How can machine learning methods be used to objectively measure the presence and severity of tinnitus? What are its implications?

WARWICK BUSINESS SCHOOL
THE UNIVERSITY OF WARWICK

Student ID: u1730484

Module Code: IB3K50

Module Title: Artificial Intelligence for Business

Deadline: 25th January 2021

Wordcount: 1983

Table of Contents

1. Abstract

Chronic tinnitus is a debilitating condition affecting around 5-15% of adults. There is currently no clinically used way of objectively measuring tinnitus, so researchers are solely reliant on subjective feedback to assess responses to treatments. Previous studies already explored the plausibility of using functional near-infrared spectroscopy due to its sensitivity to detect tinnitus related neural activity. Statistical methods applied to the collected data allow machine learning (ML) methods to discover non-linear relationships in data, achieving higher accuracies in distinguishing patients with tinnitus from those without, whilst also predicting its severity. Due to the non-linear nature of neural activity, these methods could potentially lead researchers closer to understanding the relationships between different regions of the brain, leading to numerous other breakthroughs in neurological sciences. However, researchers must stay vigilant of employing ML methods carelessly as there exists a trade-off between predictive accuracy and explicability, which could lead to biased results.

2. Introduction

It is well accepted amongst scientists that the human brain is an interconnected web that contains billions of neurons interacting with one another in response to various stimuli, but it is still unclear how these neurons interact and what determines their response patterns (Herculano-Houzel, 2012). There already exist several methods to studying this field, however, the rapid pace of technological development now allows for more precise measurements to be conducted (Husain and Schmidt, 2014). In the past, linear models and independent component analysis were commonly used to study these findings, but today scientists are drawn more towards exploring artificial intelligence (AI) based approaches.

There is currently no clinically used way of measuring the presence or severity of tinnitus, but the development of such a technology could help better understand it. AI can offer a lot in terms of neurological research, diagnosis and therapeutic interventions as it closely follows the computational power of the brain, so researchers are increasingly applying this technology to drive their investigations (Belic et al., 2019).

3. Literature Review

The first major breakthrough in understanding tinnitus came with the introduction of animal models, which demonstrated that the “phantom auditory percepts” are alterations of neural activity in the central auditory system (Lonsbury-Martin, 1981; Jastreboff and Sasaki, 1986; Chen and Jastreboff, 1995). Soon it was identified that tinnitus is a systemic problem that stems from an imbalance in the inputs to the auditory neurons (Heffner and Harrington, 2002; Kaltenbach, 2011), but there is a clash on opinions over understanding the nature of the neural code behind it (Eggermont and Roberts, 2004). Researchers in the profession agree that exploring the neural origins of tinnitus would greatly advance the development of a treatment (Eggermont and Roberts, 2004; Kaltenbach, 2011; Husain and Schmidt, 2014).

Several studies have used functional near-infrared spectroscopy (fNIRS) to record brain activity in the resting state and when evoked in response to sound, showing an effectiveness of fNIRS to detect tinnitus-related neural activity (Martin Schecklmann et al., 2014; Mohamad et al., 2016; Juan San Juan et al., 2017; Basura et al., 2018). These reports used simple statistical analysis to report findings, however, ML algorithms are better suited to finding patterns in complex data with non-linear relationships such as fNIRS recordings are, with multiple channels, conditions, and demographics (Bzdok et al., 2018). ML methods are able to reduce the number of input channels necessary, by identifying channels unrelated to tinnitus (Shoushtarian, 2020). A previous study used similar ML methods to classify pain type with an accuracy of 90% using fNIRS features (Raul Fernandez et al., 2019), and have demonstrated their power in aiding healthcare professionals to better understand the nervous system and the brain (Seo et al., 2020; Clifford, 2020; Han et al., 2020).

This paper will examine an application of machine learning methods to fNIRS data in order to establish the first scientifically reviewed way to objectively measure tinnitus, improving the treatment prospects of the condition.

4. The Application of AI in Objectively Measuring Tinnitus

4.1 Significance of Understanding Tinnitus

Tinnitus is the perception of a phantom noise affecting around 5-15% of the population, with 1-3% of the population suffering a significant deterioration of quality of life such as sleep disturbance, psychiatric distress and general work impairment. (Eggermont and Roberts, 2004; Schaette and McAlpine, 2011; De Ridder et al., 2014). An estimated 14 to 16 million people are constantly seeking medical help, however, there currently exist no known clinically used treatment of tinnitus, nor is there a clinically used way to objectively measure the presence and severity of the condition, which considerably hinders the development of a treatment (De Ridder et al., 2014; Rosen, 2018). Fortunately, developments in our ability to better understand the relationships between brain regions, demonstrate positive prospects in understanding the origin of tinnitus. The employment of ML classification algorithms put clinical trials onto an entirely new path as a reliable objective measure of the condition will enable the monitoring of changes induced by potential treatments (Alturi et al., 2016; Shoushtarian et al., 2020).

4.2 Objective Measurement of Tinnitus Using fNIRS and Machine Learning Methods

A study conducted by researchers collaborating with The Bionics Institute, the Victorian Government's Operational Infrastructure Program, and Action on Hearing Loss used fNIRS scans of the brain, which uses near-infrared light and signal processing to allow real-time monitoring of changes in blood-haemoglobin (NASA Technology Transfer Program). Neuronal activity in the brain utilises oxygen that is transported through red blood cells in the form of oxygenated haemoglobin, and fNIRS measures this change (Alturi et al., 2016; Shoushtarian et al., 2020).

Data were collected using a total of 16 sources and 16 detectors that are placed over the head of study participants to form channels between different brain regions known to be associated with tinnitus in a way illustrated below.

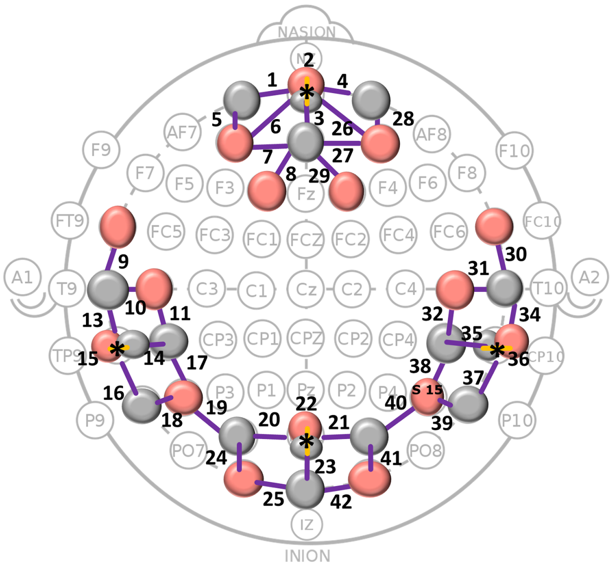

Figure 1 – Sixteen sources (red) and sixteen detectors (grey) forming 4 short (*) and 36 long channels (line) (Source: Shoushtarian et al., 2020)

Data were collected of the 36 long channels and 4 short ones. Long channels collected data from responses to auditory and visual stimuli, while the short channels were controls to improve the veracity of the data. The short channels collected signals from the superficial regions, such as the skull and scalp, which added noise to the data, so any interference was easily filtered out using custom MATLAB functions.

Measurements were taken of participant's brain activity in a resting state, with no external stimuli, and in evoked state with visual and audible stimuli. The data collected followed the "Data Iceberg" model which is an excellent support to discover underlying patterns and behaviours that cause an observable event, which in this case is the increase in blood-haemoglobin levels (Yang, 2020).

4.3 Machine Learning Classification Methods

Machine learning methods, such as feature selection and classifiers were used to compare features of the resting state and evoked state signals from fNIRS channels across the different brain regions. Feature selection algorithms automatically filtered channels which can best be used to explain distinctions between groups. Information Gain, which is a way to measure entropy in data, was used to select the most relevant features. Then four classification methods were used to classify participants as controls, or patients with tinnitus, and to differentiate between the severity of their tinnitus. The classification methods were Naïve Bayes (NB), K-nearest neighbour (KNN), Rule Induction and Artificial Neural Networks (ANN) (Shoushtarian et al., 2020).

NB and ANN are the most common ways used in pattern recognition in fNIRS scans, therefore, their more detailed explanation is necessary to understand their workings. NB is a simple, but highly scalable collection of algorithms, that is extremely fast and have worked quite well in many-real world situations, requiring only a small amount of data to estimate the necessary parameters. NB looks at each pair of fNIRS channels independently and classifies as them "Yes" or "No" for being associated with tinnitus, which then it aggregates using the maximum likelihood method (Kupervasser and Vardy, 2002). ANN is a more complex computing system mimicking the functioning of biological neural networks organised into aggregated layers, associated with a weight. Each fNIRS channel is classified as an input node interconnected through hidden layers, where signals are passed through a weight-based activation function-network that ultimately formulates the output, which is tinnitus (Shoushtarian, 2020). The function is trained to identify the weights of the input channels leading to the output of tinnitus through back propagation until it has adjusted the network to correctly assign a weight to each channel (Medium, 2017).

In the study 10-fold cross validation was used which is the random partitioning of the dataset into 10 subsets, keeping one for testing, while the other nine are used for training, iterating through the whole 10 subsets, one by one. Naïve Bayes classifiers were 78.3% accurate in predicting participants with tinnitus, and the ANN was 87.32% accurate in predicting the severity of tinnitus (Appendix 1).

5.0 A Critical Evaluation of the Benefits of Using Machine Learning Algorithms

An advantage of using AI classification models is that they can quickly review large quantities of data and discover trends and patterns that would otherwise not be apparent to us (Johnson, 2019). Previous research has identified changes in a variety of locations within the central nervous system associated with tinnitus but used simple statistical analysis to study either resting state, or evoked brain activity. This left researchers no better than guessing when attempting to identify factual relationships between multi-state neural activity in the brain regions investigated (Lanting et al., 2009; Chen et al., 2017). The model developed through the study has a 78.3% accuracy in identifying patients suffering from tinnitus, and an 87.32% accuracy in predicting the severity of the condition, which is a crucial development in the objective measurability of tinnitus (Shoushtarian, 2020). This gives researchers the ability to accurately test potential treatments of tinnitus with an objective way of measuring the responses. More importantly, this finding has wider implications in the neurological sciences, and neurological disease monitoring and management. Under similar research design, illnesses such as Alzheimer's, ALS or Dementia can be investigated with ML algorithms uncovering previously unknown relationships between the gradual deterioration in neural activity giving us an ability to develop better ways of slowing disease progression, or even allow possible reversal.

Another advantage of applying ML in studying the origins of tinnitus is the self-learning capabilities of the algorithm over time. The more data an algorithm analyses, the more accurate it becomes. Feature extraction algorithms can identify the most relevant input channels, thus redundant channels can be eliminated leading to faster computation time and improved accuracy over time, which allows the model to be scaled with larger clinical trials (Shoustharian et al., 2020). Moreover, classifiers such as ANN work without the need to rely on explicit knowledge of parameters prior to learning, having the ability to derive outputs not limited to inputs provided. These new relevant relationships might result in the discovery of significant new connections driving research.

5.1 A Critical Evaluation of the Limitations of Using Machine Learning Algorithms

In 2016, Microsoft designed an AI-powered social chatbot, Tay, to engage with people on social media and to learn in the process, with the purpose of demonstrating the advantages of AI's self-learning capabilities. Within hours of interacting with pranksters, she began posting racist and controversial tweets, supporting conspiracy theories and making very questionable comments, all because the development team overlooked basic best practice principles during the development phase (Vanian, 2018). Reflecting on this example, we can identify a bias problem when dealing with self-learning algorithms, with a trade-off between the predictive accuracy of classifier algorithms and their explicability (Kaushal et al., 2003). Biased ANN algorithms will express outputs confidently even when incorrect, having no ability to explain their line of thinking, self-reinforcing their own biases (Clifford, 2020). Introducing biased technology as such to clinical trials can be dangerous for two reasons. Firstly, it might lead to conclusions incorrectly contradicting the findings of previous studies leading to a halt in progression and expended resources. Secondly, the majority of neurological diseases are life-threatening, meaning biased algorithms can lead to fatal outcomes in clinical trials, let alone in the wider health care system if clinically implemented.

Another limitation that is important to consider is the nature of data collected. fNIRS is a relatively simple technology to study the workings of the brain which is useful only to study the outer regions of the brain. This makes the findings to be not fully representative. Functional magnetic resonance imaging (fMRI), another brain imaging technology used in studying tinnitus, can be used to investigate the brain as a whole, but this technology produces spaciotemporal data represented as a 4D matrix: data in a 3D space, and in time (Atluri et al., 2016). These fMRI scans require categorically more sophisticated storage and data analytics capabilities if a similar number of input channels are to be investigated (Ugurbil, 2013). This is why a reduction in the number input channels would assist in developing more clinically usable set-ups to further investigate tinnitus related activity.

6.0 Conclusion

Despite the risks associated with the application of ML methods in healthcare, they provide enormous potential to revolutionise research, diagnostics, management, and progression monitoring of neurological disorders. The technology might be in its early stages, but the course for further improvement necessary in data analytics is clearly established. fNIRS scans proved to be effective in providing a clear framework to which classification algorithms can be applied to in order to objectively measure the presence and severity of tinnitus. Although classification is not 100% accurate, applying the model to larger quantities of data will result in the continuous improvement of its predictive accuracy if kept free from biases. Tackling these data science challenges arising from neurological applications will have implications beyond the domain of neuroscience, such as in climate science, sociology and epidemiology, areas in which spatiotemporal data-characteristics are inherent (Ugurbil, 2013).

7.0 References

Atluri, G. et al. (2016) 'The Brain-Network Paradigm: Using Functional Imaging Data to Study How the Brain Works', Computer, 49(10), pp. 65–71. doi: 10.1109/MC.2016.307.

Basura, G. J. et al. (2018) 'Human central auditory plasticity: A review of functional near-infrared spectroscopy (fNIRS) to measure cochlear implant performance and tinnitus perception', Laryngoscope investigative otolaryngology, 3(6), pp. 463–472. doi: 10.1002/lio2.185.

Bzdok, D., Altman, N. and Krzywinski, M. (2018) 'Statistics versus machine learning', Nature methods, 15(4), pp. 233–234. doi: 10.1038/nmeth.4642.

Belić, M. et al. (2019) 'Artificial intelligence for assisting diagnostics and assessment of Parkinson's disease—A review', Clinical Neurology and Neurosurgery, 184, p. 105442. doi: 10.1016/j.clineuro.2019.105442.

Chen, G. D. and Jastreboff, P. J. (1995) 'Salicylate-induced abnormal activity in the inferior colliculus of rats', Hearing research, 82(2), pp. 158–178. doi: 10.1016/0378-5955(94)00174-o.

Chen, Y.-C. et al. (2017) 'Resting-State Brain Abnormalities in Chronic Subjective Tinnitus: A Meta-Analysis', Frontiers in human neuroscience, 11, p. 22. doi: 10.3389/fnhum.2017.00022.

Clifford, G. D. (2020) 'The Future AI in Healthcare: A Tsunami of False Alarms or a Product of Experts?' Available at: http://0-search.ebscohost.com.pugwash.lib.warwick.ac.uk/login.aspx?direct=true&db=edsarx&AN=edsarx.2007.10502&site=eds-live (Accessed: 7 January 2021).

De Ridder, D. et al. (2014) 'An integrative model of auditory phantom perception: Tinnitus as a unified percept of interacting separable subnetworks', Neuroscience and Biobehavioral Reviews, 44, pp. 16–32. doi: 10.1016/j.neubiorev.2013.03.021.

Eggermont, Jos J, and Larry E Roberts. "The neuroscience of tinnitus." Trends in neurosciences vol. 27,11 (2004): 676-82. doi:10.1016/j.tins.2004.08.010

Han, C. et al. (2020) 'Bridging the gap between AI and Healthcare sides: towards developing clinically relevant AI-powered diagnosis systems'. Available at: http://0-search.ebscohost.com.pugwash.lib.warwick.ac.uk/login.aspx?direct=true&db=edsarx&AN=edsarx.2001.03923&site=eds-live (Accessed: 7 January 2021).

Heffner, H. E. and Harrington, I. A. (2002) 'Tinnitus in hamsters following exposure to intense sound', Hearing Research, 170(1), pp. 83–95. doi: 10.1016/S0378-5955(02)00343-X.

Herculano-Houzel, S., 2012. The remarkable, yet not extraordinary, human brain as a scaled-up primate brain and its associated cost. PNAS, 109(1), pp.661-668.

Husain, F. T. and Schmidt, S. A. (2014) 'Using resting state functional connectivity to unravel networks of tinnitus', Hearing Research, 307, pp. 153–162. doi: 10.1016/j.heares.2013.07.010.

Jastreboff, P. J. and Sasaki, C. T. (1986) 'Salicylate-induced changes in spontaneous activity of single units in the inferior colliculus of the guinea pig', The Journal of the Acoustical Society of America, 80(5), pp. 1384–1391. doi: 10.1121/1.394391.

Johnson, S. L. J. (2019) 'AI, Machine Learning, and Ethics in Health Care', Journal of Legal Medicine, 39(4), pp. 427–442. Available at: http://0-search.ebscohost.com.pugwash.lib.warwick.ac.uk/login.aspx?direct=true&db=edshol&AN=edshol.hein.journals.jlm39.34&site=eds-live (Accessed: 8 January 2021).

Juan San Juan et al. (2017) 'Tinnitus alters resting state functional connectivity (RSFC) in human auditory and non-auditory brain regions as measured by functional near-infrared spectroscopy (fNIRS)', PLoS ONE, 12(6), p. e0179150. doi: 10.1371/journal.pone.0179150.

Kaltenbach, J. A. (2011) ‘Tinnitus: Models and mechanisms’, Hearing Research, 276(1), pp. 52–60. doi: 10.1016/j.heares.2010.12.003.

Kaushal, R., Shojania, K. G. and Bates, D. W. (2003) ‘Effects of computerized physician order entry and clinical decision support systems on medication safety: a systematic review’, Archives of internal medicine, 163(12), pp. 1409–1416. doi: 10.1001/archinte.163.12.1409.

Kupervasser, O. and Vardy, A. (2002) ‘The Mysterious Optimality of Naive Bayes: Estimation of the Probability in the System of “Classifiers”’. doi: 10.1134/S1054661814010088.

Lanting, C. P., de Kleine, E. and van Dijk, P. (2009) ‘Neural activity underlying tinnitus generation: Results from PET and fMRI’, Hearing Research, 255(1), pp. 1–13. doi: 10.1016/j.heares.2009.06.009.

Lonsbury-Martin, B. L. and Martin, G. K. (1981) ‘Effects of moderately intense sound on auditory sensitivity in rhesus monkeys: behavioral and neural observations’, Journal of neurophysiology, 46(3), pp. 563–586. doi: 10.1152/jn.1981.46.3.563.

Martin Schecklmann et al. (2014) ‘Functional Near-Infrared Spectroscopy to Probe State- and Trait-Like Conditions in Chronic Tinnitus: A Proof-of-Principle Study’, Neural Plasticity, 2014. doi: 10.1155/2014/894203.

Medium. 2017. *Applied Deep Learning - Part 1: Artificial Neural Networks*. [online] Available at: <https://towardsdatascience.com/applied-deep-learning-part-1-artificial-neural-networks-d7834f67a4f6> [Accessed 25 January 2021].

Mohamad Issa et al. (2016) ‘Human Auditory and Adjacent Nonauditory Cerebral Cortices Are Hypermetabolic in Tinnitus as Measured by Functional Near-Infrared Spectroscopy (fNIRS)’, Neural Plasticity, 2016. doi: 10.1155/2016/7453149.

NASA Technology Transfer Program. 2021. Patent Details. [online] Available at: <https://technology.nasa.gov/patent/LEW-TOPS-84> [Accessed 20 January 2021].

Raul Fernandez Rojas, Xu Huang and Keng-Liang Ou (2019) ‘A Machine Learning Approach for the Identification of a Biomarker of Human Pain using fNIRS’, Scientific Reports, 9(1), pp. 1–12. doi: 10.1038/s41598-019-42098-w.

Rosen, M., 2018. Tinnitus Prevention, Treatment, Ringing In Ears. [online] AARP. Available at: <https://www.aarp.org/health/healthy-living/info-2014/6-ways-to-tame-tinnitus.html> [Accessed 23 January 2021].

Schaette, R. and McAlpine, D. (2011) “Tinnitus with a Normal Audiogram: Physiological Evidence for Hidden Hearing Loss and Computational Model” Journal of Neuroscience, 31 (38) 13452-13457; DOI:10.1523/JNEUROSCI.2156-11.2011

Seo, S. et al. (2020) ‘Artificial neural network for Slice Encoding for Metal Artifact Correction (SEMAC) MRI’, Magnetic Resonance in Medicine, 84(1), p. 263. Available at: http://0-search.ebscohost.com.pugwash.lib.warwick.ac.uk/login.aspx?direct=true&db=edb&AN=142337018&site=eds-live (Accessed: 23 January 2021).

Shoushtarian, M. et al. (2020) ‘Objective measurement of tinnitus using functional near-infrared spectroscopy and machine learning’, PloS one, 15(11), p. e0241695. doi: 10.1371/journal.pone.0241695.

Uğurbil, K. et al. (2013) ‘Pushing spatial and temporal resolution for functional and diffusion MRI in the Human Connectome Project’, NeuroImage, 80, pp. 80–104. doi: 10.1016/j.neuroimage.2013.05.012.

Vanian, J., 2018. Unmasking A.I.’S Bias Problem. [online] Fortune. Available at: <https://fortune.com/longform/ai-bias-problem/> [Accessed 24 January 2021].

Yang, Y 2020, Lecture Resources Week 1 Video 2: Big Data Analytics, lecture notes, Artificial Intelligence for Business IB3K50, University of Warwick, delivered October 2020.

8.0 Appendix

Classifiers and features with highest accuracy for predicting participants with tinnitus and controls.

Classifier	features	Sensitivity	Specificity	Accuracy
Naïve Bayes	Auditory response	72.33%	64.25%	78.3%
Rule Induction	Combined auditory, visual and connectivity	80.66%	67.33%	75.09%
Naïve Bayes	Combined auditory, visual and connectivity	86.42%	61.25%	74.75%
Neural Network	Combined auditory, visual and connectivity	71.41%	74.62%	72.33%

https://doi.org/10.1371/journal.pone.0241695.t003

Figure 2 – "Classifiers and features with highest accuracy for predicting participants with tinnitus and controls"
Source: https://doi.org/10.1371/journal.pone.0241695.t003

Classifiers and features with highest accuracy for predicting severity of tinnitus (slight/ mild n = 18, versus moderate/ severe n = 7) as rated using the Tinnitus Handicap Inventory (THI).

Classifier	features	Sensitivity	Specificity	Accuracy
Neural network	Connectivity features	51.23%	95.12%	87.32%
KNN(K = 1)	Connectivity features	50.86%	90.21%	81.22%
Rule Induction	Connectivity features	34.63%	90.06%	76.53%

https://doi.org/10.1371/journal.pone.0241695.t004

Figure 3 – "Classifiers and features with highest accuracy for predicting severity of tinnitus
Source: https://doi.org/10.1371/journal.pone.0241695.t003