Brain Rise Foundation
Research to Equip Frontline Treatment

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White Paper for Non-Invasive Synaptic Dopamine Measurement

The Brain Rise Foundation (a 501c3 non-profit research organization)

ABSTRACT

This white paper outlines an effort to develop a reliable, artificial intelligence (AI), non-invasive diagnostic tool to measure changes in neural synaptic dopamine via stable webcam. There are numerous interdisciplinary use cases for the proposed technology ranging from the treatment of addiction, neurological conditions (e.g. Parkinson's, Huntington's), health communication (e.g. vaccine confidence, HIV prevention, tobacco cessation), consumer marketing, defense against information warfare (e.g. propaganda, disinformation), and general scientific inquiry in the areas of neuroscience and artificial intelligence. This effort will extend recent success in the use of facial expression recognition (FER) for consumer neuroscience by developing an improved software platform and conducting a series of rigorous experiments to validate several hypotheses necessary for clinical trials.

1. INTRODUCTION:

Addiction is arguably the number one public health crisis in the US. today, responsible for over a third of annual deaths. Addiction is typically viewed on a substance-by-substance basis: opioids, alcohol, tobacco, obesity (food addiction), however, the neurobiology of addiction is remarkably similar across substances. Aside from its direct health impacts, addiction is a key factor in numerous other social problems: 85% of the US prison population has a substance abuse problem [1]; 90% of children in the foster care system have a family history of drug/alcohol abuse with almost half having abused substances in the last six months [2]; similar impacts on homelessness; food insecurity; domestic violence; and gun violence. It is difficult to find a social problem that does not have some connection to addiction.

Addiction targets an individual's reward system in the brain primarily through the hormone dopamine which is responsible for a person's sense of motivation and action. This can be seen across individuals' motivation to eat, engage in activities and is even involved in social interactions [3], [4], [5]. Dopaminergic reward circuits are similar across species [6]. In humans, reward circuits of the ventral striatum processes homeostasis signals, sensory perceptions, emotions, learning, and decision-making [7]. Chronic substance abuse initially hijacks the brain's reward system. When individuals experience repeated high spikes in dopamine, their brain compensates by eliminating dopamine receptors [4], [8]. This creates drug/alcohol tolerance. Then, without the substance, dopamine levels drop to dangerous levels and the individual no longer feels the effects of the substance in a manner that produces a "high". They need the drug to stabilize their dopamine levels and function.

Over time, mid-brain structures predict the events and cues that lead to dopamine spikes [9], [10]. Much like Pavlov's dogs begin to salivate at the smell of meat, people with addiction become conditioned to experience initial dopamine spikes in response to cues from their environment, actions, and social interactions. This creates feelings of craving and hunger which reinforces drug (or food) seeking behavior.

Initially the brain experiences neuroplasticity, which allows the brain to rewire itself and function differently than before. In the case of the addicted patient, this rewiring predominantly occurs in the frontal cortex which affects decision-making [8], [11]. It also converts anxiety, realized in the midbrain, into long-term memories [12], [13]. The combined effect is that drug (or food) seeking behavior becomes hardwired into neural pathways, triggered by dopamine spikes in conditioned response to drug cues and impaired by damaged self-control that favors drugs (or food) over the negative emotional and physical consequences.

There are some medical treatments for a damaged dopamine system. Methadone and buprenorphine were discovered in the 1960s and 70s to treat opioid addiction, but their discovery pre-dates neuroscience advancements to understand the brain. They allow people to establish a normal baseline, without getting "high". It does not reverse the damaged neural circuits in the brain, however, it may help patients with withdrawal and transition into a more functional lifestyle and healthier environments. Hopefully, patients will eventually wean off the maintenance medication. It can take years for a dopamine system to return to normal function. Some patients find ways to abuse the medication. Without effective diagnostic tools to measure a patient's level of dopamine, it is extremely difficult to properly dose patients, verify medication adherence, or diagnose co-morbid conditions.

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2. BACKGROUND AND PROMISING SOLUTIONS:

Debashis Chanda developed a rapid blood test for dopamine [14]. He designed a microfluid whole-blood plasma separator and optically detects changes in dopamine levels. It is unclear, however, whether dopamine measured in whole-blood plasma is the best approach for treating patients with addiction or neurological conditions. Unpublished work involving surgical implants in the brain to measure synaptic dopamine in Parkinson's patients and patients with epilepsy reveal that dopamine levels change over milliseconds and may not be reflected in blood tests. Furthermore, dopamine is involved in more than just the brain's reward and motor systems. Surgical implants are invasive, costly and cannot be realistically used for the treatment of addiction. Still, this work has allowed colleagues to develop laboratory protocols using choice-reward-punishment stimuli that create reliable spikes in synaptic dopamine in the brain's reward circuit. Extending this work, it is possible to create laboratory conditions of changing dopamine to develop training data for artificial intelligence (AI).

Advances in the use of AI for consumer neuroscience have already been recognized. Dr. Christophe Morin of SalesBrain, a consumer neuromarketing firm, uses a two-stage brain model in their commercial work, based off system one and two thinking proposed by Nobel laureate Daniel Kahneman [15]. Morin argues that there is a primal brain (system 1) that is primarily responsible for our actions and decisions and there is a rational brain (system 2) that rationally justifies and explains our actions [16]. They achieve much stronger and more accurate results of consumer behavior and response to marketing campaigns with far fewer human research participants by measuring brain reactions in the primal brain regions. They call this the "buy" button of the brain. Their typical technologies for measuring primal brain response include EEG, galvanic skin response, eye-tracking, pupillometry, among others. Recently, they have been using facial expression recognition during COVID to approximate primal brain response to stimuli to include reaching target audiences in Ukraine and Russia for assessing Avon advertisements. Their use of facial expression recognition has been proven to be comparable in performance to traditional EEG and other neuroscientific measurements. The current tool used by SalesBrain is not extensible and has high license costs.

The James-Lange theory provides a similar approach to that of Kahneman and Morin. The James-Lange Theory is one of the oldest in neuroscience, first published in 1922. James and Lange describe the sequence of neural responses to stimuli [17]. The first stage is physiological, where people experience a conditioned physiological response to stimuli. For example, a person that sees a wasp may experience elevated heart rate or begin to perspire. The second stage is emotional, where people experience emotions in response to the physiological changes in their body. For example, the person with elevated heart rate and perspiration may feel fear and anxiety. The third state is conscious rationalization, where the person is aware of and rationally explains their emotion.

3. PROPOSED HYPOTHESES

H1: We posit that at each stage in the James-Lange model, error can be introduced as demonstrated thru existing consumer neuroscience. Thus, we can extend Morin's "two-brain" model to a "three-brain" model consisting of: 1) sub-primal brain involving physiological response; 2) primal brain, involving emotional response; and 3) rational brain, involving conscious thought.

H2: We further posit that dopamine may be a suitable proxy for sub-primal brain response. Given that certain cues in the environment can be stimuli that causes a conditioned dopamine release [12], [13], measurement of synaptic dopamine is likely to capture the effect of physiological response in the "three-brain" model.

H3: Measurement of synaptic dopamine will reduce error in estimating ad efficacy in the same way measuring emotion reduces error compared to self-reported rational response to ads. This will enable significant findings with fewer respondents.

H4: Measurement of synaptic dopamine, combined with existing eye-tracking models may provide improved models for early detection and distinguishing between different neurological conditions such as Parkinson's, Huntington's, and others.

4. TECHNOLOGY INTEGRATION:

The minimal viable product will seamlessly combine eye-tracking and facial expression recognition technologies, enabling real-time analysis of human responses. This integrated tool will serve as a foundational platform for subsequent scientific experiments and the development of the dopamine measurement model. Partial development of this tool has already begun and can be tested at http://brain-gaze.com. The current prototype is an AWS-hosted tool that captures eye-tracking data via webcam for a single video

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media file. We are extending the tool to capture users' facial images to allow training a facial expression recognition model. The tool can be used with a number of deployment protocols to include crowdsourcing thru Amazon Mechanical Turk (AMT).

5. SCIENTIFIC EXPERIMENTATION:

This project will consist of three phases. In phase 1, the Brain-Gaze application will be further developed to create a user interface for the analysis of eye-tracking and facial expression data. This will be tested and validated using FeelPix [18], an open-source resource for validating facial expression recognition tools available at https://github.com/ludovicalamonica/FeelPix. We may also validate the tool against previously collected content from SalesBrain. This will establish an initial MVP that can be used for evaluating the effectiveness of both adversary and friendly influential content.

The second phase will involve a slight modification to the Brain-Gaze application to modify the stimulus presentation to consist of the dopamine stimulating computer game used by Ken Kishida at Wake Forest University [19]. Dr. Kishida has used fast-scan cyclic voltammetry, an electrochemical technique, paired with machine learning, to detect and measure dopamine levels in real-time on patients undergoing invasive procedures such as deep brain stimulation. Kishida's protocol demonstrates the ability to create reliable changes in dopamine levels in a laboratory setting without the need for invasive surgical procedures. We will use this protocol within the Brain-Gaze application to collect eye-tracking and facial expression data for training new computer vision machine learning algorithms.

Depending on available resources, we may be able to utilize an innovative technology for non-invasive rapid dopamine measurement developed by Debashis Chanda at University of Central Florida [14]. The problem with dopamine measurement from blood is that it detects general dopamine in the body and may not be as temporally responsive to changing stimuli and associated brain activity.

The third phase will test the Brain-Gaze application on dopamine-compromised individuals and healthy controls to create a proof of concept for dopamine detection. This will be limited to testing the tool's ability to measure changing dopamine levels in individuals. We may be able to test retrospective facial expressions collected by SalesBrain to test whether dopamine detection provides a better measure of neuromarketing success than current emotion detection. At this time, it is unclear if the data will lend itself to this type of test and whether we will be permitted to use the data due to client restrictions on their content.

The Brain Rise Foundation often uses a third party IRB service for human subjects testing and all employees are certified in human subject research. Depending upon our collaboration with partners at the University of Central Florida and Wake Forest University, we may use one of the university IRBs. Human subjects research will follow all ethical guidelines for this type of research.

6. DOPAMINE MEASUREMENT MODEL:

The proposed prototype dopamine measurement model will leverage signals from eye-tracking and facial expression recognition to infer dopamine levels. This innovative approach aims to enhance our understanding of cognitive and emotional states, providing valuable insights for a range of applications. During the development of dopamine detection models, we may set-up a laboratory environment with multiple cameras with higher resolution than expected with a typical webcam. This will be used to create better baseline computer vision models that may be fine-tuned for webcam application later.

7. EXPECTED OUTCOMES:

The technology's practical application provides a diagnostic capability for physicians treating a wide range of medical conditions from substance abuse disorder to neurological conditions such as Parkinson's or Huntington's disease. It may also improve health communication influence products (e.g. vaccine confidence, harm prevention) in a more effective way. It will allow unprecedented capability to test whether a malign meme or video is likely to achieve effects and require a response or be ignored. Moreover, we can reverse engineer influential effects and design more effective campaigns while assuring decision makers that those campaigns are of reduced risk. This is a game-changing technology that can help health professionals more effectively develop persuasive interventions in the rapidly changing information domain.

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8. KEY PERSONNEL:

Dr. Ian McCulloh will be the PI. He co-founded the Brain Rise Foundation to conduct neuroscience and AI research to better equip frontline treatment centers to help those suffering from addiction, mental health, and neurological disorders. He is a retired Army officer, culminating as the Chief of Strategy and Assessments for the US Central Command's Information Operations Division (J39). He is a veteran of Afghanistan and Iraq, West Point professor (Math, Comp. Sci), established the Army Network Science Center, and has been a PI on 38 competitive federal research programs to include 4 DARPA programs. He was faculty at Johns Hopkins University with joint appointments in computer science, public health, and the Applied Physics Lab. He maintains an adjunct faculty position teaching graduate AI/ML and neuroscience courses. He established Accenture's Federal AI practice, growing it from 36 to 1200 people between 2019-2023, established an $80M competitive research program, and delivered five of the largest at-scale AI programs in the US Government. He holds a PhD in computer science from Carnegie Mellon, has authored three books and over 100 peer-reviewed academic papers.

Dr. Christophe Morin will be the co-PI. With over 30 years of experience in consumer research and advertising strategy, Christophe's passion is to understand and predict consumer behavior using cutting-edge science. Christophe has run and started many businesses as well as held senior positions in several publicly traded companies. Christophe holds an MBA from Bowling Green State University, an MA in Media Psychology and a Ph.D. in Media Psychology from Fielding Graduate University in Santa Barbara, California. He joined the Adjunct Faculty of the Media Psychology department of Fielding in 2013 as a professor of Media Neuroscience. Christophe has received numerous awards during his career as a speaker (Vistage 2011 and 2013) and a consumer researcher (ARF 2011, 2014 and 2015). He has given over 1200 talks and lectures on the subject of neuromarketing and consumer neuroscience since 2003. Most recently, Christophe published The Persuasion Code in 2018, the first book decoding the effect of advertising messages on the brain. His latest book is entitled The Serenity Code (9/2020). In it, Christophe unveils a unique model to help millions of people rewire their brains to experience life without stress, anxiety and depression.

9. REFERENCES

[1] https://nida.nih.gov/publications/drugfacts/criminal-justice

[2]

[3] Vickstrom, C. R., Snarrenberg, S. T., Friedman, V., & Liu, Q. S. (2022). Application of optogenetics and in vivo imaging approaches for elucidating the neurobiology of addiction. Molecular psychiatry, (27)1: 640-651, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9190069/

[4] Volkow ND, Michaelides M, Baler R. The Neuroscience of Drug Reward and Addiction. Physiol Rev. 2019 Oct 1;(99)4: 2115-2140. doi: 10.1152/physrev.00014.2018. PMID: 31507244; PMCID: PMC6890985. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6890985/

[5] Sinha R. Role of addiction and stress neurobiology on food intake and obesity. Biol Psychol. 2018 Jan;131:5-13. doi: 10.1016/j.biopsycho.2017.05.001. Epub 2017 May 4. PMID: 28479142; PMCID: PMC6784832. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6784832/

[6] Scaplen KM, Kaun KR. Reward from bugs to bipeds: a comparative approach to understanding how reward circuits function. J Neurogenet. 2016 Jun; (30)2:133-48. doi: 10.1080/01677063.2016.1180385. PMID: 27328845; PMCID: PMC4926782. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4926782/

[7] Daniel R, Pollmann S. A universal role of the ventral striatum in reward-based learning: evidence from human studies. Neurobiol Learn Mem. 2014 Oct;114:90-100. doi: 10.1016/j.nlm.2014.05.002. Epub 2014 May 10. PMID: 24825620; PMCID: PMC4143465. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4143465/

[8] Worhunsky PD, Angarita GA, Zhai ZW, Matuskey D, Gallezot JD, Malison RT, Carson RE, Potenza MN. Multimodal investigation of dopamine D2/D3 receptors, default mode network suppression, and cognitive control in cocaine-use disorder. Neuropsychopharmacology. 2021 Jan;46(2):316-324. doi: 10.1038/s41386-020-00874-7. Epub 2020 Oct 2. PMID: 33007778; PMCID: PMC7852666. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7852666/

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www.brainrisefoundation.org

[9] Ekhtiari H, Nasseri P, Yavari F, Mokri A, Monterosso J. Neuroscience of drug craving for addiction medicine: From circuits to therapies. Prog Brain Res. 2016; (223):115-41. doi: 10.1016/bs.pbr.2015.10.002. Epub 2015 Dec 19. PMID: 26806774. https://www.sciencedirect.com/science/article/abs/pii/S0079612315001909?via%3Dihub

[10] Stewart, J., de Wit, H., Eikelboom, R., 1984. Role of unconditioned and conditioned drug effects in the self-administration of opiates and stimulants. Psychol. Rev. (91)2: 251–268. https://pubmed.ncbi.nlm.nih.gov/6571424/

[11] Alizadehgoradel J, Nejati V, Sadeghi Movahed F, Imani S, Taherifard M, Mosayebi-Samani M, Vicario CM, Ntsche MA, Salehinejad MA. Repeated stimulation of the dorsolateral-prefrontal cortex improves executive dysfunctions and craving in drug addiction: A randomized, double-blind, parallel-group study. Brain Stimul. 2020 May-Jun; (13)3:582-593. doi: 10.1016/j.brs.2019.12.028. Epub 2020 Jan 3. Erratum in: Brain Stimul. 2021 Jan-Feb;14(1):182. PMID: 32289681. https://www.brainstimjrnl.com/article/S1935-861X(19)30499-1/fulltext

[12] Koob GF, Volkow ND. Neurobiology of addiction: a neurocircuitry analysis. Lancet Psychiatry. 2016 Aug; (3)8:760-773. doi: 10.1016/S2215-0366(16)00104-8. PMID: 27475769; PMCID: PMC6135092. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6135092/

[13] Uhl GR, Koob GF, Cable J. The neurobiology of addiction. Ann NY Acad Sci. 2019 Sep; (1451)1:5-28. doi: 10.1111/nyas.13989. Epub 2019 Jan 15. PMID: 30644552; PMCID: PMC6767400. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6767400/

[14] D. Chanda et.al., Nano Letters, vol.19, pp. 449-454, 2019.

[15] Kahneman, D. (2011). Thinking, fast and slow. Macmillan.

[16] Morin, C. (2011). Neuromarketing: the new science of consumer behavior. Society, 48(2), 131-135.

[17] Lange, C. G. E., & James, W. E. (1922). The emotions, Vol. 1.

[18] La Monica, L., Cenerini, C., Vollero, L., Pennazza, G., Santonico, M., & Keller, F. (2023). Development of a Universal Validation Protocol and an Open-Source Database for Multi-Contextual Facial Expression Recognition. Sensors, 23(20), 8376.

[19] https://newsroom.wakehealth.edu/news-releases/2023/12/research-shows-human-behavior-guided-by-fast-changes-in-dopamine-levels