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Music as Medicine: LUCID Science + Technology White Paper

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Executive Summary

As the digital health space continues to expand and the use of experiential therapeutics becomes more commonplace, there is a growing opportunity to leverage the power of music for health outcomes. LUCID is a digital therapeutics company creating music-based tools for targeted outcomes in mental and neuropsychiatric health. Our core technology is predicated on the hypothesis that through the use of biometrics, quantitative musical features, big data analysis, and robust machine learning techniques, functional music can be optimized to achieve more significant and predictable effects on more specific outcomes. This whitepaper gives a high-level insight into LUCID's technical and scientific basis as well as our offerings. A brief overview of relevant scientific literature around the use of music and auditory entrainment for health and wellness outcomes is provided, along with our research results and real-world evidence to date. Our core technology is outlined at a high level, followed by licensing opportunities. Current developments in various clinical areas are also described. 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 led to its development.

Problem Statement

Over the past decade the incidence of mental health challenges has continued to rise, along with the dialogue around mental health and the demand for mental health services. The volume of mental healthcare providers is insufficient to meet this demand, leaving countless individuals in crisis on waiting lists for months or without care altogether. Additionally, provider-driven care is high-cost with limited scalability. As a result, there is a growing demand for low-cost and effective mental health interventions. Despite the saturation of mental wellness tools on the market, there are relatively few evidence-based, self-guided tools for mental and neuropsychiatric health outcomes.

Anxiety and mood-related challenges are also highly comorbid with many diseases, including dementia, epilepsy, cardiovascular diseases, diabetes, and Parkinson's disease (Latas et al., 2019). In fact, people living with chronic health conditions face depression and anxiety at twice the prevalence of the general population (Canadian Mental Health Association, n.d.). In spite of the high incidence of mental and behavioral health challenges faced by patients with chronic or acute medical conditions, these challenges often go unaddressed, and health outcomes can suffer as a result (Patten, 1999).

LUCID has developed technology to address mental health challenges using a familiar modality that has stood the test of time: music. The earliest documentation of the use of music in healing contexts is from 4000 BCE (Conrad, 2010) and contemporary research continues to indicate the benefits of music in health and wellness applications. Using cutting-edge AI, biometric measurement, and proprietary music production capabilities, LUCID's technology is positioned to unlock the full breadth and depth of music's impact on health.

Background

Digital therapeutics

Digital therapeutics (DTx) have been on the market for about a decade and are defined as software-driven, evidence-based tools to prevent, treat, or manage a medical condition (Makin, 2019). DTx are part of the broader digital health landscape, which includes digital innovations like telemedicine and diagnostic support tools, but are distinct in that evidence-based claims are made about DTx with respect to specific clinical outcomes.

Pharmacological therapies consist of two parts: the *active ingredient*, which is responsible for the clinical effect, and *excipients*, which are secondary features of the therapy that have no direct clinical effect but support the administration and uptake of the active ingredient. DTx follow this model as well: the active ingredient being the protocol or intervention that the DTx software is designed to deliver, and the excipients being features to ensure the *digital bioavailability*, or the successful interaction between the DTx and the patient. As with pharmacological therapies, DTx can only be effective if the patient 'takes the medicine'. As a result, digital excipients are largely centered around increasing patient engagement, compliance, and adherence with the therapy. Unlike drug therapies, which are largely equivalent in terms of user experience, the opportunity to engineer the user experience within DTx to support engagement presents a distinct advantage of this type of therapy.

There are two key changes within healthcare that are driving innovation within digital health. The first of these is the growing population and, more succinctly, the aging population: as an increasing number of people are living longer and requiring more complex care in their later years, the demand for high-cost health services grows. Health systems are not positioned to absorb this increased demand. Secondly, as health sciences produce increasingly complex and individualized therapies like gene and cellular therapies, the standard of care increases commensurately - but the high cost of many personalized therapies inhibits widespread use.

DTx are well-positioned to respond to these challenges. DTx allow healthcare providers to efficiently provide quality care to a greater number of patients, aiding the healthcare system in absorbing the growing demand for services (Makin, 2019). Furthermore, the computational power behind DTx allows for the automation of personalization methods, presenting a highly scalable and cost-effective delivery method of personalized care. LUCID's technology leverages both of these traits by using artificial intelligence (AI) and biometric measurement competencies to provide highly personalized interventions at scale. Moreover, music is a highly engaging medium, with Americans listening to over 32 hours of music per week on average (McIntyre, 2017). LUCID leverages people's natural enjoyment and use of music to enhance the digital bioavailability of DTx, and uses cutting-edge methods to optimize the active components of music for mental health outcomes.

Music for health and wellbeing: effects and hypothesized mechanisms

The psychological and physiological effects of music-listening are tangible and wide-ranging. 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 (Koelsch, 2014; Choppin et al., 2016), and has also been shown to modulate brain activity (Koelsch, 2011), sympathetic nervous system activity (Pérez Lloret et al., 2014), 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).

Music can also expedite recovery from stress. Sandstrom & Russo (2010) conducted a randomized controlled trial in which participants were subjected to an acute stressor prior to being exposed to music or a white noise control. Results indicated that positively-valenced music most effectively promoted subjective and physiological recovery as measured via skin conductance level and heart rate.

Music-listening can induce drug-like effects. On the level of subjective experience, music-listening interventions have been shown to soothe physical pain and negative mood states, including anxiety and depression (Phipps et al., 2010; as cited in Bernatzky et al., 2011). Moreover, music-listening engages the reward pathways in the brain in similar fashions as primary rewards, like sex or food, and secondary rewards, like money (as cited in Ferreri et al., 2019).

Music-listening can noninvasively catalyze mental and physiological change and has been found to positively impact a broad array of health outcomes (see Table 1 for a selection of evidence). The fact that music can instantiate measurable changes in varied populations implies the existence of underlying biological mechanisms. Although the nature of these mechanisms remains the subject of contemporary academic research in music science, three core theories are outlined below.

1. *Music shifts the balance of the autonomic nervous system and reduces the stress response.*

   Listening to music has been shown to alter activity in the autonomic nervous system, consisting of the sympathetic and parasympathetic branches, which regulate body processes such as blood pressure, breathing rate, heart rate, and digestion. Music-listening can decrease activity in the sympathetic branch (Ellis et al., 2010) and boost parasympathetic nervous system activity, enabling physiological functions involved in rest and recovery (Jia et al., 2016). This autonomic shifting of resources from sympathetic to parasympathetic branches indicates a transition from responsiveness to stress, to recovery from stress. Music has also been shown to reduce cortisol levels (Koelsch, 2011) and attenuate stress in pediatric emergency room patients (Hartling et al., 2013). This attenuation of the stress response may further prime a patient to engage with and benefit from concurrent or subsequent interventions including Cognitive Behavioral Therapy, mindfulness, or biofeedback.

2. *Music taps into neural centers of memory and emotion.*

   Midline cortical structures such as the medial prefrontal cortex, anterior cingulate cortex, and medial temporal lobes appear to be involved in music-evoked autobiographical memories (Belfi et al., 2018; Janata, 2009). In addition, regions of the brain that are associated with emotional processing including the limbic and paralimbic systems, ventral striatum, amygdala, and anterior cingulate, show significant activity changes associated with music-listening (Blood et al., 1999; Blood & Zatorre, 2001). By altering activity in these cortical and subcortical brain regions, music interventions may assist users in accessing and processing memories or emotions as well as influencing emotional state.

3. *Music can deeply absorb the listener’s attention and direct emotional experiences.*

   Listening to pleasurable music produces an increase in frontal midline theta power (Bernatzky et al., 2011), which is associated with states of focused attention (Ishii et al., 2014). As such, music can absorb a listener’s complete attention and draw them into a rich experience (Hall, Schubert & Wilson, 2016; Sandstrom & Russo, 2013). This is thought to be mediated by the effects of music-listening on activity in mesolimbic structures involved in reward processing as well as the hypothalamus and the insula, which are involved in regulating autonomic and physiological responses to rewarding and emotional stimuli (Menon & Levitin, 2005). By effectively absorbing the listener’s attention and diverting their awareness from their typical thought patterns, stressors, and understanding of their current life circumstances (especially if they self-identify as someone who faces a chronic condition like anxiety or pain), music-based interventions can mitigate rumination and help the listener experience more positive mental and emotional states.

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Table 1: Known areas of benefit of music listening

Outcome	Effects	References
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, lower cortisol levels	Chanda et al. (2013), Hartling et al. (2013), Koelsch (2011); Sandstrom & Russo (2010)
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 postoperatively	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)
mood	Improves mood state in people affected by psychiatric conditions	Koelsch (2010), Angelucci et al. (2007)
dementia	ameliorate cognitive deficits, improve emotional wellbeing and quality of life, reduce anxiety, reduce depressive symptoms	Angelucci et al. (2007), Orgeta et al. (2014); Peck et al. (2016)
neurogenesis	increase connectivity of different areas of the brain; increase BDNF expression	Angelucci et al. (2007), GCBH (2020)
pain	reduce pain peri- and postoperatively, during labor, in 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)
Parkinson's disease	Increase motor coordination	Bernatzky et al. (2004)
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)
cancer treatment	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)

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The past, present, and future of music-based interventions: practices and limitations

Past

According to the ancient Greeks, the god Apollo was responsible for both medicine and music (Simon, 2014). Music is considered one of the few human universals (Brown, 1991), with the oldest-known instrument, a simple bone flute carbon-dated as over 40,000 years old (Higham et al., 2012). The ubiquity of music is succinctly framed by Harvey Simon in The American Journal of Medicine:

> “Virtually all cultures, from the most primitive to the most advanced, make music. It's been true through history, and it's true throughout an individual's lifespan. In tune or not, we humans sing and hum; in time or not, we clap and sway; in step or not, we dance and bounce.” (Simon, 2014)

Some scholars hypothesize that ancient musical rituals may have been the seeds of religious practices, serving to invoke feelings of de-individuation and heighten group experiences (Conrad, 2010). Some maintain that music co-evolved with language to support communication, as there is considerable overlap between the regions of the brain that process language and music (Patel, 2010; Mithen, 2006; Barrett et al., 2018). Moreover, the use of music as a medicinal tool was long used in pre-industrial societies across time and geographies (Merriam, 1964). The oldest physical evidence for the use of music for healing purposes dates to 4000 BCE (Conrad, 2010) and music has been used as a key component of psychedelic healing ceremonies since a similar era, from the Iracos sung during ayahuasca ceremonies in South America to the polyrhythms used in ibogaine rites of passage in Western Africa to the musical accompaniment to mushroom rituals of the Mazatec people in southern Mexico. See LUCID’s **Music and Psychedelics Whitepaper** for more detail.

Considering both the long-standing history of musical practices and the profound emotional experiences that can be produced as a result, it is reasonable to expect that the human brain is hard-wired to process and respond to music. The explosion of widespread access to music in contemporary times raises questions about how music can be best created, selected, and curated to optimize listening experiences for health outcomes.

Present

Like caffeine or alcohol, music can be considered a drug that people use ubiquitously in a self-directed manner to control their mood, energy, and mental state, with some examples being concentration enhancement, movement coordination, stress management, pain reduction, and athletic stamina (Chanda & Levitin, 2013). The use of music for these targeted outcomes is only growing in popularity with the advent of mood- and function-based playlists on popular streaming platforms. Functional music generally takes one of three forms: generic playlists, self-selected music, or human-delivered music therapy. The utility and limitations of each are outlined below and are summarized in Table 2.

Generic functional playlists

The vast majority of functional music offerings take the form of fixed playlists curated by hand. Although this type of functional music is widely accessible, it is limited in efficacy due to an absence of theoretical underpinning, predictive modeling, and personalization. Most music is composed and produced for entertainment purposes, with no eye to targeted health or wellness outcomes. Moreover, most generic functional playlists lack systematic methods predicating the song selection or ordering. Although many music selections can be relaxing and emotive, most functional playlists are not tailored to meaningfully leverage these qualities. In addition to this, individuals' experience of music is colored by personal factors like preference, demographic, personality, and current mood. Generic functional playlists are limited to a static experience in which no element of personalization is possible, either for the music selections that an individual is likely to enjoy nor for their current affective state. There is strong evidence to suggest that the positive outcomes of music-listening are significantly more potent when the listener finds the music selection pleasurable (David & Thaut, 1989), which a canned playlist cannot accommodate. Likewise, responses to music are not time-invariant; the same music selection played while the listener is in a state of distress is unlikely to invoke the same reaction as it would if they were in a calm or sleepy state. A static playlist cannot account for such a dynamic response. See the **Validation Research: Comparison to Generic Relaxation Music** section below for supporting data.

Self-selected music

Music is ubiquitously used for both entertainment and functional outcomes in many contexts, including relaxation, setting an emotional 'tone' in social gatherings, and fitness performance. Self-selected or self-curated playlists constitute much of this use. This addresses the lack of personalization in generic functional playlists and ensures that the listener finds the musical selection pleasurable. However, self-selected music is not well-suited to many health applications in that it places the burden on the listener to essentially develop their own 'functional music protocol' by selecting and curating the appropriate songs for their desired outcome. If a user is in a state of distress, such as anxiety or pain, self-selecting the optimal music may be challenging or stress-inducing. Moreover, proprietary data analysis conducted by LUCID suggests that the psychoacoustic features underpinning the induction of mood states are complex and context dependent, and thus difficult to perceive by an average listener. Self-selected music is also limited to music that is previously known to the listener. This is problematic in the context of therapeutic music for two reasons. First: one may not be familiar with the music that would be the most effective for them to achieve a specific functional outcome. Second: familiar music may anchor the listener in their understanding of themselves and reinforce their current state. This could be

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especially problematic for an individual who identifies as a person who experiences anxiety, chronic pain, or some other ongoing condition for which they seek relief. As a result, the effects of self-directed functional music selections are likely to be less potent, more variable, and less reproducible than those of a data-driven music selection and curation process.

Professional music therapy

Music therapy is defined by the American Music Therapy Association (ATMA) as 'the clinical and evidence-based use of music interventions to accomplish individualized goals...by a credentialed professional who has completed an approved music therapy program' (American Music Therapy Association, 2005). Music therapists employ a variety of methods, including both music-listening and music-making, to achieve clinical aims. Music therapy has been shown to be effective across a multitude of outcomes, including postoperative pain (Lin et al., 2019); quality of life, anxiety, depression, and pain in cancer patients (Li et al., 2020); and mood and behavioral challenges in patients living with dementia (McDermott et al., 2012). As a result, many healthcare institutions like hospitals and long-term care homes employ music therapists as an integral part of patients' care teams. However, scalability remains challenging, as the number of patients that a care provider can see in a day is limited and not all care facilities can afford to provide this type of care. As a result, many patients who would benefit from access to music therapy are unable to receive it.

Table 2: Overview of common delivery methods of functional music as compared to LUCID's technology.

Music intervention	Evidence	Personalization	Real-time responsivity	Burden of music selection	Measurability of methods & outcomes	Scalability
Generic functional playlists	Low	Low	None	Moderate	Low	High
Self-selected music	Moderate	High	High	High	Low	High
Music therapy	High	High	High	Low	Low	Low
LUCID's Affective Music Recommendation System	High	High	High	Low	High	High

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Future

With access to digital music services becoming more widespread globally, people are increasingly incorporating music into their daily routines for entertainment and self-improvement alike. Functional music offerings for relaxation, sleep, focus, and performance dominate music platforms like Spotify and Apple Music. This growing acceptance of the use of music for health and wellness is likely to encourage the uptake of more rigorous, effective, and engaging functional music interventions. At the same time, personalized medicine is becoming mainstream in many branches of healthcare; neuropsychiatric wellbeing is no different. The integration of personalization techniques to optimize for the listener's needs, preferences, and current mental, emotional, and physiological state is a natural progression from one-size-fits-all music interventions to more potent and absorptive sound-based therapeutics.

Furthermore, the use of big-data techniques to support intelligent music creation and curation is a notable lack in the music industry at present. Almost all music is composed for entertainment, although it may be used for other purposes. The use of tools for assisted functional music composition is likely to reduce variability in effects and increase confidence regarding outcomes. As such, quantitative music informatics are likely to become highly relevant in functional music offerings.

Optimized for success: LUCID's approach to therapeutic music

LUCID's technology is predicated on the hypothesis that through quantitative measurement and robust machine learning techniques that incorporate personalization, functional music can be optimized to achieve more significant and predictable effects on more specific outcomes. See Figure 1 for an overview of how this approach is instantiated in our solution and protected by our patents, and the **Solution** section below for technical details.

Absorption

Absorption is defined as a state of total attention in which all mental resources are engaged and a strong emotional involvement in the experience at hand is present (Tellegen & Atkinson, 1974). The 'rational, reality-focused' awareness typical of everyday experiences is replaced by a more involuntary and non-judgemental involvement in the experience (Vroegh, 2019). Absorption consists of two related but independent constructs: *state absorption*, which is the acute experience of absorption, and *trait absorption*, which is an individual's propensity to enter into absorptive states. In the case of music-listening, absorption is related to the extent to which a listener allows themselves to be drawn into an emotional experience. This construct is important to consider in the context of therapeutic music interventions because it explains some interpersonal variability in response to music (Sandstrom & Russo, 2011). This further speaks to the value of personalization of music interventions: by taking individuals' state and trait absorption scores into account, more potent and reliable outcomes may be achieved.

Absorption is important for achieving therapeutic outcomes from music because it predicates the effectiveness of both the 'active ingredient' and the 'excipients' of the therapeutic (see the **Background: Digital therapeutics** section above for definitions).

Active ingredient: emotion induction

Trait absorption is a significant predictor of physiological recovery from acute stress using music (Sandstrom & Russo, 2013). State absorption in music has been shown to be a mandatory requirement for emotional and physiological responses, including the experience of chills (Panksepp, 1995). Strong identification with the emotional content of music is essential for mood induction (Kreutz, 2008), which in many clinical applications spanning mental and neuropsychiatric health is the desired outcome, the mechanism of therapeutic change, or both.

Emotion induction is leveraged in existing music therapy methodologies including the iso principle, a technique that involves matching musical stimuli to a patient's current mood and gradually driving the music toward the desired emotional state (Heidersheit and Madson, 2015; Wilgram et al., 2013). Curiously, the first reference to the iso principle is found in Boethius' Da Musica, a highly-regarded 6th century body of work on the functions of music, which attributes the iso principle to the great mathematician Pythagoras, often referred to as the "father of numbers" (Gouk, 2001). Although the iso principle never went away, it was famously revived by Altshuler (1948) in his work on mood induction in psychiatric patients. The method has since been tested and found to be an efficacious method of mood induction in both psychotic and healthy subjects. Further studies have indicated that music sequences based on the iso principle are more effective than conventional "relaxing" music sequences at achieving desired outcomes, including reducing muscle tension as assessed by electromyography (Rider, 1985). One hypothesized mechanism of the iso principle's efficacy proposed by Shatin (1970) hinges on the concept of absorption: an individual should be more likely to become absorbed in music that is congruent with their current mood. This provides a rich theoretical framework for understanding why we gravitate to sad music when we feel sad. By first acknowledging one's current mood and facilitating absorption, the listener should be more receptive to the emotional trajectory of the music intervention. In Shatin's words:

> "If we do not match the music to [their] mood, the patient will reject the attempt to approach [them] via music. For example, a restless mood will not respond to tranquil music; rather we must match restless music to the restless mood. Then by degrees we can shift the music thereby carrying with it the subject's mood to a more tranquil state."

On another note, trait absorption has been correlated with enjoyment of negatively-valenced and complex music (Garrido & Schubert, 2011; Hall et al., 2016). One proposed explanation for this is that individuals high in trait absorption are able to become fully immersed in complex or negative emotional content within music from an aesthetic point of view, allowing these emotions to be at once felt and enjoyed. In fact, absorbing or self-transcending experiences have been associated with reduced activity in the default mode network (DMN; van Elk et al., 2019). The DMN is a large-scale network that is primarily composed of the medial prefrontal cortex, posterior cingulate cortex/precuneus and angular gyru. This network tends to be most active when a person is engaged in self-related thinking (e.g., what are people thinking about me right now?; what do I need to do to leave a positive impression?). Reducing DMN activity through a music experience that is absorbing should help listeners to non-judgmentally access emotions or emotionally-dense autobiographical experiences, which may support therapeutic processing. The ability to feel emotions (both pleasant and unpleasant) without attaching ego-based judgements to those feelings is relevant in many contexts; for example, during psychotherapy with or without psychedelic assistance in which individuals are working through aspects of their personal history, or when individuals are processing difficult emotional experiences in real-time such as anxiety, depression, or burnout.

Excipient: enjoyment

There is a strong positive correlation between state absorption and the enjoyment of music (Hall et al., 2016). This relationship is likely underpinned by the activation of mesolimbic reward pathways while listening to music that is considered absorbing (Cardona et al., under review). Absorption is also correlated with musical preferences (Hall et al., 2016). Taken together, this evidence implies that musical experiences which are more absorbing are also more rewarding, and hence enjoyable. This is relevant in the context of therapeutic music interventions; if the patient or user enjoys the act of ‘taking the medicine’, so to speak, then engagement and compliance are likely to be higher. Moreover, the listener is more likely to be receptive to the active components of the intervention if they find it pleasant. As a result, accounting for absorption is likely to augment the efficacy of music-based interventions by supporting consistent engagement.

LUCID’s Approach to optimizing absorption

LUCID’s core technology was developed with the aim of providing highly absorptive music-based interventions. Our core technology currently creates these conditions by providing personalized music sequences that account for the user’s musical preferences and current mood (iso principle) in the music selection and curation processes. Moreover, the soundscapes and music used in our products are recorded and produced using 3-dimensional spatialization techniques to support a more immersive experience, which are likely to further contribute to absorption (Guastavino et al., 2007). Soundscapes are recorded using binaural technology, and music undergoes a post-processing step to localize the musical instrumentation within a three-dimensional sonic space. By creating an auditory simulation of a spatialized environment including both nature soundscapes and music 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.

We are continuing to build on those core technical competencies. Assuming that state absorption is an indicator of whether a current music sequence is effective and considering that trait absorption influences musical preferences, objective measurements of these characteristics will be integrated into the music selection and adaptation process. LUCID is currently developing modules to (1) quantify the characteristics of music that induce the highest state absorption in an individual and (2) develop their capacity for music absorption as a trait. These modules will add value in all instantiations, but will be particularly relevant for developments in psychedelic-assisted therapies, in which high trait absorption has been strongly associated with the intensity of altered states of consciousness (Studerus et al., 2012) as well as pleasant and mystical experiences (Nichols, 2016), which have in turn been associated with positive therapeutic outcomes (Roseman et al., 2018). See LUCID's **Music and Psychedelics** whitepaper for more detail.

Natural soundscapes

The benefits derived from exposure to natural environments are well-documented. Spending time in nature has been associated with reductions in rumination (Bratman et al., 2015), reductions in physiological markers of stress (Park et al., 2010), and positive effects on mood and memory for people living with major depression (Bergman et al., 2012).

Two core theories have been developed to explain these restorative effects: Stress Recovery Therapy (SRT), which examines the effects of nature on emotional states and physiological markers of stress, and Attention Restoration Therapy (ART), which focuses on the cognitive effects. See Yannick & Siegfried (2018) for a review. SRT is predicated on evolutionary psychology, and more specifically on the idea that human beings have evolved in natural, vegetation-rich environments; we are biologically predisposed to thrive emotionally in these environments as a result. Conversely, ART is centered around the claim that natural environments are more conducive to states of focus and directed attention on account of the wealth of interesting stimuli that are often found in natural settings, which capture one's attention in an automatic, bottom-up way. According to ART research, spending time in natural environments can help to restore one's ability to exercise focused attention, which can be depleted and challenged by modern life. The notable differences between highly urbanized environments and natural landscapes is likely to contribute to stress, considering the environments within which we have evolved to flourish (Song et al., 2018). With more than 50% of people currently living in urban areas globally and with that proportion projected to increase to 70% by 2050 (Bratman et al., 2015), the question of how we can mitigate the detrimental effects of urban life for our psychological wellbeing remains open and relevant.

Interestingly, simulations of natural environments have shown similar effects. Experimental research conducted by Annerstedt et al. (2011) showed greater stress reduction following an acute stressor when participants were placed in a virtual forest as compared to a standard room. Gwan-Woo et al. (2010) conducted a study using fMRI to assess the effects of natural and urban imagery on participants' brain activity. Exposure to images of natural scenes resulted in increased activation of the anterior cingulate gyrus and the insula, which have been associated with empathy, whereas exposure to images of urban scenes resulted in increased activation of areas including the amygdala, which is associated with fear and anxiety. These results support the idea that exposure to nature - even simulations thereof - significantly changes the predominant regions of brain activation, likely corresponding to changes in emotional states. Simulated natural environments have also been shown to modulate behavior: Nadkarni et al. (2017) randomized maximum-security prisoners to exercise in either a plain gym or a room with nature videos playing. Inmates who watched nature videos reported feeling significantly calmer, less irritable, and more empathetic, and committed a staggering 26% fewer violent infractions as compared to those who did not watch the videos. Prison staff corroborated these findings.

In order to leverage these deep-seated psychological cues imparted by immersion in natural environments, LUCID embeds recordings of natural soundscapes within the music-based experiences delivered through our products. These soundscapes are recorded using 3D spatialization technology, as outlined in the **Absorption** section above.

Auditory beat stimulation

Auditory beat stimulation (ABS) is a family of auditory stimuli designed to induce brainwave entrainment; meaning, the synchronization of neuronal activity with the ABS frequency (Vernon et al., 2014). The effects of ABS are contingent on the frequency used. A summary of some relevant areas in which ABS techniques have shown efficacy is outlined in Table 3. Of particular note, ABS in the theta and delta frequency ranges may reduce anxiety and promote increased self-reported relaxation (Isik et al., 2017; McConnell et al., 2014; Padmanabhan et al., 2005; Wahbeh et al., 2007).

Table 3: Overview of some effects of ABS of varying frequencies.

	Outcomes	ABS Frequency	Sources
Migraine	Reduce attack frequency	12 H, decreasing to 8 Hz	Lovati et al. (2019)
Pain	Reduce perceived pain	6 Hz; range from 8-12 Hz	Zampi (2016); Ecsy et al. (2017), Dabu-Bondoc et al. (2010)
	Reduce pain and primary symptom severity in conditions related to chronic pain	Self-selected frequency	Huang & Charyton (2008)
Anxiety	Reduce anxiety severity	Range from 1-10 Hz	Huang & Charyton (2008); McConnell et al. (2014); Isik et al. (2017); Padmanabhan et al. (2005)
Sleep	Induce relaxation; increase theta and reduce beta brainwave power in adults with subclinical insomnia, thereby reducing hyper-arousal state and assisting in sleep induction	6 Hz	Choi et al. (2020)
	Produced deeper sleep, longer N3 phases	3 Hz	Jirakittayakorn & Wongsawat (2018)
	Significantly improved ratings of sleep and wakefulness quality, sleepiness, and motivation	2-8 Hz	Abeln et al. (2014)
Memory	Associated with improvements in long- and short-term memory	15 Hz	Beauchene et al. (2016), Beauchene et al. (2017)
Focus	Associated with improvements in attention and vigilance tasks	40 Hz, 16-24 Hz	Colzato et al. (2017), Hommel et al. (2016), Lane et al. (1998), Reedijk et al. (2015)

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Solution: Core Technology & Offerings

Intellectual property

LUCID's intervention is rooted in three core technologies. The first is a novel audio engineering technique that integrates auditory beat stimulation of varying frequencies into music (see **Patent 1** below for more details). 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 deep reinforcement learning system that personalizes music curation for particular outcomes in real-time. (See **Patent 2** below). This second technology produces correlated data that can then be used in deep learning systems to uncover a deeper understanding of human responses to music and their mechanisms. These insights are used to enable a third core technology, BioMIR, which includes a set of tools and generative systems to supercharge the human composition process of functional music (see the **Music Production Practices** section below). All of these technologies are protected under two patents that have both received positive PCT reviews (most claims deemed 'novel' and 'inventive' after international patent search). See Figure 1 for a visual depiction of the relationships between these technical modules.

Patents

Patent 1: Device, Method, and Medium for Integrating Auditory Beat Stimulation Into Music *(PCT/CA2020/050585 PCT 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.

Patent 2: Method, System, and Medium for Affective Music Recommendation and Composition *(PCT/CA2021/050220 PCT Status, Priority Date: February 24th, 2020)*

A method, system, and medium for affective music recommendation and composition. A listener's current affective state and target affective state are identified, and 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 effecting 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 auditory stimulus. Over time, the machine learning system gains a

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robust understanding of the relationship between music and human affect, and thus the machine learning system may also be used to compose, master, and/or adapt music configured to induce specific affective responses in listeners.

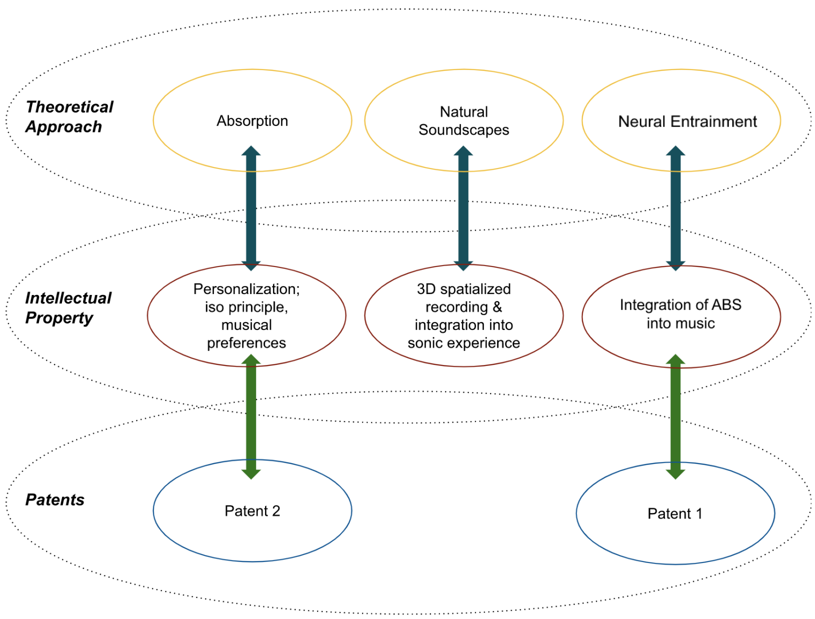

Figure 1: Connecting the dots between LUCID's approach, intellectual property, and patents.

API & Service Offerings

LUCID's tech stack consists of stand-alone components that can be leveraged in varying combinations, supporting LUCID's partnership model in delivering functional music to multiple markets (see Figure 2). Three licensable components of our tech stack are outlined below.

1 - LUCID API

LUCID's API provides the patent-pending affective music recommendation system ('AMRS') as a service. The AMRS engine can optimize any music library for functional music outcomes. This patent-pending engine curates music sequences based on the user's current and target state while personalizing them based on the user's unique reactions to music. The core recommendation functionality is complemented by LUCID's patent-pending audio engineering framework for integrating auditory beat stimulation into music. Each component is isolated and available for use as desired. This system is 'content agnostic' meaning that it can be used with any music library) and has been used with LUCID's core content library and with external catalogues provided by Universal Music Group (UMG). The LUCID API is used to power LUCID's VIBE mobile application, along with other DTx productions both internally (in development) and for our partners.

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2 - Functional Music Library

LUCID's functional music library has grown exponentially through licensing sourced content and extensive in-house composition. 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.

3 - BioMIR

Currently in its alpha stage, BioMIR will soon be available as a software-as-a-service platform to provide 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.

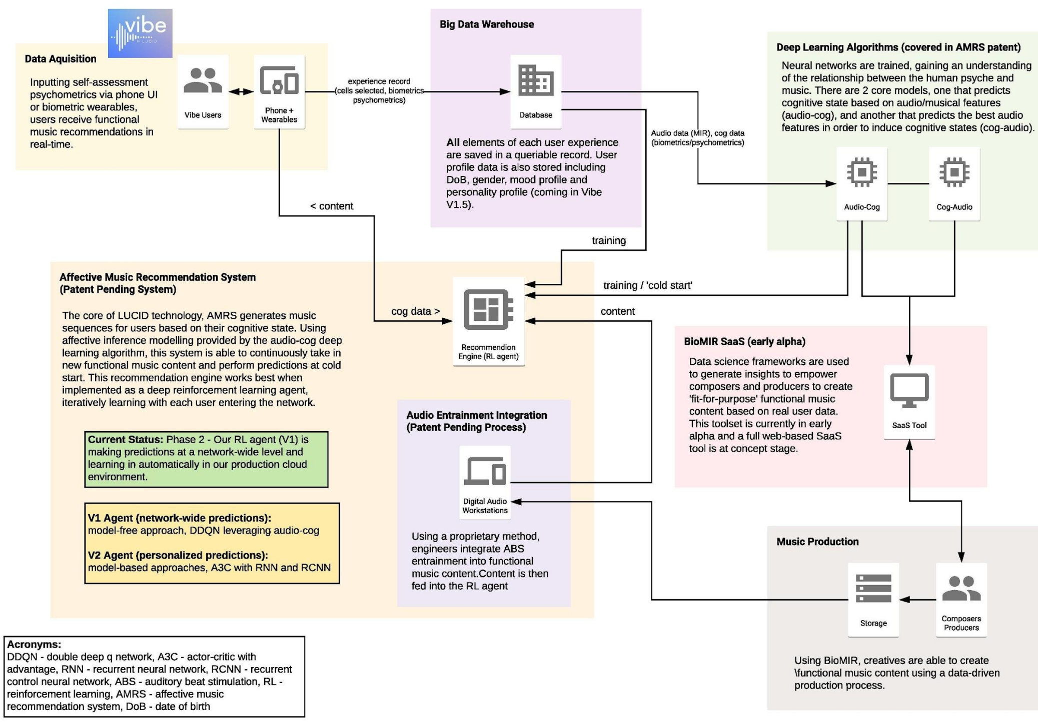

Figure 2: Tech Ecosystem.

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Overview: Supporting Data

Validation Research

Adult Acute Anxiety Study

Motivation:

This randomized controlled study was conducted to assess the effects of a single use of LUCID's auditory intervention on acute anxiety symptoms. For increased transparency, this study was pre-registered prior to data collection using the Open Science Framework.

Methods:

Participants (n=318, mean age: 28.95 years, 232 females, 86 males) currently taking anti-anxiety medication were recruited using Prolific, a remote research platform. Following a screening procedure, participants were randomly assigned to listen to 24 minutes of either a personalized music intervention curated by LUCID's affective recommendation system combined with 4 Hz ABS using the algorithm outlined in **Patent 1** above, a LUCID-personalized music curation alone, or one of two active comparator conditions (4 Hz ABS alone or pink noise). The primary outcome measure in this study was the change in the State-Trait Inventory of Cognitive and Somatic Anxiety-State (STICSA-s) scores, and the design was structured to allow for the additive effects of two of LUCID's core competencies (ABS integration and functional music curated using AMRS) to be assessed.

Results:

Among individuals with moderate trait anxiety, we observed reductions in somatic anxiety that were statistically greater in both the combined music and ABS and music-alone conditions than in the pink noise condition (medium to large effect sizes). The combined music and ABS condition also outperformed the condition of ABS alone. Reductions in cognitive anxiety were significantly higher for the combined music and ABS condition than for all other groups. (See Figure 2 and supporting data in Tables 4 and 5.) Reductions in anxiety were also observed in participants with high trait anxiety; however, these effects were not as well differentiated and further study is required. We expect that the efficacy of treatment will be amplified across all groups over the course of longitudinal use.

It is worth noting that the effect size of the comparison between the combined condition (music and ABS) and the control condition (pink noise) is 0.83. According to a review by Hidalgo et al. (2007), documented effect sizes for benzodiazepines (pharmaceuticals used to reduce acute anxiety) are approximately 0.38. This finding demonstrates the efficacy of LUCID's intervention for

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individuals with moderate trait anxiety relative to other treatment options and supports further study.

Table 4: 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 (one-tailed)	0.004	0.005	0.05	0.04
Effect size (Cohen's d)	0.83	0.86	0.52	0.57
Power	0.84	0.79	0.52	0.45

Table 5: Comparisons of cognitive 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 (one-tailed)	0.05	0.02	0.15	0.43
Effect size (Cohen's d)	0.49	0.78	0.30	0.06
Power	0.50	0.72	0.16	0.07

According to multiple linear regression analysis, music preferences also played a significant role: for individuals who reported a stronger appreciation for music characterized as 'Intense and Rebellious,' a smaller reduction in state anxiety was observed ($p=0.02$). We have dubbed this as the 'heavy metal effect': individuals who prefer music of higher intensity may be less likely to experience anxiolytic effects from music with a traditionally calming aesthetic. This result supports the findings of Renfrow & Gosling (2003) and speaks to the value of a personalized music intervention which accounts for these individual differences. No adverse events were reported.

Table 6: Mean & standard error of mean of somatic state anxiety reduction.

	Music & ABS	Music	Pink Noise	ABS
Mean reduction	4.36	3.43	2.09	1.86
Percent reduction (%)	13.2	10.4	6.3	5.6
Standard Error of Mean	0.93	0.75	0.46	0.40

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Table 7: Mean and standard error of mean of cognitive state anxiety reduction.

	Music & ABS	Music	Pink Noise	ABS
Mean reduction	6.38	3.35	4.42	3.13
Percent reduction (%)	21.3	11.2	14.7	10.4
Standard Error of Mean	0.90	0.71	0.75	0.87

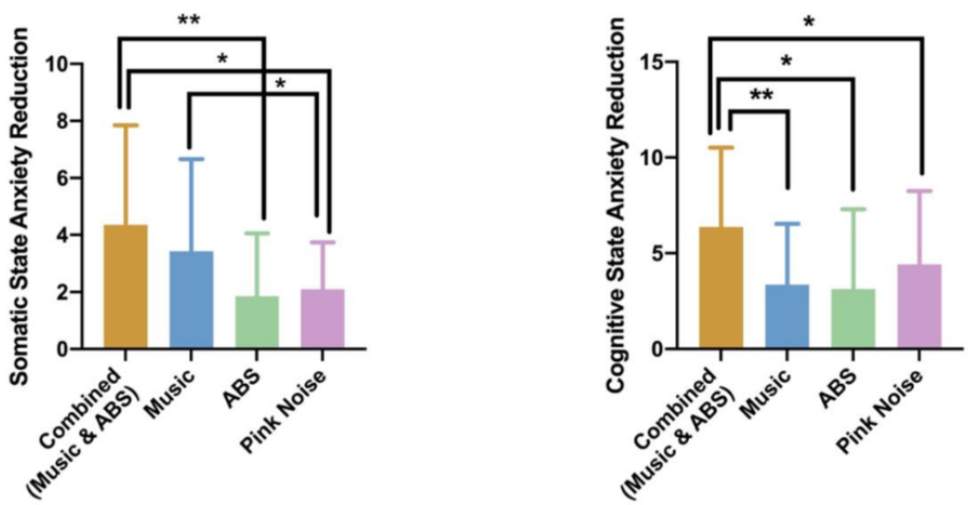

Figure 2: Somatic and cognitive state anxiety reduction in moderate trait anxiety participants as compared between intervention groups. (* indicates p < 0.05)

Results have been presented at the McMaster Institute for Music and the Mind NeuroMusic conference (November 14th, 2020) and the international Conference on Music Perception and Cognition (July 28 2021). A preprint has been archivd at PsychArXiiv (https://psyarxiv.com/qnhu4/) and has been accepted for publication in the journal PLOS1.

Comparison to Generic Relaxation Music

Motivation:

This pilot study was conducted in order to compare the efficacy of LUCID's personalized music curation with embedded ABS to generic relaxation music with respect to stress and mood outcomes.

Methods:

Participants (n=40, mean age: 25.05 years, 22 males, 17 females, 1 undisclosed gender) were recruited using the remote research platform Prolific, and were pre-screened for moderate anxiety symptoms using the STICSA trait and cutoffs reported in a previous study (Amaral et al., 2013). This population was selected based on the hypothesis that a single intervention use is likely to be most effective for participants with moderate trait anxiety: participants with low trait anxiety are more likely to present with low levels of acute state anxiety and due to this low effect size, a very large sample would be needed to observe statistically significant effects; conversely, participants with severe anxiety may find the first use of any experiential therapy to be anxiety-inducing, and may show more consistent effects in a longitudinal study. This hypothesis was supported by the results of the **Adult Acute Anxiety Study** described above. Participants were randomized to listen to either a 24-minute personalized music curation with embedded 4 Hz ABS or 24 minutes of the Spotify-curated relaxation playlist with the highest number of followers at the time of data collection.

The primary outcome measure of this study was self-reported stress, using a visual analog scale (VAS) and the following question: 'Indicate how stressed you feel in this moment.' Secondary outcome measures included the Self-Assessment Manikin (SAM), which measures emotion on two axes: valence, indicating positivity/negativity, and arousal, indicating high/low activation.

Results:

LUCID's music intervention produced significantly greater reductions in stress (VAS) and activation (SAM) and significantly greater increases in positive mood (SAM) as compared to the generic 'Calm' playlist. (See Table 8 and Figures 3 & 4.) No adverse events were reported.

Table 8: Changes and comparisons in primary and secondary outcomes.

	LUCID (n = 34)	Spotify (n = 17)	p-value	Cohen's d
Change in stress VAS	-2.25 (-20.5%)	-1.35 (-12.3%)	0.05	0.63
Change in SAM-Activation	-0.63 (-12.6%)	0.12 (2.4%)	0.01	0.81
Change in SAM-Valence	0.58 (11.6%)	0.18 (3.6%)	0.05	0.54

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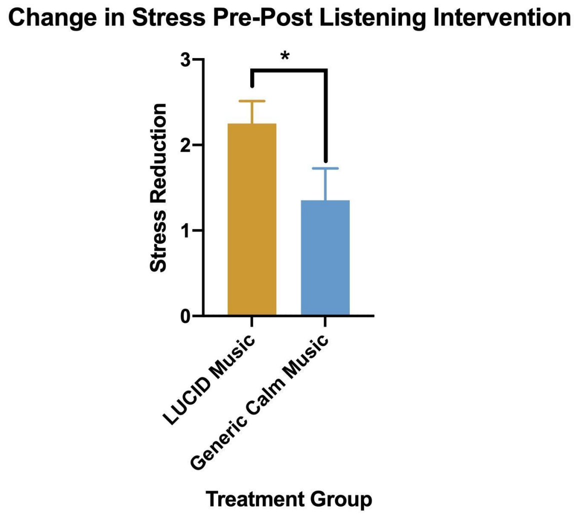

Figure 3: Reduction in stress (VAS). (* indicates p≤0.05.)

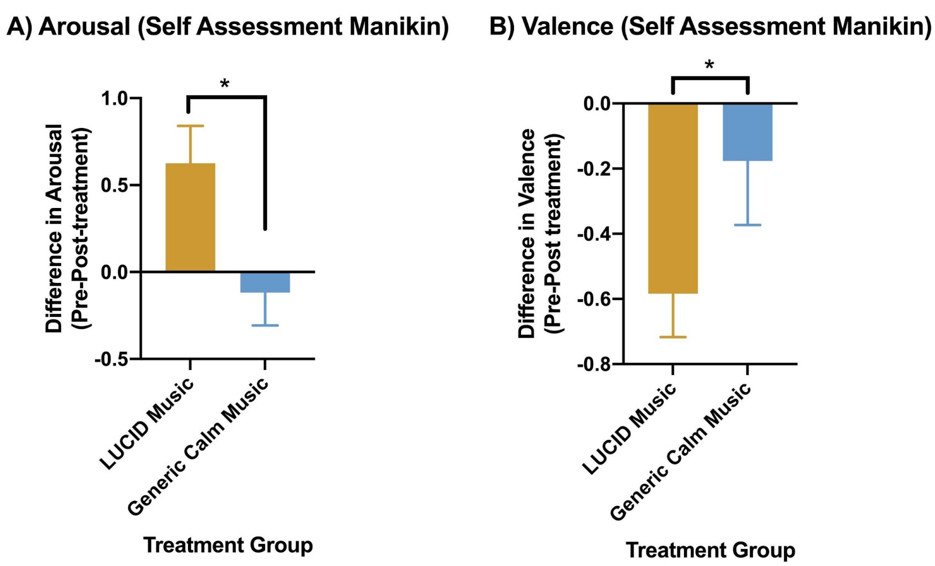

Figure 4: Reduction in Self-Assessed Mood (SAM). (* indicates p≤0.05.)

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Real-World Evidence

In-App Data Analysis

Analysis was performed on anonymized data from real-world use of LUCID's consumer-facing app, VIBE, over an 8-week period to assess the efficacy of VIBE (see Table 9 for overview). At the time of this analysis, clean data of completed uses of VIBE was available for 1347 app uses from 408 users.

This analysis indicates that VIBE is largely effective at reducing anxiety. For 57% of users, it is effective at reducing anxiety the majority of the time; for 41% of users, it is effective every time. On average, VIBE users demonstrated 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 their target emotional state.

Table 9: 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%

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Applications: Current Developments

Dementia: Music-Based Digital Therapeutic

In the US alone, approximately 6.2 million people are currently living with dementia (Alzheimer's Association, n.d.). These individuals, even those with advanced symptoms, typically retain musical appreciation longer than other faculties (GCBH, 2020). As a result, listening to familiar music can connect individuals living with dementia to their identity, helping to mitigate confusion and associated agitation. Moreover, neuroimaging studies have demonstrated that passive music listening can lead to activations of the anterior portion of the hippocampus, a key brain area involved in memory formation that shows volume reduction in response to dementia and depression, particularly if the music conveys emotion (Blood & Zatorre, 2001; Koelsch, 2009). It has thus been hypothesized that frequent engagement in passive music-listening may lead to neurogenesis, which may slow the rate of brain aging (Koelsch, 2009). In addition, the neurotoxic modifiers produced in response to stress cause gray matter atrophy in the hippocampus; as a result, interventions that target stress reduction may reduce the advancement of symptoms (Baumgartner et al., 2006; Blood & Zatorre, 2001). Music interventions are widely used at present as adjunctive therapies for people living with dementia; however, they often entail high-cost music therapy providers or are high-burden for family members or caregivers to administer.

Noncognitive psychiatric symptoms (NPS) in AD include agitation and depression, and affect 98% of patients at some point in their disease progression (Kales et al., 2014). These symptoms are known to correlate with advancing cognitive decline (Mayor, 2015), are associated with increased morbidity, mortality, and faster disease progression, and result in 30% of the cost of care in AD (Kales et al., 2014). Moreover, the vast majority of treatments for AD are focused on addressing the neurological cause of the disease and do not directly address this branch of symptoms. There is a distinct lack of effective interventions for the behavioral health symptoms so widely associated with AD, although these symptoms contribute significantly to the economic costs and burden of care of the disease. Current practice entails widespread use of psychotropic medication to reduce agitation and subsequent aggressive behaviors, which does not align with the wishes of all providers, families, or patients. As a result, there is a significant impetus to address this challenging symptom from both a health economics and an ethical point of view.

LUCID is engaging in a collaboration with a global pharmaceutical company to develop a digital music-based intervention to optimally select and curate music to support acute cognition and minimize agitation in people living with dementia and mild cognitive impairment. This tool will be optimized to select music that has a high probability of being familiar to the patient, and will adapt over time to what music is most effective for that patient. This tool will also generate broad insights into the effects of music-listening interventions for this population and how sound can be further optimized as part of a holistic approach to care.

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Healthcare Provider Burnout: Combination Digital Therapeutic

Burnout is a cumulative reaction to ongoing occupational stressors (Rossi et al., 2006). At its core, burnout is underpinned by stress (Khamisa et al., 2015), although stress and burnout are experientially different: acute stress is characterized by hyperreactivity and over-engagement of the sympathetic nervous system, while burnout more often presents as a disengagement and a sense of helplessness or hopelessness. Additional mental health challenges like anxiety and depression also contribute to the risk of burnout (Hu et al., 2020). Models of burnout proposed in the literature demonstrate that both *cognitive* and *emotional* symptoms may be present, and that symptoms may vary based on both the *stage* of burnout and interpersonal differences (see Figure 5, below).

		Stages			
		Enthusiasm	**Stress & Overload**	**Experience**	**Reaction**
Dimensions	**Cognitive**	High hopes, unrealistic expectations	Inability to cope	Lack of feelings of personal & professional accomplishment	Frustration & apathy
	Emotional			Exhaustion	Depersonalization

Figure 5: Model of burnout based on Friedman (1996).

Effects of burnout include *absenteeism* (increased sick leave and turnover), *presenteeism* (reduced job performance and elevated errors at work), detrimental effects on physical health (Dall'Ora et al., 2020), and an overall negative influence on workplace culture. These effects culminate into reduced wellbeing and quality of life for workers, increased risks for patients, and detrimental economic effects for employers. In 2017, around half of physicians presented with at least one symptom of burnout (Shanafelt et al., 2017).

Some solutions, including Cognitive Behavioral Therapy (Ahola et al., 2017), mindfulness (Ahola et al., 2017), social support (Khamisa et al., 2015), and music-based interventions (Kacem et al., 2020), have demonstrated efficacy for burnout symptoms. However, these tools are not optimized for the unique needs, challenges, and lifestyles of frontline healthcare workers. Moreover, these existing solutions typically exist as single-featured tools; a stand-alone digital solution encompassing multiple effective modalities for improved ease of use and data capture capabilities has not been identified in the market.

LUCID is collaborating with a large US-based healthcare delivery network boasting 90 hospitals across 22 states with over 70,000 employees to co-develop and validate a digital solution for burnout prevention and management. A preliminary research pilot will be conducted to assess which types of tools are most effective and engaging for frontline healthcare workers at different stages in burnout progression. Tested tools will be selected to address different areas of burnout symptomology and include LUCID's flagship Digital Music Therapy, digital Cognitive Behavioral Therapy, digital mindfulness/meditation, and circadian support technology optimized for shift workers. Findings from the preliminary pilot will inform a user-centered design process, followed by prototype development and a controlled trial.

Psychedelic-Assisted Therapy: Digital Music Therapy Adjunctive Treatment

Music has been a consistent feature within psychedelic practices and interventions, both in ritualistic uses that have been taking place over millennia and in contemporary Western medical contexts. Though there has been a considerable uptick in the study and development of the compounds themselves and the clinical outcomes they can produce, the music which almost always accompanies the psychedelic therapy is typically not evidence-based or selected with any quantitative rigor. Moreover, many providers are currently using music offerings with limited flexibility to personalize the music experience to the patient's needs or experience, though this type of dynamic personalization is often recommended in the literature (Bonny & Pahnke, 1972; Grof, 1980; Hoffer, 1965).

LUCID currently offers static playlists and an API to partners who are building digital platforms for this indication space. In the static playlists, LUCID leverages it's affective music recommendation system to curate emotional journeys in line with the desired protocols for the therapeutic intervention. These protocols are co-designed by the clinical partner and the LUCID team, and they take into account the psychedelic molecule and consumption method being experienced by the patient (i.e. sublingual vs. IV) and the therapeutic intention of the session. The stages of the psychedelic experience is also taken into account when making aesthetic decisions for this curation, consulting the body of scientific literature on the subject (Bonny & Pahnke, 1972). In the API offering, this same level of library curation is provided but with the ability to provide a dynamic and personalized experience for the patient. Emotional journeys are created in real-time by the practitioner and the music can be further personalized through biometric measurement on the listener. These generative playlists can then be offered to the listener via download during the integration stage in order to best optimize the therapeutic outcomes of the treatment.

Future Directions: Indication Pipeline

LUCID plans to continue employing a partnership model in the research and development of music-based interventions for specific populations. Based on existing literature regarding the use of music for clinical outcomes, we have identified several indications as high-potential areas for future development. See Table 10 below for an overview. By coupling our core competencies in music and machine learning with world-class expertise, LUCID is positioned to increase access to high-quality digital interventions optimized for targeted outcomes. People are naturally compelled to engage with music both for pleasure and for its drug-like effects on mental state. We are creating tools to leverage this natural tendency and to bolster the benefits that individuals stand to gain from music.

Table 10: Areas of future development.

Indication	Evidence	Relevance
Chronic & episodic pain	Music-listening can reduce stress, distress, depressive effects, perceived pain intensity, and opioid requirements in individuals suffering from acute and chronic pain (Cepeda et al., 2006; Smith et al., 2018; Bernatzky et al., 2011).	Pain is often treated with pharmaceuticals with a high potential for abuse and that sometimes lose their efficacy over prolonged use. Chronic and episodic pain can further cause depression and anxiety. About 20% of American adults suffer from chronic pain (Yong et al., 2021).
Tinnitus	Tinnitus, or chronic ringing in the ears, is often exacerbated by stress, which music is well-indicated to reduce (see **Music for health outcomes** section above). There is also some literature support for auditory habituation therapies (Neff et al., 2019; Reavis et al., 2012).	Sound therapies are currently used by tinnitus patients, but are largely limited to masking. Around 10% of American adults suffer from tinnitus (U.S. Department of Health and Human Services, n.d.), and there is a lack of effective treatments available.
Pre- and intra-operative anxiety and discomfort in diverse healthcare settings (surgical, dental, etc.)	Music-listening can reduce perioperative pain and anxiety; is as effective as diazepam at reducing vital signs of anxiety and is more effective than benzodiazepines at reducing preoperative anxiety (Shabonlei et al., 2010; Good et al., 2005; Jangsirikul et al., 2017; Berbel et al., 2007; Chanda et al., 2013).	In inpatient settings, pain is often treated with pharmaceuticals that have a high potential for abuse and anxiety is often treated with sedation. Around 50 million surgical procedures are conducted per year in the US (Stanford Health Care, n.d.).

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