical and Experimental Neuropsychology*, *42*(5), 516–529. https://doi.org/10.1080/13803395.2020.1773765

Basner, M., Savitt, A., Moore, T. M., Port, A. M., McGuire, S., Ecker, A. J., Nasrini, J., Mollicone, D. J., Mott, C. M., McCann, T., Dinges, D. F., & Gur, R. C. (2015). Development and Validation of the Cognition Test Battery for Spaceflight. *Aerospace Medicine and Human Performance*, *86*(11), 942–952. https://doi.org/10.3357/AMHP.4343.2015

Beisteiner, R., Matt, E., Fan, C., Baldysiak, H., Schönfeld, M., Philippi Novak, T., Amini, A., Aslan, T., Reinecke, R., Lehrner, J., Weber, A., Reime, U., Goldenstedt, C., Marlinghaus, E., Hallett, M., & Lohse-Busch, H. (2020). Transcranial Pulse Stimulation with

Ultrasound in Alzheimer's Disease—A New Navigated Focal Brain Therapy. *Advanced Science*, *7*(3), 1902583. https://doi.org/10.1002/advs.201902583

Benyamin, R. (2008). Opioid Complications and Side Effects. *Pain Physician*, *2s;11*(3;2s), S105–S120. https://doi.org/10.36076/ppj.2008/11/S105

Benzi, R., Sutera, A., & Vulpiani, A. (1981). The mechanism of stochastic resonance. *Journal of Physics A: Mathematical and General*, *14*(11), L453–L457. https://doi.org/10.1088/0305-4470/14/11/006

Berryhill, M. E., & Martin, D. (2018). Cognitive Effects of Transcranial Direct Current Stimulation in Healthy and Clinical Populations: An Overview. *The Journal of ECT*, *34*(3), e25–e35. https://doi.org/10.1097/YCT.0000000000000534

Bigelow, R. T., & Agrawal, Y. (2014). *Vestibular involvement in cognition: Visuospatial ability, attention, executive function, and memory*. 18.

Bikson, M., Grossman, P., Thomas, C., Zannou, A. L., Jiang, J., Adnan, T., Mourdoukoutas, A. P., Kronberg, G., Truong, D., Boggio, P., Brunoni, A. R., Charvet, L., Fregni, F., Fritsch, B., Gillick, B., Hamilton, R. H., Hampstead, B. M., Jankord, R., Kirton, A., … Woods, A. J. (2016). Safety of Transcranial Direct Current Stimulation: Evidence Based Update 2016. *Brain Stimulation*, *9*(5), 641–661. https://doi.org/10.1016/j.brs.2016.06.004

Boring, R. L. (Ed.). (2020). *Advances in Human Error, Reliability, Resilience, and Performance: Proceedings of the AHFE 2019 International Conference on Human Error, Reliability, Resilience, and Performance, July 24-28, 2019, Washington D.C., USA* (Vol. 956). Springer International Publishing. https://doi.org/10.1007/978-3-030-20037-4

Bosch Bruguera, M., Fink, A., Schröder, V., López Bermúdez, S., Dessy, E., van den Berg, F. P., Lawson, G., Dangoisse, C., Possnig, C., Albertsen, N., Pattyn, N., & Ewald, R. (2021). Assessment of the effects of isolation, confinement and hypoxia on spaceflight piloting performance for future space missions—The SIMSKILL experiment in Antarctica. *Acta Astronautica*, *179*, 471–483. https://doi.org/10.1016/j.actaastro.2020.11.019

Bostrom, N., & Sandberg, A. (2009). Cognitive Enhancement: Methods, Ethics, Regulatory Challenges. *Science and Engineering Ethics*, *15*(3), 311–341. https://doi.org/10.1007/s11948-009-9142-5

Bowary, P., & Greenberg, B. D. (2018). Noninvasive Focused Ultrasound for Neuromodulation. *Psychiatric Clinics of North America*, *41*(3), 505–514. https://doi.org/10.1016/j.psc.2018.04.010

Brem, A., Ran, K., & Pascual-leone, A. (2013). Learning and memory. In *Handbook of Clinical Neurology* (Vol. 116, pp. 693–737). Elsevier. https://doi.org/10.1016/B978-0-444-53497-2.00055-3

Brunoni, A. R., Amadera, J., Berbel, B., Volz, M. S., Rizzerio, B. G., & Fregni, F. (2011). A systematic review on reporting and assessment of adverse effects associated with transcranial direct current stimulation. *International Journal of Neuropsychopharmacology*, *14*(8), 1133–1145. https://doi.org/10.1017/S1461145710001690

Bystritsky, A., Korb, A. S., Douglas, P. K., Cohen, M. S., Melega, W. P., Mulgaonkar, A. P., DeSalles, A., Min, B.-K., & Yoo, S.-S. (2011). A review of low-intensity focused ultrasound pulsation. *Brain Stimulation*, *4*(3), 125–136. https://doi.org/10.1016/j.brs.2011.03.007

Caccianiga, P., Carminati, I., & Caccianiga, G. (2023). Photobiomodulation with Laser Technology to Reduce Pain Perception during Fixed Orthodontic Treatment: Literature Review and New Perspectives with LED Devices. *Inventions*, *8*(1), 46. https://doi.org/10.3390/inventions8010046

Carey, S., Ross, J. M., & Balasubramaniam, R. (2023). Auditory, tactile, and multimodal noise reduce balance variability. *Experimental Brain Research*, *241*(5), 1241–1249. https://doi.org/10.1007/s00221-023-06598-6

Carney, C. E., Buysse, D. J., Ancoli-Israel, S., Edinger, J. D., Krystal, A. D., Lichstein, K. L., & Morin, C. M. (2012). The Consensus Sleep Diary: Standardizing Prospective Sleep Self-Monitoring. *Sleep*, *35*(2), 287–302. https://doi.org/10.5665/sleep.1642

Carr, C. (2001). *Distributed Architectures for Mars Surface Exploration* [Master's]. Massachusetts Institute of Technology.

Chan, A. S., Lee, T., Hamblin, M. R., & Cheung, M. (2021). Photobiomodulation Enhances Memory Processing in Older Adults with Mild Cognitive Impairment: A Functional Near-Infrared Spectroscopy Study. *Journal of Alzheimer's Disease*, *83*(4), 1471–1480. https://doi.org/10.3233/JAD-201600

Chen, I.-C., Chan, H.-Y., Lin, K.-C., Huang, Y.-T., Tsai, P.-L., & Huang, Y.-M. (2022). Listening to White Noise Improved Verbal Working Memory in Children with Attention-Deficit/Hyperactivity Disorder: A Pilot Study. *International Journal of Environmental Research and Public Health*, *19*(12), 7283. https://doi.org/10.3390/ijerph19127283

Chi, M. T. H. (2009). Active-Constructive-Interactive: A Conceptual Framework for Differentiating Learning Activities. *Topics in Cognitive Science*, *1*(1), 73–105. https://doi.org/10.1111/j.1756-8765.2008.01005.x

Choe, J., Coffman, B. A., Bergstedt, D. T., Ziegler, M. D., & Phillips, M. E. (2016). Transcranial Direct Current Stimulation Modulates Neuronal Activity and Learning in Pilot Training. *Frontiers in Human Neuroscience*, *10*. https://doi.org/10.3389/fnhum.2016.00034

Ciechanski, P., Cheng, A., Damji, O., Lopushinsky, S., Hecker, K., Jadavji, Z., & Kirton, A. (2018). Effects of transcranial direct-current stimulation on laparoscopic surgical skill acquisition. *BJS Open*, *2*(2), 70–78. https://doi.org/10.1002/bjs5.43

Ciechanski, P., Cheng, A., Lopushinsky, S., Hecker, K., Gan, L. S., Lang, S., Zareinia, K., & Kirton, A. (2017). Effects of Transcranial Direct-Current Stimulation on Neurosurgical Skill Acquisition: A Randomized Controlled Trial. *World Neurosurgery*, *108*, 876-884.e4. https://doi.org/10.1016/j.wneu.2017.08.123

Clark, V. P., Coffman, B. A., Mayer, A. R., Weisend, M. P., Lane, T. D. R., Calhoun, V. D., Raybourn, E. M., Garcia, C. M., & Wassermann, E. M. (2012). TDCS guided using fMRI significantly accelerates learning to identify concealed objects. *NeuroImage*, *59*(1), 117–128. https://doi.org/10.1016/j.neuroimage.2010.11.036

Clément, G. R., Boyle, R. D., George, K. A., Nelson, G. A., Reschke, M. F., Williams, T. J., & Paloski, W. H. (2020). Challenges to the central nervous system during human spaceflight missions to Mars. *Journal of Neurophysiology*, *123*(5), 2037–2063. https://doi.org/10.1152/jn.00476.2019

Cole, J. C., Green Bernacki, C., Helmer, A., Pinninti, N., & O'reardon, J. P. (2015). Efficacy of Transcranial Magnetic Stimulation (TMS) in the Treatment of Schizophrenia: A Review of the Literature to Date. *Innovations in Clinical Neuroscience*, *12*(7–8), 12–19.

Collins, J. J., Imhoff, T. T., & Grigg, P. (1996). Noise-enhanced information transmission in rat SA1 cutaneous mechanoreceptors via aperiodic stochastic resonance. *Journal of Neurophysiology*, *76*(1), 642–645. https://doi.org/10.1152/jn.1996.76.1.642

Collins, J. J., Imhoff, T. T., & Grigg, P. (1997). Noise-mediated enhancements and decrements in human tactile sensation. *Physical Review E*, *56*(1), 923–926. https://doi.org/10.1103/PhysRevE.56.923

Costa, F., Ambesi-Impiombato, F. S., Beccari, T., Conte, C., Cataldi, S., Curcio, F., & Albi, E. (2021). Spaceflight Induced Disorders: Potential Nutritional Countermeasures. *Frontiers in Bioengineering and Biotechnology*, *9*, 666683. https://doi.org/10.3389/fbioe.2021.666683

Dockery, C. A., Hueckel-Weng, R., Birbaumer, N., & Plewnia, C. (2009). Enhancement of Planning Ability by Transcranial Direct Current Stimulation. *The Journal of Neuroscience*, *29*(22), 7271–7277. https://doi.org/10.1523/JNEUROSCI.0065-09.2009

Dole, M., Auboiroux, V., Langar, L., & Mitrofanis, J. (2023). A systematic review of the effects of transcranial photobiomodulation on brain activity in humans. *Reviews in the Neurosciences*, *0*(0). https://doi.org/10.1515/revneuro-2023-0003

Dompe, C., Moncrieff, L., Matys, J., Grzech-Leśniak, K., Kocherova, I., Bryja, A., Bruska, M., Dominiak, M., Mozdziak, P., Skiba, T., Shibli, J., Angelova Volponi, A., Kempisty, B., & Dyszkiewicz-Konwińska, M. (2020). Photobiomodulation—Underlying Mechanism and Clinical Applications. *Journal of Clinical Medicine*, *9*(6), 1724. https://doi.org/10.3390/jcm9061724

Downs, M. E., Teichert, T., Buch, A., Karakatsani, M. E., Sierra, C., Chen, S., Konofagou, E. E., & Ferrera, V. P. (2017). Toward a Cognitive Neural Prosthesis Using Focused Ultrasound. *Frontiers in Neuroscience*, *11*, 607. https://doi.org/10.3389/fnins.2017.00607

Ekhtiari, H., Tavakoli, H., Addolorato, G., Baeken, C., Bonci, A., Campanella, S., Castelo-Branco, L., Challet-Bouju, G., Clark, V. P., Claus, E., Dannon, P. N., Del Felice, A., den Uyl, T., Diana, M., di Giannantonio, M., Fedota, J. R., Fitzgerald, P., Gallimberti, L., Grall-Bronnec, M., … Hanlon, C. A. (2019). Transcranial electrical and magnetic stimulation (tES and TMS) for addiction medicine: A consensus paper on the present state of the science and the road ahead. *Neuroscience & Biobehavioral Reviews*, *104*, 118–140. https://doi.org/10.1016/j.neubiorev.2019.06.007

Employer-Reported Workplace Injuries and Illnesses – 2019. (2020). 9.

Friedman, E., & Bui, B. (2017). A Psychiatric Formulary for Long-Duration Spaceflight. *Aerospace Medicine and Human Performance*, *88*(11), 1024–1033. https://doi.org/10.3357/AMHP.4901.2017

Fuller, J. A., Stanton, J. M., Fisher, G. G., Spitzmüller, C., Russell, S. S., & Smith, P. C. (2003). A Lengthy Look at the Daily Grind: Time Series Analysis of Events, Mood, Stress, and Satisfaction. *Journal of Applied Psychology*, *88*(6), 1019–1033. https://doi.org/10.1037/0021-9010.88.6.1019

Fuster, J. M., Bodner, M., & Kroger, J. K. (2000). *Cross-modal and cross-temporal association in neurons of frontal cortex*. *405*, 5.

Gallop, L., Westwood, S. J., Lewis, Y., Campbell, I. C., & Schmidt, U. (2023). Effects of transcranial direct current stimulation in children and young people with psychiatric disorders: A systematic review. *European Child & Adolescent Psychiatry*. https://doi.org/10.1007/s00787-023-02157-0

Galvan-Garza, R. C. (2018). Exhibition of stochastic resonance in vestibular tilt motion perception. *Brain Stimulation*, 7.

Gammaitoni, L., Hänggi, P., Jung, P., & Marchesoni, F. (1998). Stochastic resonance. *Reviews of Modern Physics*, *70*(1), 223–287. https://doi.org/10.1103/RevModPhys.70.223

Garrett-Bakelman, F. E., Darshi, M., Green, S. J., Gur, R. C., Lin, L., Macias, B. R., McKenna, M. J., Meydan, C., Mishra, T., Nasrini, J., Piening, B. D., Rizzardi, L. F., Sharma, K., Siamwala, J. H., Taylor, L., Vitaterna, M. H., Afkarian, M., Afshinnekoo, E., Ahadi, S., … Turek, F. W. (2019). The NASA Twins Study: A multidimensional analysis of a year-long human spaceflight. *Science*, *364*(6436), eaau8650. https://doi.org/10.1126/science.aau8650

Gingl, Z., Kiss, L. B., & Moss, F. (1995). Non-Dynamical Stochastic Resonance: Theory and Experiments with White and Arbitrarily Coloured Noise. *Europhysics Letters (EPL)*, *29*(3), 191–196. https://doi.org/10.1209/0295-5075/29/3/001

Goel, R., Kofman, I., Jeevarajan, J., De Dios, Y., Cohen, H. S., Bloomberg, J. J., & Mulavara, A. P. (2015). Using Low Levels of Stochastic Vestibular Stimulation to Improve Balance Function. *PLOS ONE*, *10*(8), e0136335. https://doi.org/10.1371/journal.pone.0136335

Gold, A. K., Ornelas, A. C., Cirillo, P., Caldieraro, M. A., Nardi, A. E., Nierenberg, A. A., & Kinrys, G. (2019). Clinical applications of transcranial magnetic stimulation in bipolar disorder. *Brain and Behavior*, *9*(10). https://doi.org/10.1002/brb3.1419

Gutiérrez-Menéndez, A., Marcos-Nistal, M., Méndez, M., & Arias, J. L. (2020). Photobiomodulation as a promising new tool in the management of psychological disorders: A systematic review. *Neuroscience & Biobehavioral Reviews*, *119*, 242–254. https://doi.org/10.1016/j.neubiorev.2020.10.002

Hallett, M. (2007). Transcranial Magnetic Stimulation: A Primer. *Neuron*, *55*(2), 187–199. https://doi.org/10.1016/j.neuron.2007.06.026

Harper, J. D., Sorensen, M. D., Cunitz, B. W., Wang, Y.-N., Simon, J. C., Starr, F., Paun, M., Dunmire, B., Liggitt, H. D., Evan, A. P., McAteer, J. A., Hsi, R. S., & Bailey, M. R. (2013). Focused Ultrasound to Expel Calculi from the Kidney: Safety and Efficacy of a Clinical Prototype Device. *Journal of Urology*, *190*(3), 1090–1095. https://doi.org/10.1016/j.juro.2013.03.120

Harvey, P. (2019). Domains of cognition and their assessment. *Dialogues in Clinical Neuroscience*, *21*(3), 227–237. https://doi.org/10.31887/DCNS.2019.21.3/pharvey

Heidbreder, R. (2015). ADHD symptomatology is best conceptualized as a spectrum: A dimensional versus unitary approach to diagnosis. *ADHD Attention Deficit and Hyperactivity Disorders*, *7*(4), 249–269. https://doi.org/10.1007/s12402-015-0171-4

Helps, S. K., Bamford, S., Sonuga-Barke, E. J. S., & Söderlund, G. B. W. (2014). Different Effects of Adding White Noise on Cognitive Performance of Sub-, Normal and Super-Attentive School Children. *PLoS ONE*, *9*(11), e112768. https://doi.org/10.1371/journal.pone.0112768

Helton, W. S. (2004). Validation of a Short Stress State Questionnaire. *PROCEEDINGS of the HUMAN FACTORS AND ERGONOMICS SOCIETY 48th ANNUAL MEETING*, 5.

Hidaka, I., Nozaki, D., & Yamamoto, Y. (2000). Functional Stochastic Resonance in the Human Brain: Noise Induced Sensitization of Baroreflex System. *Physical Review Letters*, *85*(17), 3740–3743. https://doi.org/10.1103/PhysRevLett.85.3740

Hilliard, D., Passow, S., Thurm, F., Schuck, N. W., Garthe, A., Kempermann, G., & Li, S.-C. (2019). Noisy galvanic vestibular stimulation modulates spatial memory in young healthy adults. *Scientific Reports*, *9*(1), 9310. https://doi.org/10.1038/s41598-019-45757-0

Horn, A., & Fox, M. D. (2020). Opportunities of connectomic neuromodulation. *NeuroImage*, *221*, 117180. https://doi.org/10.1016/j.neuroimage.2020.117180

Hosseinabadi, M., Mohammadkhani, G., Rostami, R., & Aalmasi, A. (2021). Inhibitory function and sustained attention following galvanic vestibular stimulation in children with attention-deficit/hyperactivity disorder. *Auditory and Vestibular Research*. https://doi.org/10.18502/avr.v30i3.6533

Huidobro, N. (2020). Augmenting Global Coherence in EEG Signals with Binaural or Monaural Noises. *Brain Topography*, 16.

Human Factors Training Manual. (1998). ICAO; DOC 9683-AN/950.

Hyde, J., Carr, H., Kelley, N., Seneviratne, R., Reed, C., Parlatini, V., Garner, M., Solmi, M., Rosson, S., Cortese, S., & Brandt, V. (2022). Efficacy of neurostimulation across mental disorders: Systematic review and meta-analysis of 208 randomized controlled trials. *Molecular Psychiatry*, *27*(6), 2709–2719. https://doi.org/10.1038/s41380-022-01524-8

Inukai, Y., Otsuru, N., Masaki, M., Saito, K., Miyaguchi, S., Kojima, S., & Onishi, H. (2018). Effect of noisy galvanic vestibular stimulation on center of pressure sway of static standing posture. *Brain Stimulation*, *11*(1), 85–93. https://doi.org/10.1016/j.brs.2017.10.007

Inukai, Y., Saito, K., Sasaki, R., Tsuiki, S., Miyaguchi, S., Kojima, S., Masaki, M., Otsuru, N., & Onishi, H. (2016). Comparison of Three Non-Invasive Transcranial Electrical Stimulation Methods for Increasing Cortical Excitability. *Frontiers in Human Neuroscience*, *10*. https://doi.org/10.3389/fnhum.2016.00668

Kandel, E. R., Schwartz, J. H., & Jessell, T. M. (Eds.). (2000). *Principles of neural science* (4th ed). McGraw-Hill, Health Professions Division.

Karsen, E. F., Watts, B. V., & Holtzheimer, P. E. (2014). Review of the Effectiveness of Transcranial Magnetic Stimulation for Post-traumatic Stress Disorder. *Brain Stimulation*, *7*(2), 151–157. https://doi.org/10.1016/j.brs.2013.10.006

Keywan, A., Badarna, H., Jahn, K., & Wuehr, M. (2020). No evidence for after-effects of noisy galvanic vestibular stimulation on motion perception. *Scientific Reports*, *10*(1), 2545. https://doi.org/10.1038/s41598-020-59374-9

Keywan, A., Jahn, K., & Wuehr, M. (2019). Noisy Galvanic Vestibular Stimulation Primarily Affects Otolith-Mediated Motion Perception. *Neuroscience*, *399*, 161–166. https://doi.org/10.1016/j.neuroscience.2018.12.031

Keywan, A., Wuehr, M., Pradhan, C., & Jahn, K. (2018). Noisy Galvanic Stimulation Improves Roll-Tilt Vestibular Perception in Healthy Subjects. *Frontiers in Neurology*, *9*, 83. https://doi.org/10.3389/fneur.2018.00083

Kim, D. J., Yogendrakumar, V., Chiang, J., Ty, E., Wang, Z. J., & McKeown, M. J. (2013). Noisy Galvanic Vestibular Stimulation Modulates the Amplitude of EEG Synchrony Patterns. *PLOS ONE*, *8*(7), 10.

Kintz, J. R., Banerjee, N. T., Zhang, J. Y., Anderson, A. P., & Clark, T. K. (2022). Estimation of Subjectively Reported Trust, Mental Workload, and Situation Awareness Using Unobtrusive Measures. *Human Factors: The Journal of the Human Factors and Ergonomics Society*, 001872082211293. https://doi.org/10.1177/00187208221129371

Klein, G., Ross, K. G., Moon, B. M., Klein, D. E., Hoffman, R. R., & Hollnagel, E. (2003). Macrocognition. *IEEE Intelligent Systems*, *18*(3), 81–85. https://doi.org/10.1109/MIS.2003.1200735

Lajoie, K., Marigold, D. S., Valdés, B. A., & Menon, C. (2021). The potential of noisy galvanic vestibular stimulation for optimizing and assisting human performance. *Neuropsychologia*, *152*, 107751. https://doi.org/10.1016/j.neuropsychologia.2021.107751

Lantrip, C., Gunning, F. M., Flashman, L., Roth, R. M., & Holtzheimer, P. E. (2017). Effects of Transcranial Magnetic Stimulation on the Cognitive Control of Emotion: Potential Antidepressant Mechanisms. *The Journal of ECT*, *33*(2), 73–80. https://doi.org/10.1097/YCT.0000000000000386

Lavezzi, G. D., Sanz Galan, S., Andersen, H., Tomer, D., & Cacciamani, L. (2022). The effects of tDCS on object perception: A systematic review and meta-analysis. *Behavioural Brain Research*, *430*, 113927. https://doi.org/10.1016/j.bbr.2022.113927

Lee, J.-W., Lee, G.-E., An, J.-H., Yoon, S.-W., Heo, M., & Kim, H.-Y. (2014). Effects of Galvanic Vestibular Stimulation on Visual Memory Recall and EEG. *Journal of Physical Therapy Science*, *26*(9), 1333–1336. https://doi.org/10.1589/jpts.26.1333

Lee, T., Ding, Z., & Chan, A. S. (2023). Can transcranial photobiomodulation improve cognitive function? A systematic review of human studies. *Ageing Research Reviews*, *83*, 101786. https://doi.org/10.1016/j.arr.2022.101786

Lee, W., Chung, Y. A., Jung, Y., Song, I.-U., & Yoo, S.-S. (2016). Simultaneous acoustic stimulation of human primary and secondary somatosensory cortices using transcranial focused ultrasound. *BMC Neuroscience*, *17*(1), 68. https://doi.org/10.1186/s12868-016-0303-6

Lin, H.-Y. (2022). The Effects of White Noise on Attentional Performance and On-Task Behaviors in Preschoolers with ADHD. *International Journal of Environmental Research and Public Health*, *19*(22), 15391. https://doi.org/10.3390/ijerph192215391

Luber, B., & Lisanby, S. H. (2014). Enhancement of human cognitive performance using transcranial magnetic stimulation (TMS). *NeuroImage*, *85*, 961–970. https://doi.org/10.1016/j.neuroimage.2013.06.007

Lugo, E., Doti, R., & Faubert, J. (2008). Ubiquitous Crossmodal Stochastic Resonance in Humans: Auditory Noise Facilitates Tactile, Visual and Proprioceptive Sensations. *PLoS ONE*, *3*(8), e2860. https://doi.org/10.1371/journal.pone.0002860

Luigjes, J., Segrave, R., De Joode, N., Figee, M., & Denys, D. (2019). Efficacy of Invasive and Non-Invasive Brain Modulation Interventions for Addiction. *Neuropsychology Review*, *29*(1), 116–138. https://doi.org/10.1007/s11065-018-9393-5

Manan, H. A., Franz, E. A., Yusoff, A. N., & Mukari, S. Z.-M. S. (2012). Hippocampal-cerebellar involvement in enhancement of performance in word-based BRT with the presence of background noise: An initial fMRI study. *Psychology & Neuroscience*, *5*(2), 247–256. https://doi.org/10.3922/j.psns.2012.2.16

Manjarrez, E., Mendez, I., Martinez, L., Flores, A., & Mirasso, C. R. (2007). Effects of auditory noise on the psychophysical detection of visual signals: Cross-modal stochastic resonance. *Neuroscience Letters*, *415*(3), 231–236. https://doi.org/10.1016/j.neulet.2007.01.030

Mankins, J. C. (1995). *TECHNOLOGY READINESS LEVELS*.

Mantovani, A., Pavlicova, M., Avery, D., Nahas, Z., McDonald, W. M., Wajdik, C. D., Holtzheimer, P. E., George, M. S., Sackeim, H. A., & Lisanby, S. H. (2012). LONG-TERM EFFICACY OF REPEATED DAILY PREFRONTAL TRANSCRANIAL MAGNETIC STIMULATION (TMS) IN TREATMNT-RESISTANT DEPRESSION: Research Article: Long-Term Efficacy of TMS in TRD. *Depression and Anxiety*, *29*(10), 883–890. https://doi.org/10.1002/da.21967

Manuel, A. L., & Schnider, A. (2016). Effect of prefrontal and parietal tDCS on learning and recognition of verbal and non-verbal material. *Clinical Neurophysiology*, *127*(7), 2592–2598. https://doi.org/10.1016/j.clinph.2016.04.015

McDonnell, M. D., Stocks, N. G., Pearce, C. E., & Abbott, D. (2008). *Stochastic resonance: From suprathreshold stochastic resonance to stochastic signal quantization.* Cambridge University Press.

McGuire, S, Walker, M, McGinley, J, Ahmed, N, Szafir, D, & Clark, Torin. (2018). TRAADRE : TRust in Autonomous ADvisors for Robotic Exploration. *Robotics Science and Systems Autonomous Space Robotics Workshop*.

Medeiros, L. F., de Souza, I. C. C., Vidor, L. P., de Souza, A., Deitos, A., Volz, M. S., Fregni, F., Caumo, W., & Torres, I. L. S. (2012). Neurobiological Effects of Transcranial Direct Current Stimulation: A Review. *Frontiers in Psychiatry*, *3*. https://doi.org/10.3389/fpsyt.2012.00110

Mendez-Balbuena, I., Arrieta, P., Huidobro, N., Flores, A., Lemuz-Lopez, R., Trenado, C., & Manjarrez, E. (2018). Augmenting EEG-global-coherence with auditory and visual noise: Multisensory internal stochastic resonance. *Medicine*, *97*(35), e12008. https://doi.org/10.1097/MD.0000000000012008

Moore, S. T., Dilda, V., Morris, T. R., Yungher, D. A., & MacDougall, H. G. (2015). Pre-adaptation to noisy Galvanic vestibular stimulation is associated with enhanced sensorimotor performance in novel vestibular environments. *Frontiers in Systems Neuroscience*, *9*. https://doi.org/10.3389/fnsys.2015.00088

Moore, T. M., Basner, M., Nasrini, J., Hermosillo, E., Kabadi, S., Roalf, D. R., McGuire, S., Ecker, A. J., Ruparel, K., Port, A. M., Jackson, C. T., Dinges, D. F., & Gur, R. C. (2017). Validation of the Cognition Test Battery for Spaceflight in a Sample of Highly Educated Adults. *Aerospace Medicine and Human Performance*, *88*(10), 937–946. https://doi.org/10.3357/AMHP.4801.2017

Mori, T., & Kai, S. (2002). Noise-Induced Entrainment and Stochastic Resonance in Human Brain Waves. *Physical Review Letters*, *88*(21), 218101. https://doi.org/10.1103/PhysRevLett.88.218101

Morphew, E. (2020). Psychological and Human Factors in Long Duration Spaceflight. *McGill Journal of Medicine*, *6*(1). https://doi.org/10.26443/mjm.v6i1.555

Moss, F., Ward, L. M., & Sannita, W. G. (2004). Stochastic resonance and sensory information processing: A tutorial and review of application. *Clinical Neurophysiology*, *115*, 267–281. https://doi.org/10.1016/j.clinph.2003.09.014

Mulavara, A. P., Kofman, I. S., De Dios, Y. E., Miller, C., Peters, B. T., Goel, R., Galvan-Garza, R., & Bloomberg, J. J. (2015). Using low levels of stochastic vestibular stimulation to improve locomotor stability. *Frontiers in Systems Neuroscience*, *9*. https://doi.org/10.3389/fnsys.2015.00117

Munoz, F., Meaney, A., Gross, A., Liu, K., Pouliopoulos, A. N., Liu, D., Konofagou, E. E., & Ferrera, V. P. (2022). Long term study of motivational and cognitive effects of low-intensity focused ultrasound neuromodulation in the dorsal striatum of nonhuman primates. *Brain Stimulation*, *15*(2), 360–372. https://doi.org/10.1016/j.brs.2022.01.014

Myczkowski, M., Dias, A., Luvisotto, T., Arnaut, D., Bellini, B. B., Marcolin, M. A., Mansur, C. G., Rennó, J., Tortella De Souza, G., & Ribeiro, P. L. (2012). Effects of repetitive transcranial magnetic stimulation on clinical, social, and cognitive performance in postpartum depression. *Neuropsychiatric Disease and Treatment*, 491. https://doi.org/10.2147/NDT.S33851

National Census of Fatal Occupational Injuries in 2019. (2020). 10.

Nhut, D. T., & Nam, N. B. (2010). Light-Emitting Diodes (LEDs): An Artificial Lighting Source for Biological Studies. In V. Van Toi & T. Q. D. Khoa (Eds.), *The Third International Conference on the Development of Biomedical Engineering in Vietnam* (Vol. 27, pp. 134–139). Springer Berlin Heidelberg. https://doi.org/10.1007/978-3-642-12020-6_33

Nollet, H., Van Ham, L., Deprez, P., & Vanderstraeten, G. (2003). Transcranial magnetic stimulation: Review of the technique, basic principles and applications. *The Veterinary Journal*, *166*(1), 28–42. https://doi.org/10.1016/S1090-0233(03)00025-X

Nooristani, M., Maheu, M., Houde, M.-S., Bacon, B.-A., & Champoux, F. (2019). Questioning the lasting effect of galvanic vestibular stimulation on postural control. *PLOS ONE*, *14*(11), e0224619. https://doi.org/10.1371/journal.pone.0224619

Oberman, L. M., Enticott, P. G., Casanova, M. F., Rotenberg, A., Pascual-Leone, A., McCracken, J. T., & the TMS in ASD Consensus Group. (2016). Transcranial magnetic stimulation in autism spectrum disorder: Challenges, promise, and roadmap for future research: TMS in ASD. *Autism Research*, *9*(2), 184–203. https://doi.org/10.1002/aur.1567

Oluwafemi, F. A., Abdelbaki, R., Lai, J. C.-Y., Mora-Almanza, J. G., & Afolayan, E. M. (2021). A review of astronaut mental health in manned missions: Potential interventions for cognitive and mental health challenges. *Life Sciences in Space Research*, *28*, 26–31. https://doi.org/10.1016/j.lssr.2020.12.002

Othman, E., Yusoff, A. N., Mohamad, M., Abdul Manan, H., Giampietro, V., Abd Hamid, A. I., Dzulkifli, M. A., Osman, S. S., & Wan Burhanuddin, W. I. D. (2019). Low intensity white noise improves performance in auditory working memory task: An fMRI study. *Heliyon*, *5*(9), e02444. https://doi.org/10.1016/j.heliyon.2019.e02444

Patel, Z. S., Brunstetter, T. J., Tarver, W. J., Whitmire, A. M., Zwart, S. R., Smith, S. M., & Huff, J. L. (2020). Red risks for a journey to the red planet: The highest priority human health risks for a mission to Mars. *Npj Microgravity*, *6*(1), 33. https://doi.org/10.1038/s41526-020-00124-6

Pathak, Y. V., Araújo Dos Santos, M., & Zea, L. (Eds.). (2022). *Handbook of Space Pharmaceuticals*. Springer International Publishing. https://doi.org/10.1007/978-3-030-05526-4

Pereira, L. S., Müller, V. T., da Mota Gomes, M., Rotenberg, A., & Fregni, F. (2016). Safety of repetitive transcranial magnetic stimulation in patients with epilepsy: A systematic review. *Epilepsy & Behavior*, *57*, 167–176. https://doi.org/10.1016/j.yebeh.2016.01.015

Petersen, D. (2003). *Human Error*. ASSE.

Pieters, M. A., & Zaal, P. M. T. (2019). Training for Long-Duration Space Missions: A Literature Review into Skill Retention and Generalizability. *IFAC-PapersOnLine*, *52*(19), 247–252. https://doi.org/10.1016/j.ifacol.2019.12.099

Pineault, K., Pearson, D., Wei, E., Kamil, R., Klatt, B., & Agrawal, Y. (2020). Association Between Saccule and Semicircular Canal Impairments and Cognitive Performance Among Vestibular Patients. *Ear & Hearing*, *41*(3), 686–692. https://doi.org/10.1097/AUD.0000000000000795

Pinedo, C. (2021). *Design and Evaluation of an Achievability Limit Display and Control Response Types for Piloted Planetary Landing*. ProQuest Dissertations & Theses.

Polanía, R., Nitsche, M. A., & Ruff, C. C. (2018). Studying and modifying brain function with non-invasive brain stimulation. *Nature Neuroscience*, *21*(2), 174–187. https://doi.org/10.1038/s41593-017-0054-4

Putman, E. J., Galvan-Garza, R. C., & Clark, T. K. (2021). The Effect of Noisy Galvanic Vestibular Stimulation on Learning of Functional Mobility and Manual Control Nulling Sensorimotor Tasks. *Frontiers in Human Neuroscience, 15*, 756674. https://doi.org/10.3389/fnhum.2021.756674

Rausch, V. H., Bauch, E. M., & Bunzeck, N. (2014). White Noise Improves Learning by Modulating Activity in Dopaminergic Midbrain Regions and Right Superior Temporal Sulcus. *Journal of Cognitive Neuroscience*, *26*(7), 1469–1480. https://doi.org/10.1162/jocn_a_00537

Razza, L. B., De Smet, S., Moffa, A., Sudbrack-Oliveira, P., Vanderhasselt, M.-A., & Brunoni, A. R. (2021). Follow-up effects of transcranial direct current stimulation (tDCS) for the major depressive episode: A systematic review and meta-analysis. *Psychiatry Research*, *302*, 114024. https://doi.org/10.1016/j.psychres.2021.114024

Reis, J., Robertson, E. M., Krakauer, J. W., Rothwell, J., Marshall, L., Gerloff, C., Wassermann, E. M., Pascual-Leone, A., Hummel, F., Celnik, P. A., Classen, J., Floel, A., Ziemann, U., Paulus, W., Siebner, H. R., Born, J., & Cohen, L. G. (2008). Consensus: Can transcranial direct current stimulation and transcranial magnetic stimulation enhance motor learning and memory formation? *Brain Stimulation*, *1*(4), 363–369. https://doi.org/10.1016/j.brs.2008.08.001

Ries, D. T. (2007). The influence of noise type and level upon stochastic resonance in human audition. *Hearing Research*, *228*(1–2), 136–143. https://doi.org/10.1016/j.heares.2007.01.027

Rollock, A. (2023). *Guiding Principles for Prioritizing Use of Emergent Technology Towards Self-Reliant Deep Space Habitats*. Doctoral Dissertation, University of Colorado Boulder. ProQuest.

Romanella, S. M., Mencarelli, L., Seyedmadani, K., Jillings, S., Tomilovskaya, E., Rukavishnikov, I., Sprugnoli, G., Rossi, S., Wuyts, F. L., & Santarnecchi, E. (2023). Optimizing transcranial magnetic stimulation for spaceflight applications. *Npj Microgravity*, *9*(1), 26. https://doi.org/10.1038/s41526-023-00249-4

Romanella, S. M., Sprugnoli, G., Ruffini, G., Seyedmadani, K., Rossi, S., & Santarnecchi, E. (2020). Noninvasive Brain Stimulation & Space Exploration: Opportunities and Challenges. *Neuroscience & Biobehavioral Reviews*, *119*, 294–319. https://doi.org/10.1016/j.neubiorev.2020.09.005

Roscoe, A., & Ellis, G. (1990). *A subjective rating scale for assessing pilot workload in flight: A decade of practical use.* Royal Aerospace Establishment Farnborough (United Kingdom). https://apps.dtic.mil/sti/citations/ADA227864

Rose, R. D., Buckey, J. C., Zbozinek, T. D., Motivala, S. J., Glenn, D. E., Cartreine, J. A., & Craske, M. G. (2013). A randomized controlled trial of a self-guided, multimedia, stress management and resilience training program. *Behaviour Research and Therapy*, *51*(2), 106–112. https://doi.org/10.1016/j.brat.2012.11.003

Roy-O'Reilly, M., Mulavara, A., & Williams, T. (2021). A review of alterations to the brain during spaceflight and the potential relevance to crew in long-duration space exploration. *Npj Microgravity*, *7*(1), 5. https://doi.org/10.1038/s41526-021-00133-z

Rusticus, S. A., & Lovato, C. Y. (2011). *Applying Tests of Equivalence for Multiple Group Comparisons: Demonstration of the Confidence Interval Approach*. https://doi.org/10.7275/D5WF-5P77

Ruzzoli, M., Marzi, C. A., & Miniussi, C. (2010). The Neural Mechanisms of the Effects of Transcranial Magnetic Stimulation on Perception. *Journal of Neurophysiology*, *103*(6), 2982–2989. https://doi.org/10.1152/jn.01096.2009

Salehpour, F., Gholipour-Khalili, S., Farajdokht, F., Kamari, F., Walski, T., Hamblin, M. R., DiDuro, J. O., & Cassano, P. (2020). Therapeutic potential of intranasal photobiomodulation therapy for neurological and neuropsychiatric disorders: A narrative review. *Reviews in the Neurosciences*, *31*(3), 269–286. https://doi.org/10.1515/revneuro-2019-0063

Salehpour, F., Mahmoudi, J., Kamari, F., Sadigh-Eteghad, S., Rasta, S. H., & Hamblin, M. R. (2018). Brain Photobiomodulation Therapy: A Narrative Review. *Molecular Neurobiology*, *55*(8), 6601–6636. https://doi.org/10.1007/s12035-017-0852-4

Salehpour, F., Majdi, A., Pazhuhi, M., Ghasemi, F., Khademi, M., Pashazadeh, F., Hamblin, M. R., & Cassano, P. (2019). Transcranial Photobiomodulation Improves Cognitive Performance in Young Healthy Adults: A Systematic Review and Meta-Analysis. *Photobiomodulation, Photomedicine, and Laser Surgery*, *37*(10), 635–643. https://doi.org/10.1089/photob.2019.4673

Sarica, C., Nankoo, J.-F., Fomenko, A., Grippe, T. C., Yamamoto, K., Samuel, N., Milano, V., Vetkas, A., Darmani, G., Cizmeci, M. N., Lozano, A. M., & Chen, R. (2022). Human Studies of Transcranial Ultrasound neuromodulation: A systematic review of effectiveness and safety. *Brain Stimulation*, *15*(3), 737–746. https://doi.org/10.1016/j.brs.2022.05.002

Sasaki, H., Sakane, S., Ishida, T., Todorokihara, M., Kitamura, T., & Aoki, R. (2008). Suprathreshold stochastic resonance in visual signal detection. *Behavioural Brain Research*, *193*(1), 152–155. https://doi.org/10.1016/j.bbr.2008.05.003

Sayed Daud, S. N. S., & Sudirman, R. (2023). Effect of auditory noise circumstance on visual images encoding based electroencephalography analysis. *International Journal of Healthcare Management*, 1–15. https://doi.org/10.1080/20479700.2023.2198902

Scheldrup, M., Greenwood, P. M., McKendrick, R., Strohl, J., Bikson, M., Alam, M., McKinley, R. A., & Parasuraman, R. (2014). Transcranial direct current stimulation facilitates cognitive multi-task performance differentially depending on anode location and subtask. *Frontiers in Human Neuroscience, 8*. https://doi.org/10.3389/fnhum.2014.00665

Scully, R. R., Basner, M., Nasrini, J., Lam, C., Hermosillo, E., Gur, R. C., Moore, T., Alexander, D. J., Satish, U., & Ryder, V. E. (2019). Effects of acute exposures to carbon dioxide on decision making and cognition in astronaut-like subjects. *Npj Microgravity*, *5*(1), 17. https://doi.org/10.1038/s41526-019-0071-6

Sellaro, R., Nitsche, M. A., & Colzato, L. S. (2016). The stimulated social brain: Effects of transcranial direct current stimulation on social cognition: tDCS and social cognition. *Annals of the New York Academy of Sciences*, *1369*(1), 218–239. https://doi.org/10.1111/nyas.13098

Serafini, G., Pompili, M., Belvederi Murri, M., Respino, M., Ghio, L., Girardi, P., Fitzgerald, P. B., & Amore, M. (2015). The Effects of Repetitive Transcranial Magnetic Stimulation on Cognitive Performance in Treatment-Resistant Depression. A Systematic Review. *Neuropsychobiology*, *71*(3), 125–139. https://doi.org/10.1159/000381351

Sherman, S. O., Greenstein, M., Basner, M., Clark, T. K., & Anderson, A. P. (2023a). Effects of additive sensory noise on cognition. *Frontiers in Human Neuroscience*, *17*, 1092154. https://doi.org/10.3389/fnhum.2023.1092154

Sherman, S. O., Jonsen, A., Lewis, Q., Schlittenhart, M., Szafir, D., Clark, T. K., & Anderson, A. P. (2023b). Training augmentation using additive sensory noise in a lunar rover navigation task. *Frontiers in Neuroscience*, *17*, 1180314. https://doi.org/10.3389/fnins.2023.1180314

Sherman, S. O., Shen, Y.-Y., Gutierrez-Mendoza, D., Schlittenhart, M., Watson, C., Clark, T. K., & Anderson, A. P. (2023c). Additive Sensory Noise Effects on Operator Performance in a Lunar Landing Simulation. *Aerospace Medicine and Human Performance*.

Simonotto, E., Riani, M., Seife, C., Roberts, M., Twitty, J., & Moss, F. (1997). Visual Perception of Stochastic Resonance. *PHYSICAL REVIEW LETTERS*, *78*(6), 4.

Simonotto, E., Spano, F., Riani, M., Ferrari, A., Levrero, F., Pilot, A., Renzetti, P., Parodi, R. C., Sardanelli, F., Vitali, P., Twitty, J., Chiou-Tan, F., & Moss, F. (1999). *FMRI studies of visual cortical activity during noise stimulation*ଝ. 6.

Slack, K. J., Williams, T. J., Schneiderman, J. S., Whitmire, A. M., & Picano, J. J. (2016). *Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders*. 123.

Söderlund, G. B., Sikström, S., Loftesnes, J. M., & Sonuga-Barke, E. J. (2010). *The effects of background white noise on memory performance in inattentive school children*. 10.

Söderlund, G., & Sikström, S. (2008). *Positive effects of noise on cognitve performance: Explaining the Moderate Brain Arousal model*.

Spektr of Failure. (2010). 4.

Stangor, D. C., Jhangiani, D. R., & Tarry, D. H. (2014). *Principles of Social Psychology—1st International Edition*. Victoria, B.C.: BCcampus. Retrieved from https://opentextbc.ca/socialpsychology/

Stefani, S. P., Serrador, J. M., Breen, P. P., & Camp, A. J. (2020). Impact of galvanic vestibular stimulation-induced stochastic resonance on the output of the vestibular system: A systematic review. *Brain Stimulation*, *13*(3), 533–535. https://doi.org/10.1016/j.brs.2020.01.006

Stilling, J. M., Monchi, O., Amoozegar, F., & Debert, C. T. (2019). Transcranial Magnetic and Direct Current Stimulation (TMS/tDCS) for the Treatment of Headache: A Systematic Review. *Headache: The Journal of Head and Face Pain*, *59*(3), 339–357. https://doi.org/10.1111/head.13479

Strangman, G. E., Sipes, W., & Beven, G. (2014). Human Cognitive Performance in Spaceflight and Analogue Environments. *Aviation, Space, and Environmental Medicine*, *85*(10), 1033–1048. https://doi.org/10.3357/ASEM.3961.2014

Summers, J. J., Kang, N., & Cauraugh, J. H. (2016). Does transcranial direct current stimulation enhance cognitive and motor functions in the ageing brain? A systematic review and meta- analysis. *Ageing Research Reviews*, *25*, 42–54. https://doi.org/10.1016/j.arr.2015.11.004

Terry, P. C., Lane, A. M., & Fogarty, G. J. (2003). Construct validity of the Profile of Mood States—Adolescents for use with adults. *Psychology of Sport and Exercise*, *4*(2), 125–139. https://doi.org/10.1016/S1469-0292(01)00035-8

Thair, H., Holloway, A. L., Newport, R., & Smith, A. D. (2017). Transcranial Direct Current Stimulation (tDCS): A Beginner's Guide for Design and Implementation. *Frontiers in Neuroscience*, *11*, 641. https://doi.org/10.3389/fnins.2017.00641

Thirsk, R., Kuipers, A., Mukai, C., & Williams, D. (2009). The space-flight environment: The International Space Station and beyond. *Canadian Medical Association Journal*, *180*(12), 1216–1220. https://doi.org/10.1503/cmaj.081125

Torres, J., Drebing, D., & Hamilton, R. (2013). TMS and tDCS in post-stroke aphasia: Integrating novel treatment approaches with mechanisms of plasticity. *Restorative Neurology and Neuroscience*, *31*(4), 501–515. https://doi.org/10.3233/RNN-130314

Trung, J., Hanganu, A., Jobert, S., Degroot, C., Mejia-Constain, B., Kibreab, M., Bruneau, M.-A., Lafontaine, A.-L., Strafella, A., & Monchi, O. (2019). Transcranial magnetic stimulation improves cognition over time in Parkinson's disease. *Parkinsonism & Related Disorders*, *66*, 3–8. https://doi.org/10.1016/j.parkreldis.2019.07.006

Tyng, C. M., Amin, H. U., Saad, M. N. M., & Malik, A. S. (2017). The Influences of Emotion on Learning and Memory. *Frontiers in Psychology*, *8*, 1454. https://doi.org/10.3389/fpsyg.2017.01454

Usher, M., & Feingold, M. (2000). Stochastic resonance in the speed of memory retrieval. Biological Cybernetics. 83, L11-L16.

van der Groen, O., & Wenderoth, N. (2016). Transcranial Random Noise Stimulation of Visual Cortex: Stochastic Resonance Enhances Central Mechanisms of Perception. *The Journal of Neuroscience*, *36*(19), 5289–5298. https://doi.org/10.1523/JNEUROSCI.4519-15.2016

Van Rooij, S. J. H., Arulpragasam, A. R., McDonald, W. M., & Philip, N. S. (2023). Accelerated TMS - moving quickly into the future of depression treatment. *Neuropsychopharmacology*. https://doi.org/10.1038/s41386-023-01599-z

Voros, J. L., Sherman, S. O., Rise, R., Kryuchkov, A., Stine, P., Anderson, A. P., & Clark, T. K. (2021). Galvanic Vestibular Stimulation Produces Cross-Modal Improvements in Visual Thresholds. *Frontiers in Neuroscience*, *15*, 640984. https://doi.org/10.3389/fnins.2021.640984

Voros, J., Rise, R., Sherman, S., Durell, A., Anderson, A. P., & Clark, T. K. (2022). A machine learning approach to identify stochastic resonance in human perceptual thresholds. *Journal of Neuroscience Methods*, *374*, 109559. https://doi.org/10.1016/j.jneumeth.2022.109559

Waterston, M. L., & Pack, C. C. (2010). Improved Discrimination of Visual Stimuli Following Repetitive Transcranial Magnetic Stimulation. *PLoS ONE*, *5*(4), e10354. https://doi.org/10.1371/journal.pone.0010354

Weigmann, D. A., & Shappell, S. A. (1997). Human Factors Analysis of Postaccident Data: Applying Theoretical Taxonomies of Human Error. *The International Journal of Aviation Psychology*, *7*(1), 67–81. https://doi.org/10.1207/s15327108ijap0701_4

Wen, T. (2020, April 9). An astronaut's guide to surviving isolation. *BBC*. https://www.bbc.com/future/article/20200408-an-astronauts-guide-to-surviving-isolation

Whelan, H. T. (2000). The NASA light-emitting diode medical program—Progress in space flight and terrestrial applications. *AIP Conference Proceedings*, *504*, 37–43. https://doi.org/10.1063/1.1302454

Wickens, C. D., Hollands, J. G., Banbury, S., & Parasuraman, R. (2013). *Engineering psychology and human performance* (Fourth edition). Pearson.

Wicklegren, Wayne. (1977). Speed-Accuracy Tradeoff and Information Processing Dynamics. *Acta Psychologica*, *67*(85).

Wilkinson, A., Patel, R., Darzi, A., Singh, H., & Leff, D. R. (2022). Transcranial Direct-Current Stimulation (tDCS) attenuates perceived temporal demand during simulated laparoscopic tasks. In *Current Research in Neuroadaptive Technology* (pp. 139–157). Elsevier. https://doi.org/10.1016/B978-0-12-821413-8.00013-0

Wilkinson, D., Nicholls, S., Pattenden, C., Kildu, P., & Milberg, W. (2008). Galvanic vestibular stimulation speeds visual memory recall. *Exp Brain Res*, 6.

Wróbel, K. (2021). Searching for the origins of the myth: 80% human error impact on maritime safety. *Reliability Engineering & System Safety*, *216*, 107942. https://doi.org/10.1016/j.ress.2021.107942

Wuehr, M., Nusser, E., Krafczyk, S., Straube, A., Brandt, T., Jahn, K., & Schniepp, R. (2016). Noise-Enhanced Vestibular Input Improves Dynamic Walking Stability in Healthy Subjects. *Brain Stimulation*, *9*(1), 109–116. https://doi.org/10.1016/j.brs.2015.08.017

Yavari, F., Jamil, A., Mosayebi Samani, M., Vidor, L. P., & Nitsche, M. A. (2018). Basic and functional effects of transcranial Electrical Stimulation (tES)—An introduction. *Neuroscience & Biobehavioral Reviews*, *85*, 81–92. https://doi.org/10.1016/j.neubiorev.2017.06.015

Yoo, S.-S. (2018). Technical Review and Perspectives of Transcranial Focused Ultrasound Brain Stimulation for Neurorehabilitation. *Brain & Neurorehabilitation*, *11*(2), e16. https://doi.org/10.12786/bn.2018.11.e16

Zeng, F.-G., Fu, Q.-J., & Morse, R. (2000). Human hearing enhanced by noiseq,. *Brain Research*, 5.

Zuzula, E. A., Dixon, J. B., Davis, E., Bretl, K., Pinedo, C., & Clark, T. K. (2018). A numerical algorithm to estimate an achievability limit for crewed planetary landing. *2018 IEEE Aerospace Conference*, 1–7. https://doi.org/10.1109/AERO.2018.8396484