Spontaneous Neuronal Signaling is Inherently Musical and Mathematical: Insight into the Universal Human Affinity for Music

Thomas B. Shea\textsuperscript{1,}\textsuperscript{*} and Ruth Remington\textsuperscript{2}

\textsuperscript{1}Department of Biological Sciences, UMass Lowell, Lowell, MA 01821, USA  
\textsuperscript{2}Department of Nursing, Framingham State University, Framingham, MA, USA

Received: August 27, 2018 Revised: October 8, 2018 Accepted: October 20, 2018

Abstract:

Objective: Audio files of spontaneous signal streams generated by \textit{ex vivo} neuronal networks cultured on multi-electrode arrays generated an oscillating sine wave with an inherent musical quality. This was not anticipated considering that synaptic signals are “all - or – none”, and therefore digital, events.

Methods: These findings may provide insight into why music can be perceived as pleasurable and invoke a calm mood despite that music is ultimately perceived and stored as a series of digital signals; it is speculated that music may reinforce and/or enhance this spontaneous digital stream.

Results and Conclusion: These findings also support the relationship between music and mathematics.

Keywords: Multi-electrode array, Neurons, Music, Signaling, Binary, Inhibitory.

1. INTRODUCTION

Music is often referred to as a universal language [1]. While distinct differences are observed among cultures, music is prevalent in all cultures [2], which may derive from the ability of some forms of music to provoke an emotional response and to instill a calming mood [3, 4]. Music has been utilized as therapy even in preliterate cultures and currently for both children and adults affected a variety of conditions that are accompanied by depression or agitation [5 - 10].

The sound is initially perceived as sonic vibrations that induce vibration of eardrum, which is sequentially transmitted to auditory neurons. Information regarding pitch and volume is delivered by differential stimulation of auditory sensory neurons. However, continued transmission to the central nervous system is \textit{via} all - or - none synaptic signaling. Importantly, all sound, including music, is therefore ultimately perceived and stored in memory, as a series of digital signals. Pleasing sensations arising from hearing music are of necessity therefore derived from a corresponding sequence of synaptic pulses that has been stripped of the original analog nature. It remains unclear as to how the digital translation of music can retain what is perceived as pleasurable. To address this, we examined synaptic signal streams generated by neuronal networks established on multi-electrode arrays (MEAs) that interfaced with computer software.

\textsuperscript{*} Address correspondence to this author at the Department of Biological Sciences, UMass Lowell, Lowell MA 01821, USA; Tel: 978-934-2881; E-mail: thomas_shea@uml.edu
2. METHODS

Primary murine embryonic cortical neurons harvested at day 17 of gestation from C57B/6 mice were plated and maintained in commercial Multi-Electrode Array (MEA) culture chambers (Multichannel Systems; Fig. 1A). Sacrifice of the pregnant female mice and generation of cultures were according to a protocol approved by this institution’s Institutional Animal Care and Use Committee. Neuronal signaling was monitored and recorded by interfacing MEAs with MatLab software as described in detail previously [11].

Signal profiles (15 sec in duration) recorded between two electrodes that were demonstrably synaptically-connected by neuronal clusters (e.g., Fig. 1C) were processed via the voltage-controlled oscillator (VCO) with a continuous tuning range [12] as detailed in the Signal Processing Toolbox of MathWorks (https://www.mathworks.com/help/signal/ref/vco.html). Baseline tone and range for VCO were arbitrarily selected.

3. RESULTS

Within approximately one month in culture, these neurons form a functional network that elaborates regular spontaneous signals among interconnected neurons (Fig. 1) [11]. Spontaneous signals exhibited a regular amplitude (40.0 ± 5.0 µV), duration (0.8 ± 0.2 sec, mean ± SD, n=20) and periodicity (intervals of 4.2 ± 0.3 sec between events (n=7).

Audio files of spontaneous signal streams generated by a VCO generated an oscillating sine wave with an inherent musical quality (Supplemental files 1 and 2). As with graphical displays of signaling streams (Fig. 1C), audio streams contained signals of apparently identical amplitude, range and periodicity, that remained in relative synchrony with occasional drifts out of phase among signaling neurons.
4. DISCUSSION

Despite the random synaptogenesis inherent in dissociated cultures, ex vivo neuronal networks neurons retain the ability to transmit information in an organized manner [13]. Notably, synaptic signals are comprised of multiple all - or - none signals and therefore are inherently digital. While graphical representation of these signal streams revealed regular oscillations that were shared among synaptically-connected neurons, displaying them as audio files nevertheless revealed an unanticipated musical nature. While the perception of music is complex and involves multiple cortical regions [14, 15], our findings lead us to speculate that the digital input from music may also encompass an underlying reinforcement and/or augmentation of spontaneous signaling patterns. Herein, the consistent stream of spontaneous signals varied in pitch but not volume. Spontaneous signals may, therefore, represent a “background” continuous pulse. Music can modulate activity in brain structures involved in emotion [3]. While music may simply invoke a calm mood by masking background noise [16], music may also influence brain activity in the same sense as biofeedback can positively influence mood [17]. In this regard, the intrinsic oscillatory properties of neurons have been suggested to underlie brainwaves [18]. With particular regard to music, auditory feedback can be as effective as more conventional visual feedback approaches [15, 19] and auditory biofeedback can also enhance musical performance [20].

Digital and musical aspects of spontaneous signal streams provide additional potential insight with regard to the relationship between music and mathematics. Mathematics has long been regarded as a universal language since it relies on numbers and consistent operations, although this terminology has been met with a degree of a practical challenge since comprehension is dependent upon literacy [21 - 23]. Connections have been recognized between music and mathematics in terms of logic and organization [4, 24, 25]. Basic mathematical ideas can be recognized within music and, conversely, mathematical consideration of patterns can expose organizing principles of music [26]. Mathematics has been studied in the context of artificial neural networks [27]. In this regard, we have demonstrated key processing similarities between artificial neural networks (which consist of software-defined nodes that are designed to approximate neurons) and our ex vivo neuronal networks (which consist of bona-fide neurons) [28, 29]. Music consists of pitch, tone, volume and rhythm. The rhythm component is well-recognized as mathematical in that, it consists of a sequence of pulses at regular intervals [30]. The findings herein underscore that the additional components - pitch, tone and volume – are also mathematical. A corollary of these findings is that music can be considered as an analog expression of mathematics. As such, music and mathematics can be considered as two dialects of a single language.

Herein, we have only examined simple signaling generated by dissociated ex vivo neuronal networks. Since the MEA system allows external stimulation, neuronal network signaling is altered in response to external stimulation [11], this system would accommodate the analysis of synaptic signaling patterns arising from the various digitized musical input. Since these networks can display complex signaling patterns [13], this system would also allow examination of whether VCO processing of all synaptic signaling reveals an inherent musical nature or whether such is confined to only spontaneous, oscillatory patterns as observed herein. Further examination of synaptic signaling streams may provide additional insight into the human affinity for music.

CONCLUSION

The inherent musical quality of spontaneous signal streams, despite that they are digital in nature, prompts the speculation that music may provide a calming influence by reinforcement of this spontaneous digital stream. These findings also support the relationship between music and mathematics.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The protocol is approved by The University of Massachusetts Lowell’s Institutional Animal Care.

HUMAN AND ANIMAL RIGHTS

No animals/humans were used for studies that are the basis of this research.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.
ACKNOWLEDGEMENTS

This research was supported by US Army Research Office Contract W911NF1110125.

SUPPLEMENTARY MATERIAL

Supplementary material is available on the publishers Web site along with the published article.

REFERENCES

[1] Campbell PS. Music, the universal language: Fact or fallacy? Int J Music Educ 1997; 29: 32-9. [http://dx.doi.org/10.1177/025576149702900105]

[2] Cross I. Music and Biocultural Evolution In: The Cultural Study of Music (Clayton M, Herber T, Middleton R, eds) Routledge New York. 2012; pp. 17-28.

[3] Koelsch S. Brain correlates of music-evoked emotions. Nat Rev Neurosci 2014; 15: 170-80. [http://dx.doi.org/10.1038/nrn3666]

[4] Remington R. Calming music and hand massage with agitated elderly. Nurs Res 2002; 51: 312-23. [http://dx.doi.org/10.1097/00006199-200209000-00008]

[5] Clare M. Soothing sounds: Reducing agitation with music therapy. Br J Healthc Assist 2014; 8: 190-5. [http://dx.doi.org/10.12968/bjha.2014.8.4.190]

[6] Plotkin WB. On the self-regulation of the occipital alpha rhythm: Control strategies, states of consciousness, and the role of physiological feedback. J Exp Psychol Gen 1976; 105(1): 66-99. [http://dx.doi.org/10.1037/0096-3445.105.1.66]

[7] Thaut MH. Music as therapy in early history. Prog Brain Res 2015; 217: 143-58. [http://dx.doi.org/10.1016/bs.pbr.2014.11.025]

[8] van Assche E, De Backer J, Vemote R. Music therapy and depression. Tijdschr Psychiatr 2015; 57: 823-9.

[9] Whitford T. Is mathematics a universal language? Teach Child Math 2009; 16: 276-83.

[10] Yinger OS, Gooding L. Music therapy and music medicine for children and adolescents. Child Adolesc Psychiatr Clin N Am 2014; 23: 535-53. [http://dx.doi.org/10.1016/j.chc.2013.03.003]

[11] Zemianek J, Serra M, Guaraldi M, Shea TB. Stimulation with a low-amplitude, digitized synaptic signal to invoke robust activity within neuronal subpopulations on multielectrode arrays. Biotechniques 2012; 52: 177-82.

[12] Jooiay A, Chang MCF. A V-band voltage controlled oscillator with greater than 18GHz of continuous tuning-range based on orthogonal E mode and H mode control. In: Radio Frequency Integrated Circuits Symposium (RFIC). 2011; 5: pp. 1-4. IEEE

[13] Lee S, Zemianek J, Shultz A, et al. Synaptic signal streams generated by ex vivo neuronal networks contain non-random, complex patterns. Int J Dev Neurosci 2014; 38: 184-94. [http://dx.doi.org/10.1016/j.jdevneu.2014.08.008]

[14] Koelsch S, Siebel WA. Towards a neural basis of music perception. Trends Cogn Sci 2005; 9: 578-84. [http://dx.doi.org/10.1016/j.tics.2005.10.001]

[15] Platel H, Price C, Baron JC, et al. The structural components of music perception. A functional antitomical study. Brain 1997; 120: 229-43. [http://dx.doi.org/10.1093/brain/120.2.229]

[16] Goddaer J, Abraham IL. Effects of relaxing music on agitation during meals among nursing home residents with severe cognitive impairment. Arch Psychiatr Nurs 1994; 8: 150-8. [http://dx.doi.org/10.1016/0883-9417(94)90048-5]

[17] Kotozaki Y, Takeuchi H, Sekiguchi A, et al. Biofeedback-based training for stress management in daily hassles: An intervention study. Brain Behav 2014; 24: 566-79. [http://dx.doi.org/10.1002/brb3.241]

[18] de Silva L. Neural mechanisms underlying brain waves: From neural membranes to networks. Electroencephalogr Clin Neurophysiol 1991; 79: 81-93. [http://dx.doi.org/10.1016/0013-4694(91)90044-5]

[19] McCreadie KA, Coyle DH, Prasad G. Sensorimotor learning with stereo auditory feedback for a brain-computer interface. Med Biol Eng Comput 2013; 51(3): 285-93. [http://dx.doi.org/10.1007/s11517-012-0992-7]

[20] Gruzelier J. A theory of alpha/theta neurofeedback, creative performance enhancement, long distance functional connectivity and psychological integration. Cogn Process 2009; 10: 101-9. [http://dx.doi.org/10.1007/s10339-008-0248-5]

[21] Cavanah S. Math: The Not-So-Universal Language. Educ Week 2005; 24: 1.
van der Steen JT, Smaling HJ, van der Wouden JC, Bruinsma MS, Scholten RJ, Vink AC. Music-based therapeutic interventions for people with dementia. Cochrane Database Syst Rev 2018; 7: CD003477. [Epub ahead of print].
[http://dx.doi.org/10.1002/14651858.CD003477.pub4]

Waller PP, Flood CT. Mathematics as a universal language: Transcending cultural lines. J Multicult Educa 2016; 10: 294-306.
[http://dx.doi.org/10.1108/JME-01-2016-0004]

Boettcher WS, Sabrina S, Hahn SS, Shaw GF. Mathematics and music: A search for insight into higher brain function. Leonardo Music J 1994; 4: 53-8.
[http://dx.doi.org/10.2307/1513181]

Kashyap R. The Universal language: Mathematics or music?. SSRN Electronic Journal 2017.

Bamberger J, diSessa A. Music as embodied mathematics: A study of a mutually informing affinity. Int J Comput Math Learn 2003; 8: 123-60.
[http://dx.doi.org/10.1023/B:IJCO.0000003872.84260.96]

White H. Artificial Neural Networks. Cambridge, MA, USA: Approximation and Learning Theory Blackwell Publishers, Inc. 1992.

Schellenberg EG. Music and cognitive abilities. Curr Dir Psychol Sci 2005; 14: 317-20.
[http://dx.doi.org/10.1111/j.0963-7214.2005.00389.x]

Shultz A, Lee S, Shea TB, Yanco H. 2015; 13: pp. Biological and simulated neuronal networks show similar competence on a visual tracking task. In: Development and Learning and Epigenetic Robotics (ICDL-EpiRob), 2015 Joint IEEE International Conference on. 2015; 13: pp. 261-6. IEEE.

Nisbet S. Mathematics and music Australian mathematics teacher 1991; 47: 4-8.

© 2018 Shea and Remington.
This is an open access article distributed under the terms of the Creative Commons Attribution 4.0 International Public License (CC-BY 4.0), a copy of which is available at: https://creativecommons.org/licenses/by/4.0/legalcode. This license permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.