LUCID

Music as Medicine: LUCID Science + Technology White Paper

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0 - EXECUTIVE SUMMARY

This white paper gives a high-level insight into LUCID's core technical and scientific basis as well as our business offerings. A brief overview of relevant scientific literature around the use of music and auditory entrainment for specific health and wellness outcomes is provided. A review of our in-app data analytics demonstrates the efficacy of LUCID's mobile application embodiment, VIBE, regarding anxiety and mood management. Clinical trials that are in progress at the time of this white paper's development are also outlined. Our music sourcing and production practices are provided in detail, including our proprietary data-driven composition and curation tool (BioMIR) and other techniques which render our audio experience unique and bolster its experiential quality. Our core technology is outlined at a high-level, followed by licensing opportunities. Our aim is that this document gives insight into the current and potential applications of our technology and the rigorous, data-driven approach that has been taken in its development.

1 - INTRODUCTION

Anxiety disorders are the most common mental health challenge in the US, affecting nearly 20% of the population. (ADAA) Among adolescents and young adults, the prevalence of mental health challenges has skyrocketed over the past decade. (Twenge et al., 2019) Even when anxiety presents at subclinical levels, it can be disabling and can negatively impact quality of life. Music is often used as a self-directed tool to mitigate the detrimental symptoms of anxiety.

LUCID is a software platform geared to extract the full therapeutic potential of sound and music. At its core, LUCID is an affective computing environment that consists of two core technologies. The first is a novel audio engineering technique that seamlessly integrates auditory beat stimulation into music (see Sections 2-I, 6-II, and 7-I). The second is the use of psychometric and biometric measurement in conjunction with emotional modeling to estimate a user's current mood state (see Section 7-I and 7-II.ii). This estimation is then used as the input to a model-based reinforcement learning system to personalize music curation for specific outcomes in real-time.

LUCID's affective music recommendation system leverages a body of music cognition research as the 'ground truth' logic for recommending the appropriate music for specific therapeutic outcomes. The system further enhances this recommendation process using cutting-edge machine learning techniques, including model-based reinforcement learning and recurrent neural networks. Selections are optimized based on population-wide data and are hyper-personalized based on the individual users' responses to their musical interventions. This intervention is highly scalable at a low variable cost.

LUCID's long-term intent is to continue to perform literature-based, academic, and clinical research, develop robust emotion-based AI algorithms, and collect a large dataset to lead the development for the commercial and academic landscape of personalized functional music. We aspire to continue developing LUCID as a tool for users, health practitioners, researchers, and creatives. We have developed and released a mobile application (VIBE) to disseminate our technology and to collect a high volume of real-world data for algorithm development and efficacy testing. We intend to distribute our technology primarily in the form of plug-and-play SDKs that helps users on partner platforms de-escalate anxiety, stress, and burnout, improve sleep, increase cognitive performance, and practice self-directed care for their mental well-being.

2 - SCIENTIFIC BASIS

I - MUSIC FOR HEALTH

Music stimulates social and emotional processes, which can positively affect moods and result in numerous health benefits (Dileo et al., 2008; Koelsch, 2005; as cited in Bernatzky et al., 2011). Listening to music evokes a wide range of emotions (joy (Koelsch, 2014); wonder (Choppin et al., 2016)), and has also been shown to modulate both brain activity (Koelsch, 2011) and cardiac output (Sumpf et al., 2015). Music can significantly attenuate physiological indicators of stress, including heart and respiration rates. (Phipps et al., 2010; Pittman et al., 2011; as cited in Bernatzky et al., 2011) and blood pressure (Pittman et al., 2011, as cited in Bernatzky et al., 2011) On the level of subjective experience, music-listening interventions can moderate pain and negative mood states, including anxiety and depression. (Phipps et al., 2010; as cited in Bernatzky et al., 2011)

Music-listening can noninvasively catalyze mental and physiological change and has been found to positively impact a broad array of psychological and physical health outcomes (see Table 1 for a selection of evidence). The fact that music can instantiate measurable changes on such a broad spectrum of measures in varied populations implies the existence of underlying commonalities, the most prominent being the relationship between mental/emotional change and therapeutic benefit. (Bernatzky et al., 2011) Though the exact mechanisms behind this relationship remain unknown, two critical theories provide essential insight.

First: listening to music has been shown to alter activity in the autonomic nervous system, which regulates subconscious body processes such as blood pressure, breathing rate, heart rate, and digestion. Music-listening can increase activity in the parasympathetic nervous system (Jia et al., 2016) and decrease activity in the sympathetic nervous system. (Ellis et al., 2010) This shift implies a change in the body from responsiveness and reactivity to stress, to recovery from stress.

Second: research shows that music can alter activity in regions of the brain, including the limbic and paralimbic systems, responsible for memory and emotion. As stated in Bernatzky et al. (2011): ‘Because primary-process emotions which are tightly intermeshed with a host of autonomic processes that can regulate bodily state are generated by deep brain structures, a likely place to look for explanations for music’s effect is in those deep structures. Several regions in the limbic and paralimbic systems, which are centers of affective pain, show notable changes associated with listening to music.’ In simple terms, deep regions of the brain that process memory and emotion are strongly affected by music - and in this way, music can exert a bottom-up influence on both one’s emotional experience of their life and their behavior.

Table 1: Known areas of benefit of music.

Outcome	Effects	References
neurogenesis	increase connectivity of different areas of the brain; increase BDNF expression	Angelucci et al. (2007), GCBH (2020)
anxiety	calming music found to be as effective as diazepam at reducing vital signs of anxiety	Koelsch (2010)
	significantly reduce anxiety, cortisol, and norepinephrine levels	Fancourt et al. (2014), Koelsch (2010)
	modify heart rate, respiration rate, blood pressure, skin conductance, muscle tension	Chanda et al. (2013)
	music more effective than benzodiazepine at reducing preoperative anxiety; reduce anxiety and sedative use pre-, peri-, and post-operatively	Shabanloei et al. (2010), Wu et al. (2012), Bradt et al. (2013), Hepp et al. (2018), Bradt et al. (2015), Chanda et al. (2013)
	reduce anxiety in patients with heart disease	Bradt et al. (2013)
pain	reduce pain peri- and post-operatively, during labor, in an emergency room	Choi et al. (2018), Vaajoki et al. (2010), Shabanloei et al. (2010), Good et al. (2005), Smyth et al. (2018), Chai et al. (2020), Jangsirikul et al. (2017)
sleep	Music interventions improve sleep in students, in the ICU, in patients with insomnia, following invasive procedures	Harmat et al. (2008), Rong-Fang et al. (2015), Jespersen et al. (2015), Bradt et al. (2013), Cordi et al. (2019)
mood	increases oxytocin, improves mood state in people affected by psychiatric conditions	Koelsch (2010), Angelucci et al. (2007)
stress	Reduce stress and anxiety in healthy subjects, patients undergoing invasive medical procedures (e.g., surgery, colonoscopy, dental procedures), pediatric patients undergoing medical procedures, and patients with coronary heart disease	Chanda et al. (2013)
inflammation	reduce inflammatory cytokine IL-6, reduce natural killer cell levels, increase CD8+ cell levels, increase s-IgA (immunoglobulin) levels	Metcalf et al. (2019), Koelsch (2010), Chanda et al. (2013)
dementia	ameliorate cognitive deficits, improve emotional wellbeing and quality of life, reduce anxiety, reduce depressive symptoms	Angelucci et al. (2007), Orgeta et al. (2014)
cancer	Reduce anxiety, pain, fatigue, improve quality of life, reduce the need for anesthetics and analgesics, reduce recovery time and duration in hospital, lower cancer-treatment biomarker in people undergoing treatment for cancer	Bradt et al. (2016), Metcalf et al. (2019)
stroke recovery	Improve motor skills during recovery	GCBH (2020)
Parkinson's	Increase motor coordination	Angelucci (2007)
multiple sclerosis	Improve cognition, motor function, emotional wellbeing	Sihvonen et al. (2017)

II - AUDITORY BEAT STIMULATION

Beyond traditional forms of music, some sound patterns have demonstrated beneficial effects on specific outcomes. Auditory beat stimulation (ABS) is defined as the use of external rhythmic stimuli to entrain brain activity such that the external and internal rhythms become synchronized (Huang & Charyton, 2008). A form of brainwave entrainment, ABS has been used to positively impact many outcomes, including cognition and focused attention (Huang & Charyton, 2008; Carter & Russell, 1988; Kraus & Porubanova, 2015), acute stress and anxiety (Le Scouranec et al., 2001; Padnmanabhan et al., 2005, Chuter, et al., 2007; Isik et al., 2017; Wiwatwongwana et al., 2017), as well as pain and anesthesia requirements (Garcia-Argibay, 2019). See Section 6-II for more information about how LUCID's audio integrates ABS.

3 - IN-APP DATA ANALYSIS

Helping users to manage anxiety and to maintain emotional wellbeing are among our highest priorities as a company. Analysis was performed on anonymized data from real-world use of VIBE over an 8-week period to assess the efficacy of VIBE regarding these outcomes (see Table 2). Clean data of completed uses of VIBE was available for 1347 app uses from 408 users.

This analysis indicates that VIBE is very effective at reducing anxiety: for 57% of users, it is effective at reducing their anxiety the majority of the time; for 41% of users, it is effective every time. On average, VIBE users experience a 54% reduction in self-reported anxiety following a single listening session. VIBE also shows positive effects on users' mood states; 58% of app uses ended within 50% of the target emotional state.

Table 2: Results of in-app data analysis.

Metric (description	Outcome
CTSR50 (percentage of app uses which ended within 50% of the target emotional state)	58%
Change in anxiety (average difference in self-reported anxiety from pre- to post-experience, on a 10-point scale)	-2
Percent change in anxiety (average percent change in self-reported anxiety from pre- to post-experience)	-54%
Percentage of users who experienced a reduction in anxiety during >50% of their VIBE sessions	57%
Percentage of users who experienced a reduction in anxiety during 100% of their VIBE sessions	41%

4 - CLINICAL VALIDATION RESEARCH

LUCID is committed to taking a scientific and validation-forward approach to product development and marketing. We have completed the preliminary analysis for a clinical validation study to assess VIBE's efficacy for acute anxiety. This work is a collaboration with Dr. Frank Russo and Dr. Adiel Mallik of the SMART Lab in the Department of Psychology at Ryerson University. This randomized controlled trial (RCT) was performed digitally using remote research services.

Participants (n=264) who are currently taking anti-anxiety medication were randomly assigned to listen to either LUCID's calm music curation combined with ABS, LUCID's calm music curation alone, or one of two active comparator conditions (ABS alone or pink noise) for 24 minutes. The primary outcome measure in this study was the change in the State-Trait Inventory of Cognitive and Somatic Anxiety-State (STICSA-S) scores.

For individuals with moderate trait anxiety, both versions of VIBE (with and without ABS) outperformed both active comparator groups at reducing somatic state anxiety (see Figure 1, Table 2 for p-values; Table 3 for means and SEMs of Figure 1, percent reductions). No adverse events or negative side effects were reported.

Table 2: Comparisons of somatic anxiety reduction between intervention groups for moderate trait anxiety participants.

	Music & ABS vs. pink noise	**Music & ABS vs. ABS**	**Music vs. pink noise**	**Music vs. ABS**
p-value	0.03	0.019	0.039	0.031

According to multiple linear regression analysis, reductions in somatic anxiety were moderated by trait anxiety severity (cognitive trait anxiety: $p=0.048$, somatic trait anxiety: $p < 2\times10\text{-}16$) such that individuals with higher trait anxiety saw greater benefit. Music preferences also played a significant role: for individuals who reported a stronger appreciation for music characterized as 'Intense and Rebellious,' a slightly smaller reduction in state anxiety was observed ($p=0.02$). We might call this the 'heavy metal effect': individuals who prefer and are calmed by music of higher intensity may be less likely to experience anxiolytic effects from music with a traditionally calming aesthetic.

Table 3: Mean and standard error of mean of somatic state anxiety reduction for moderate trait anxiety participants.

	Music & ABS	Music	Pink Noise	ABS
Mean reduction	5.22	4.33	1.73	2.08
Percent reduction (%)	15.8	13.1	5.2	6.3
Standard Error of Mean	1.21	0.80	1.26	0.81

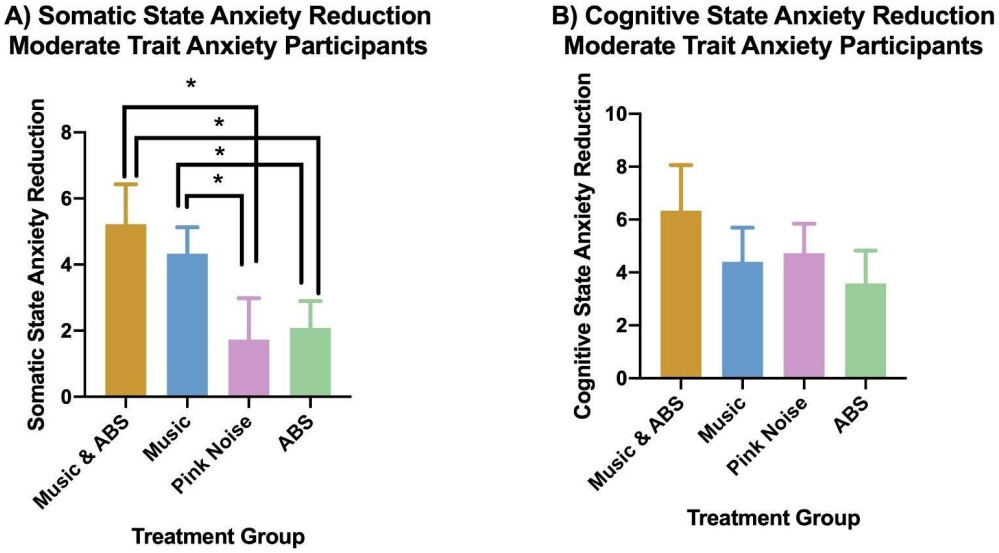

Figure 1: State anxiety reduction in moderate trait anxiety participants as compared between intervention groups. (* indicates $p < 0.05$)

Full data analysis is underway. Meanwhile, preliminary results have been presented at the McMaster Institute for Music and the Mind NeuroMusic conference (November 14th, 2020). Final results from this study will be presented at additional scientific conferences and submitted for publication in peer-reviewed journals.

5 - CLINICAL PIPELINE

LUCID is currently committed to two longitudinal studies to assess the use of VIBE for trait anxiety symptoms against different control conditions. The first of these is an extension of the existing RCT in collaboration with the SMART Lab. We will assess the effects of VIBE versus an active comparator over a 12-week intervention period on both trait anxiety and heart rate variability metrics. The second will be an RCT conducted under the supervision of Dr. Farooq Naeem, Chief of General and Health Systems Psychiatry at the Centre for Addiction and Mental Health (CAMH), and will assess the effects of 12 weeks of VIBE use relative to a waitlist condition on anxiety and depression symptoms. We have also secured funding for a third study in collaboration with the SMART Lab, which will assess both anxiety and relevant clinical outcomes for a specific population.

LUCID is also pursuing arms-length research collaborations to assess the use of VIBE for additional populations in which stress and anxiety are common challenges and where their management can assist in producing meaningful clinical outcomes.

6 - MUSIC SOURCING + PRODUCTION PRACTICES

I - DATA-DRIVEN COMPOSITION + CURATION PROCESS (BioMIR)

Using proprietary machine learning algorithms and data tools developed in-house, BioMIR was developed as a software-as-a-service tool which provides LUCID composers and music supervisors with data insights that correlate musical features to affective states. This development approach is evidence-based and is built iteratively with the network effect of real-world data generated by LUCID users. BioMIR is capable of insights like the following:

> *Time-series batch of MIR features (including genre) the most likely to induce states of calm for 18-24-year-old males from North America who are in a tense state.*

We have developed working prototypes of this model, which operate in a bi-directional format: if waveform audio is used as an input, affective state insights (i.e., what emotion that track will likely induce in people of specific demographics) are produced as an output, whereas if desired affective states and demographic information are used as an input, a sequence of desirable musical features is produced as an output. This bi-directionality effectively doubles the versatility and utility of this tool.

Using a combination of BioMIR data insights and information from pre-existing music cognition research, LUCID has developed a content framework for functional music geared toward specific outcomes. This formula is continuously adapted and revised but remains grounded in both well-established scientific principles and continuous data insights generated by LUCID users. This content spans various genres, instrumentations, and aesthetics, and is composed and sourced to elicit specific neurophysiological outcomes. In addition to in-house composed music, we source content from artists with perpetual licenses, and we are currently forming new partnerships with production houses interested in developing functional music.

II - AUDIO ENTRAINMENT OPTIMIZATION

As mentioned in Section 2, LUCID utilizes auditory entrainment to support the desired outcomes of our functional audio by inserting a synchronized set of ABS tones within the musical fabric. The entrainment is infused using a patent-pending method designed to produce an aesthetically pleasing and non-abrasive experience of listening to the tones. (See Patent i below for more information.)

III - SPATIAL AUDIO + AMBIENT SOUNDSCAPES

The effects of natural soundscapes and their digital simulations on physiological signals, subjective mood state, well-being, and behavior are well-documented. (Song et al., 2018; Bergman et al., 2012; Bratman et al., 2015; Park et al., 2010; Gwan-Woo et al., 2010; Annerstedt et al., 2013; Nadkarni et al., 2017) LUCID's custom content includes binaurally spatialized music and spatial audio recordings from a myriad of natural environments from which the users can choose. By creating an auditory simulation of a spatialized environment that emulates the dimensionality of natural space, this simulation becomes more deeply immersive and maintains the attention of the listener on the experience more effectively than a one-dimensional stereo recording.

7 - TECHNOLOGY

I - CORE IP

LUCID's intervention is rooted in two core technologies. The first is a novel audio engineering technique that integrates auditory beat stimulation into music. The second is the use of real-time affective state estimation using psychometric and/or biometric measurement in conjunction with specific emotional models. These measurements are used as the input to a model-based reinforcement learning system that personalizes music curation for particular outcomes in real-time.

This second technology produces correlated data that can then be used in deep learning systems to uncover a deeper understanding of how the human body and psyche responds to music and why those relationships exist. Currently, these two technologies are patent protected. A third patent, regarding a generative music system design, is in progress (see below for details). See Figure 2 for a visual depiction of how these modules interface with one another.

II - PATENTS

i - Device, Method, and Medium for Integrating Auditory Beat Stimulation Into Music

(US 62/842, 196 Provisional Status, Filed on May 9th, 2019)

A device, method, and medium for integrating monaural and binaural beats into music. The music is analyzed to determine the key, root tone, and spectral range. It is then remixed with monaural beats and/or binaural beats at frequencies based on the desired entrainment frequency and the root tone and lowest dominant frequency range of the music. Additional harmonics of the beats in higher octaves may be integrated into the music as well using mixing and/or equalization.

ii - Method, System, and Medium for Affective Music Recommendation

(US 62/980, 979 Provisional Status, Filed on February 24th, 2020)

A method, system, and medium for affective music recommendation. A listener's current affective state and target affective state are identified. An audio stream, such as a music playlist, is generated with the intent of effecting a controlled trajectory of the listener's affective state from the current state to the target state. The audio stream is generated by a machine learning system trained using data from the listener and/or other users indicating the effectiveness of specific audio segments, or audio segments having specific features, in producing the desired affective trajectory. The audio stream is presented to the user as an auditory stimulus. The machine learning system may be updated based on the affective state changes induced in the listener after exposure to the audio stimulus.

iii - Method, System, and Medium for Affective Music Composition

(US 63/074,109 Provisional Status, Filed on September 3rd 2020)

This application is directed to hybrid techniques for the generation of functional affective music, offering both human-machine collaboration and machine-only music generation options. In the human-machine modality it allows for a modification and assisted music creation process that is fully data-driven, leaving the human composers with the tasks that are difficult for machines (aesthetic, raw creative input) and machines are left with high computation tasks like probabilistic modelling to predict the best musical decisions to elicit particular affective responses (a goal emotional state for instance). This system is designed to render music that suits a particular functional outcome with a high level of certainty through a completely data-driven creative process. This system can also be paired with our affective music recommendation system, allowing the recommendation of content for a user that does not already exist.

8 - API + WEB SERVICE OFFERINGS

I - MUSIC OPTIMIZATION ENGINE

LUCID's optimization engine can optimize any music library for functional music outcomes. This engine leverages our patent-pending affective music recommendation system to curate music sequences based on the user's current and target state while personalizing them based on the user's unique reactions to music. It also includes the patent-pending audio engineering framework for integrating auditory beat stimulation into music. Each component is isolated and available for use as desired. This system has been used with music outside of LUCID's core content library in a proof-of-concept demo created during the Universal Music Group's Global Acceleration Program in 2019. Our optimization engine recommended playlists from a library of Universal music and infused ABS within the playback to induce specific and desirable emotional states.

II - FUNCTIONAL MUSIC CONTENT LIBRARY

LUCID's functional music library has grown exponentially through licensing sourced content and extensive in-house composition over the last three years. All content was created or sourced in line with LUCID's content formula, derived using BioMIR from data insights and ground truths in music cognition literature. This content features spatial audio and pre-rendered infusions of auditory beat stimulation.

III - BioMIR

Currently in its alpha stage, BioMIR is a platform that provides insights for the music production process, unlocking the creation of functional music content through a data-driven practice. This tool has been used to create hours of content internally and with partners in the music production space.

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