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Is music a drug? How music listening may trigger neurochemical responses in the brain

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Abstract

In this article, we explore the idea that music listening can achieve neurological and psychological effects that are somewhat similar to those facilitated by psychoactive substances. To motivate this claim, we delve into the mechanisms behind music perception, psychoactive substance use, and their mutual relationship, relying on recent developments in psychedelic therapy and neuropsychopharmacology. Using a comparative approach, we discuss some underlying mechanisms of peak experiences and their neurochemical properties and suggest that music may be regarded as an alternative psychoactive trigger, prompting neurochemical responses in the brain, with resulting feelings of coping, (aesthetic) pleasure, and reward.

Keywords

psychoactive drugs, neurochemistry, peak experiences, coping, pleasure, reward

The human tendency to alter the state of consciousness through psychoactive substance use has ancient roots (Samorini, 2019). As early as 200 million years ago, hominid species have been using drugs (Saah, 2005) and, even today, natural products and (semi-) synthesized substances are used for their psychoactive or psychotropic effects. Usually, these substances are administered to the body through intravenous or intramuscular injection, oral administration (liquid or pill), smoking, or insufflation (Panlilio & Goldberg, 2007). On the one hand, such substances are inherently pathogenic in that they bypass adaptive information processing systems and act directly on ancient brain mechanisms but, on the other hand, they can also

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improve adaptation in some circumstances, relieve symptoms of mental disorders, and induce pleasure (Nesse & Berridge, 1997). Recent research has shown that motivation for the use of psychoactive substances mainly relates to coping, pleasure, performance, and creativity (Boys et al., 2001; Novacek et al., 1991; Soussan et al., 2018).

Throughout history, and in all cultures, and in all cultures, human beings have also displayed a tendency to listen to music (Levitin, 2006; Mithen, 2009). Interestingly, their main motives for engaging in individual music listening activities are somewhat similar to those that support psychoactive substance use and relate to coping, pleasure, reward, and aesthetics (Brattico et al., 2009; Miranda, 2019; Miranda & Claes, 2009; Redman & Bugos, 2019; Schäfer & Eerola, 2020; Zatorre, 2015; Zatorre & Salimpoor, 2013). This does not mean that music should be equated with drugs. Rather, we compare them, suggesting that they can have similar effects, and revealing some overlaps between research on the effects of music and psychoactive drugs, respectively. Our aim is to broaden the scope, aims, and methods of studies of the effects of music.

First, music and drugs are not the same. Music consists of pressure waves that are registered by the senses. As such, it is not invasive in a strict sense although, in terms of vibration, it can be considered as transferable energy that affects the body and the brain (Eidsheim, 2015). These vibrations are not restricted to the auditory sense but also activate the sense of touch (Huang et al., 2013) and the vestibular system of the inner ear (Todd, 1993, 2001; Todd et al., 2000). The latter emerges early in phylogeny and ontogeny (Trainor & Unrau, 2009) and interacts with the auditory system at both the subcortical and cortical levels of processing (Oertel & Young, 2004; Phillips-Silver & Trainor, 2007, 2008). Furthermore, music also induces reactions that trigger the complex machinery of neurochemical release, up to the level of the production of endogenous opiates or related substances, which are all primarily produced in the brain (Laeng et al., 2021).

In this article, we explore the claim that music can produce neurological and psychological effects that are somewhat similar to those facilitated by psychoactive drugs. To motivate this claim, we delve into the mechanisms that underlie music perception, psychoactive drug use, and their mutual relationship, relying upon recent developments in the domains of psychedelic therapy (Carhart-Harris et al., 2012, 2014, 2016; Griffiths et al., 2016; Johnson et al., 2016) and neuropsychopharmacology (Halberstadt, 2015). In this view, music can be regarded as a multivariate phenomenon that embraces biological, psychological, and cultural factors that, together, shape and enhance an overall, full-fledged experience. As such, it can be considered as a kind of adjuvant for achieving an altered state, although it should also be considered as having existential structure and meaning in itself (Clifton, 1983; Lochhead, 1986).

We embrace four major claims that run like a red thread through what follows: (1) music is a sounding and temporal phenomenon rather than a detached object in some mental space without any connection to its sonorous unfolding in real time; (2) listening should be targeted as a lived experience rather than as a disembodied reflection or interpretation of a mere mental construct; (3) the vibrational energy of music has a major impact on our biological systems; and (4) neuroscientific perspectives can be taken on the study of the effects of music on these systems. Some caveats should be noted, however, as the neural correlates of musical reward are just one layer in the processing of the music. Several topics should be discussed in parallel, such as the role of neurotransmitters in the generation of arousal, the relation between core pleasure and aesthetic reactions, the claim that all aesthetic reactions can be reduced to their biological origins, and the distinction between lower-level hedonic reactions as core pleasure as opposed to conscious aesthetic liking that originates in higher-level cortical structures of the brain (Liu et al., 2017; Zaidel & Nadal, 2011).

Music listening, however, is only one part of our story. Given its power to induce or evoke physiological and psychological effects that can be very similar to some of those elicited by substance use, we also delve into the neurochemistry of psychoactive substances (*psychedelics*) so as to identify the commonalities and differences that are reflected in the main body of this article. We start by looking at the mechanisms and motivations that underlie music listening to elaborate on its possible effects, in both the short and long terms. We then explore the modulatory power and effects of psychedelics, and subsequently describe music, tentatively, as a psychedelic resonator. Finally, we address the question as to whether music can be considered a (non-addictive) drug.

Music listening: Underlying mechanisms and possible effects

Explanations for individual music listening are made from a multitude of perspectives. Rather than being mutually exclusive, these explanations tend to complement each other, as both biological dispositions and higher-level mechanisms of sense-making modulate lower-level sensory and affective reactions to music (Reybrouck & Eerola, 2017). In what follows, our perspective on music listening relates to the complex neurochemistry of musical engagement, revolving primarily around the hedonic systems of the brain. This is a promising neurobiological approach in which music listening is raised to the standard of a science of pleasure (Berridge & Kringelbach, 2008; Leknes & Tracey, 2008). The approach is grounded in the mechanisms underlying pleasure, which are similar in most mammalian brains. We therefore put less emphasis on the higher-level mechanisms of musical sense-making, which are less important from an evolutionary point of view, although they play a role in the transition from hedonic pleasure to aesthetic enjoyment and the modulation of lower-level processes (see Liu et al., 2017; Reybrouck, 2017, 2019, 2021; Zaidel & Nadal, 2011 for in-depth discussion).

Listening as coping behavior

The hearing system functions both as a warning and a reward system. Human beings, therefore, tend to assess their acoustic environment in terms of potential threats and opportunities (Mithen, 2009; Rylander, 2004). Music listeners, accordingly, behave as biological agents who govern their natural disposition for coping with sounds. Coping, which living organisms use as a survival mechanism in their interactions with their environment, has been defined as the "cognitive and behavioral efforts to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of the person" (Lazarus & Folkman, 1984, p. 141). Coping is believed to contribute to the maintenance of a state of equilibrium with regard to both our internal and external environments (Bernard, 1878). Translated to the realm of music, it allows listeners to avoid stimuli that are considered harmful, and invites them to search for those that might have some benefits (Reybrouck et al., 2020), relying on neural mechanisms for evaluating the sonic environment. These entail the management and regulation of attention and arousal with the exploratory function of open monitoring that is fueled by arousal to heighten the responsiveness to sensory stimulation (Filippi et al., 2017). Coping, in this view, is not limited to reacting to challenges presented by the environment. It also involves interpreting them affectively and cognitively to make sense of them. As such, it can broaden the listener's behavioral and cognitive repertoire, as advocated by the *broaden-and-build* theory (Fredrickson, 2001), which states that positive emotions may consolidate and expand human resources. This occurs when individuals attempt to take creative courses of action, broadening their scope of attention, enhancing their thought–action repertoire, augmenting their holistic processing, and increasing their openness to new experiences so as to build long-term resources such as resilience and curiosity (Jayawickreme et al., 2012).

Traditionally, the literature on coping has focused mainly on acute stress and related avoidance behavior. It typically describes how humans rely on warning or alerting responses (e.g., orienting response, startle reflex, fight-or-flight reactions) when encountering stimuli that signal potential danger (Bernstein, 1968, 1979; Błaszczyk, 2003; Salloum et al., 2014; Todd et al., 2000). These dispositional reactions trigger the release of particular neurotransmitters that heighten arousal levels (Parker et al., 2011). They are mostly associated with sensations of stress and fear but, mediated by sensation-seeking traits, they can also be intentionally provoked to increase arousal and activation. In musical interactions, this is typically exemplified by high-intensity music listening (e.g., the rock and roll threshold of around 96 dB Leq) (Todd & Cody, 2000). In this view, music can be seen as a stressor spurring endocrine systems to release a cascade of neurotransmitters and/or hormones such as cortisol, adrenaline, noradrenaline, prolactin, testosterone, corticotrophin-releasing hormones (CRH), and adrenocorticotrophic hormones (ACTH) (Chanda & Levitin, 2013; Sapolsky, 1990).

A distinction should be made here between adaptive and maladaptive music listening. *Adaptive listening* may involve avoiding those stimuli that are annoying/harmful/painful and accepting or even seeking those that are valued as beneficial/pleasurable/worthy (Ryan & Deci, 2001). The normative view is that adaptive coping does not focus exclusively on acute shifts in reactive activity, but rather entails a shift from avoidance behavior to the celebration of optimal functioning by promoting optimal navigation strategies in the surrounding environment. *Maladaptive listening*, on the contrary, refers to ways of listening that celebrate overstimulation (e.g., sound levels above the threshold of discomfort) (Garrido & Schubert, 2013; Miranda & Claes, 2009; Reybrouck et al., 2020; Saarikallio & Erkkilä, 2007; Van den Tol et al., 2016). In both cases stress, whether negative-aversive or positive-rewarding, is associated with increased activation of the hypothalamic–pituitary–adrenal axis (HPA). This implies that a potential aesthetic engagement with music (see below) connects physiological responses with both positive and negative affect, expanding our cognitive–emotional states.

Pleasure, reward, and aesthetic empowerment

The shift toward optimal functioning has prompted research on musical pleasure and reward (Reybrouck & Eerola, 2022). Recent neuroscientific work has explored the localization and connectivity of so-called hedonic hotspots in the brain, focusing on the role of neurotransmitters, among others, in the modulation of responses to music (Reybrouck et al., 2018). Pleasure generation, in particular, seems to depend on a *hedonic network* of strongly connected hotspots that prompt and train listeners to want to experience musical stimuli with potential survival benefits. These are found along the reward circuitry (i.e., the dopaminergic mesocorticolimbic circuit) in the nucleus accumbens (NAcc), the insula, the orbitofrontal cortex (OFC), and the ventral pallidum (Ferreri et al., 2019; Peciña et al., 2006), and are responsible for basic and spontaneous responses to pleasurable stimuli as well as more conscious feelings of wanting or *incentive salience* (Berridge, 2007). As such, the hedonic network displays an interesting interplay between phylogenetically more recently evolved neocortical functioning and older brain systems (Kringelbach & Berridge, 2009; Kringelbach, 2009).

This hedonic approach to an understanding of music listening revolves mainly around the subjective evaluation of quality of life, which targets the experience of pleasure, the balance between positive and negative affect, and the cognitive–affective evaluation of overall life satisfaction. It is primarily orientated toward the experience of sensations of relaxation and happiness, and the avoidance of problems (Kahneman et al., 1999), summarized by some as more positive affect, less negative affect, and greater life satisfaction (Ryan & Deci, 2001).

By extension, music listening can be described in terms of *affective regulation* and *visceral reactions* to sounding stimuli, as a way of establishing or maintaining an optimal state of internal equilibrium, fueled by both interoceptive and exteroceptive information. According to this view, listeners may interact continuously with the sonic world by monitoring and adapting their personal state to stay within the limits of their own homeostatic level setting (Reybrouck et al., 2022).

Our overall preference for rewarding stimuli, however, goes beyond mere homeostatic regulation in the sense that human beings may also display an *aesthetic orientation* toward these stimuli. The question can be raised, however, as to whether the experience of beauty, or aesthetic reactions in general, should be considered in terms of general survival mechanisms or in terms of domain-specific reactions to a particular subset of the environment. In other words, is it feasible for individuals to depend on a toolkit crafted as a general-purpose architecture (Peretz, 2006), or is it instead a cultural product comprising various faculties initially unrelated to musical functions and of marginal importance to the species' survival (Pinker, 1997)? Initially, aesthetic reactions were believed to rely on more general, nonspecific neural mechanisms that relate to processes involved in attention and motivation (Zaidel et al., 2013). Brain areas mediating aesthetic responses to art works have indeed been found to overlap with those that monitor the appraisal of (other) items of evolutionary importance, such as the appeal of food and the attractiveness of potential mates. Such findings broaden the scope from a rather narrow focus on phenomena that are positively assessed (e.g., beauty, the sublime) to a broader domain that spans a continuum from negative (e.g., disgust, dislike) to positive appraisals (e.g., awe, ecstasy) (Brown et al., 2011).

From this point of view music can be seen as a tool for *aesthetic empowerment*. As a form of sonic energy, its vibrations affect our biological systems and have the potential to trigger two major outcomes: (1) the enhancement of our mood and motivation through dopaminergic activity within the reward circuit, and (2) the modulation of our level of physiological arousal through the sympathetic and parasympathetic activity of the autonomic nervous system (Brattico & Varankaité, 2019; Chanda & Levitin, 2013; Kringelbach & Berridge, 2017; Peck et al., 2016). Through enhanced emotional processing music may trigger an elementary and spontaneous core liking reaction that involves sensations of *valence* and *arousal*, both relying on visceral and peripheral sensory systems. The empowering impact of such an experience, then, is ultimately reducible to mental representations of bodily changes that are valued as hedonic pleasure or displeasure together with some degree of physiological arousal (Brattico, 2015; Lindquist et al., 2012).

The study of the aesthetic experience of music is highly relevant to this discussion, with a growing body of empirical research in recent times grouped under the umbrella term of *neuroaesthetics*. This is a challenging new field that tries to explain musical behavior in terms of stimuli, brain physiology, and motor responses (Brattico, 2020; Brattico & Pearce, 2013; Brattico & Varankaité, 2019; Brown & Dissanayake, 2009; Chatterjee, 2010; Leder, 2013; Nadal & Skov, 2013; Pearce et al., 2016; Zaidel, 2009). Three major outcomes have been identified to date: (1) the experience of aesthetic emotions (e.g., enjoyment, chills, nostalgia, awe, being moved), (2) aesthetic judgments based on conscious and formal evaluation of beauty, and (3) judgments of liking or preference. These have led to the definition of the aesthetic experience as "one in which the individual immerses itself in the music, dedicating its attention to perceptual, cognitive, and affective interpretations based on the formal properties of the perceptual experience" (Brattico & Pearce, 2013, p. 49). The findings are not yet conclusive, however, with important recent contributions from the field of network neuroscience or *connectomics.* These contributions aim to generate a complete map of all neural connections by describing the brain as a large structural network of neural connections that consist mainly of white matter tracts and gray matter neural units. This is a new field of research that relies on techniques and analysis methods such as diffusion-tensor magnetic resonance imaging (MRI), tractography, stochastic-dynamic causal modeling (DCM), and whole-brain computational modeling for the *in vivo* examination of anatomical and functional interactions on a whole-brain scale. Its major goal is to obtain information on the amount and direction of patterns of activity in particular brain regions (see Biswal et al., 1995; Cabral et al., 2014; Fauvel et al., 2014; Reybrouck et al., 2018 for an overview). The role of functional connectivity seems to be particularly informative, as it clearly displays the temporal dependence of neuronal activity patterns of anatomically separated brain regions. One major finding corroborates the assumed connection between aesthetic listening and reward processing, besides demonstrable relationships with moral decision-making. This means that aesthetic judgments share their neural correlates in the reward system with moral appraisal, thus pointing toward common ground (Avram et al., 2013; Sachs et al., 2016). This seems to echo the beauty-is-good stereotype and the old adage that music soothes the soul.

Neural activity in the reward circuit of the brain can thus be considered a key component of conscious listening, even to the extent that it enables the transition from hedonic pleasure to eudaimonic enjoyment, often experienced as transcendence (Reybrouck & Eerola, 2022; Ryan & Deci, 2001). The distinction between pleasure and enjoyment is important because the former is primarily oriented toward the satisfaction of homeostatic needs (e.g., food, sex, and bodily comfort), whereas the latter can go beyond the mere management of physiological responses permitting the individual to live in accordance with their daimon or true self; hence the term *eudaimonic*, to use Aristotle's term (Waterman, 1993). Eudaimonia is related to being challenged and exerting effort by engaging in diverse meaning-creating and purpose-seeking life experiences (e.g., artistic performances, athletic achievements, stimulating conversations; Jayawickreme et al., 2012; Lent, 2004; McGregor & Little, 1998). These may, in turn, contribute to the individual's feeling that they are intensively alive, authentic, and fully engaged in actualizing their true potential (Seligman & Csikszentmihalyi, 2000).

The eudaimonic perspective can be easily applied to adaptive listening, which is rooted (as we have seen) in evolutionary perspectives on listeners as biological beings. According to this view listening should not be defined solely in terms of avoiding harmful and/or annoying stimuli, but should be directed at obtaining a level of aesthetic enjoyment that links pleasure or positive affect to happiness. The role of aesthetic emotions is relevant here with a central focus on peak experiences/pleasures, and on the "aesthetic trinity" (Konečni, 2005), that is, the experience of thrills, awe, and being moved. This tripartition of aesthetic emotions provides an interesting starting point for the study of affective neuroscience, although the debate about the construct validity of the terms is still ongoing. It is still unclear, for instance, whether peak pleasure should be considered as a unified psychological construct or as a set of distinct responses. Specifically, the category of chills has received growing attention in this regard (see below). Peak pleasure can be seen as an important and objective marker of emotional responses, involving distinct feelings of awe, surprise, tension, pleasure, being moved, elevation, and nostalgia, each of which can be valued either as positive/desirable or as negative/aversive (Bannister, 2019; Salimpoor et al., 2011).

Effects of music listening: Short and long term

There are (at least) two ways of understanding the sensations of coping, (aesthetic) pleasure, and reward; Tinbergen (1963), for example, distinguishes between the *proximate* and *ultimate* *stages of explanation* (see also Fitch, 2015). While these sensations may be understood in terms of their long-term survival function (the ultimate stage of explanation), the proximate stage is more appropriate when using the findings of current neurobiological and psychobiological research to inform our understanding of musical experience. These explain sensations mechanistically in terms of their biochemistry and their physiological and neural correlates, showing that music can influence brain functioning through the modulation of dopaminergic activity within the reward circuit and thus linking dopamine release with musical pleasure (Brattico & Pearce, 2013). Music therefore functions as a mediator impacting mood and motivation. Through the activity of the autonomic nervous system it can influence physiological responses (e.g., heart rate, blood pressure, respiratory rate, body temperature, skin conductance, muscle tension) and strengthen noradrenergic neurons that regulate cholinergic and dopaminergic neurotransmission (Brattico & Varankaité, 2019; Chanda & Levitin, 2013). Most of these effects are short term or acute responses to musical stimulation and two of them are related to musical pleasure and reward, namely *physiological arousal* and emotional *peak experiences*.

Physiological arousal is a short-term response, mediated by activation of the sympathetic nervous system, reliant on dopaminergic synapses in hypothalamic pathways, and involving an acute shift in reactivity to specific potential harmful stimuli. The distinction should be made, however, between acute (short term) physiological reactivity and chronic (long term) elevation of the individual's basic homeostatic settings. The former operates in the presence of challenging stimuli, the latter also in their absence (e.g., hypertension, diabetes) (Ryff & Singer, 1998). Arousal, however, is not necessarily harmful, as evidenced by work on *allostatic load* (literally, stability through change). This refers to the cumulative wear and tear exerted by the physiological effects of environmental challenges on the organs and tissues of the body because of overactive and inefficient management of the stress response (McEwen, 1998; Sterling & Eyer, 1988). Known as the *general adaptation syndrome* (Selye, 1950), it should be regarded as a basic reactive pattern revolving around the concepts of *internal milieu* (Bernard, 1878) and homeostasis (Cannon, 1932). General adaptation aims to keep the homeostatic setting within safe limits when the individual is responding adaptively to life-endangering situations.

Allostatic load is reflected in biological stress responses triggered by the neuroendocrine, autonomic, and immune systems, making high demands on the mobilization by the HPA (Chanda & Levitin, 2013) and thus increasing the risk of pathology (organ breakdown, weakened immune system, cardiovascular dysfunction, elevated hormone secretion of cortisol and insulin). Yet it is possible to conceive also of optimal allostasis. Adaptive coping, in this case, is not mainly aimed at maintaining indicators of load within normal operating ranges; it also targets the solicitation of selected brain opioids such as β-endorphins, leucine, and methionine enkephalins, which can thwart negative emotions and favor positive ones (Panksepp, 1981, 1993). Secretion of dopamine from the catecholamine systems, release of endogenous opioid peptide from the hedonic hotspots in the central nervous system, and release of oxytocin are also important (Berridge, 2004, 2007; Berridge & Kringelbach, 2008; Chanda & Levitin, 2013; Ferreri et al., 2019; Wise, 2004).

It should be noted, however, that most studies of reactive behavior have focused mainly on the comparatively recently evolved telencephalic sites of the brain, both cortical and subcortical, while neglecting evolutionary older regions such as the brain stem. These older regions house key auditory processing mechanisms as well as mechanisms for homeostatic regulation (Habibi & Damasio, 2014; Pando-Naude et al., 2020). While the telencephalic sites provide a slow route for affective evaluative processing, such as conscious appraisal and liking, the older regions are important because they provide a fast route for appraising incoming stimuli instantaneously, operating mostly below the level of consciousness (Jacobsen et al., 2006; LeDoux, 1994; Power & Dalgleish, 1999).

Emotional peak experiences, also referred to as *strong experiences in music* (SEM) (Gabrielsson, 2011), involve a state of flow in which music completely dominates the listener's attention by excluding all other input. Flow relies on dopaminergic neurotransmission triggered by the hypothalamus, with identifiable arousal patterns of both the sympathetic and parasympathetic branches of the autonomic nervous system, which regulates physiological responses via the brain stem (Blood & Zatorre, 2001; Chanda & Levitin, 2013; Rickard, 2004; Salimpoor et al., 2009).

Music-evoked *thrills* are an important subcategory of peak experiences, and should be distinguished from *chills*. Thrills are mainly linked to novelty or acquiring new insights; chills entail absorption and being moved (Bannister, 2019; Pelowski et al., 2017). Chills, specifically, have been studied with regard to their construct validity and affective valence, the characteristics of the eliciting stimuli, and individual differences between responders. Bannister (2019) provides a tentative distinction between three main physiological response categories: (1) a dimension of frowning, smiling, and feeling warm or cold; (2) feelings of tingling, shivers, and goosebumps; and (3) the occurrence of tears and feeling a lump in the throat. Other classifications have used related categories such as warm chills, cold chills, and being moved. Their eliciting factors, however, are still somewhat elusive, as listeners seem to react to musical patterns rather than to mere acoustic triggers. It seems that simple linear–causal relations between stimulus and response are not easily established, and that the musical preferences and individual learning histories must be considered as well (Grewe et al., 2007).

In sum, music listening can elicit several short-term responses. It can also elicit more lasting effects such as psychological changes and neuroplastic modifications of the brain. Psychological changes affect the overall quality of life through emotion regulation and have observable effects on our behavior and brain functioning (Matrone & Brattico, 2015). Musical engagement can therefore contribute to well-being by modulating neuroendocrine responses to the sounding music (e.g., by reducing systemic stress hormones levels, see Conrad et al., 2007) and by promoting the experience of positive emotions. Accordingly, music should be situated, on the one hand, within the context of well-being and human flourishing, embracing aspects of both emotional and physical health (McFerran & Saarikallio, 2014; Reybrouck & Brattico, 2023). Neuroplastic changes associated with music listening, on the other hand, involve structural and functional modifications of three neural networks (the default mode network, the central executive network, and the salience network), resulting in the silent imprint of musical engagement on the brain (Klein et al., 2016; Reybrouck & Brattico, 2015; Reybrouck et al., 2018).

Psychedelics: Modulatory power and effects

Given that music can evoke feelings of pleasure and reward, as well as aesthetic emotions and peak experiences that may induce altered states of consciousness, it can be asked if there is an analogy between music listening and the use of psychoactive substances to alter the individual's state of consciousness? We therefore expand, in what follows, on the mechanisms that trigger neurochemical reactions in the brain. We start with a general overview of substance use before focusing on the use of psychedelics in particular, as an isolated phenomenon and in clinical and therapeutic settings.

A common way of categorizing drugs, first, is to look at their impact on the body and the mind. Psychedelics, or hallucinogens, form one major group of drugs including psychoactive substances that produce significant changes in perception, mood, and cognitive processes. The term *psychedelic* stems from the Greek ψυχή (*mind*) and δῆλος (to *manifest*), and refers to the quality of revealing the inner workings of the mind. Those most commonly used are LSD, psilocybin, mescaline, DMT, peyote, ibogaine, 2C-B, and 25[-x]-NBOMe (Alcohol and Drugs Foundation, 2023).

Generally, psychedelics stimulate serotonin 2A receptors (serotonin 5-HT2A) directly. These receptors play a role in higher cortical brain functioning and tend to produce unusual visual distortions as well as imaginative additions to features in the actual environment. They also affect emotions, typically generating empathogenic sensations of care, love, and connection to others and the natural world (Barrett et al., 2017, Barrett, Preller, & Kaelen, 2018; Kaelen et al., 2015; Nutt, 2012; Vollenweider et al., 1998). Although these effects have been reported repeatedly, they derive from the limited amount of research on the human experience of psychoactive substance use and remain somewhat elusive within the field of psychopharmacology, with numerous unresolved questions regarding visual and transcendental/mystical experiences. Indeed the majority of studies, typically based on nonhuman animal, mostly rodent, populations, explore the roles of brain chemistry, neurotransmitters, and receptors (Nutt, 2012), and their findings may not be generalizable to human beings.

In what follows, we provide a short overview of the effects of psychedelics on brain chemistry and, by extension, the body and mind. We also elaborate on the motivations for substance use, which are mainly reducible to the experience of pleasure and reward, and the reduction of suffering or coping, and we explore possible overlaps between the psychedelic experience and peak experiences during music listening.

Psychedelic effects in clinical settings and therapy

In the scientific literature, the psychoactive effects of psychedelic substances were first reported by psychiatrists who uncovered effects of their consumption on perception and cognition, as well as the dysregulation of emotion-regulation mechanisms (Kaelen et al., 2018; Nichols, 2016; O'Callaghan et al., 2020). After an early phase lasting from the 1950s to the 1970s, when psychedelics were administered in psychotherapy with the aim of dismantling ego defenses, facilitating emotional release or catharsis, and promoting individuals' insights into their own psyche by uncovering emotions, memories, and thoughts (Kaelen et al., 2015; Pollan, 2018; Schmid et al., 2015), modern clinical studies of the effects of psychedelics-assisted therapy (PAT) have obtained promising results in the context of depression, end-of-life anxiety, post-traumatic stress disorder, and addiction (Adamska & Finc, 2022; Kaelen et al., 2018). The use of *psilocybin*, in particular, has been explored (Reiff et al., 2020) and psilocybin-assisted psychotherapy is currently used as an established research protocol for safe drug administration in combination with psychological support as a clinical intervention (Carhart-Harris et al., 2016; Horton et al., 2021; Johnson et al., 2008; Ross et al., 2016; Wall et al., 2022). The use of psilocybin in clinical settings has been promoted because it can stimulate emotional release, induce peak experiences and mystical ones, and facilitate autobiographical insight (Busch & Johnson, 1950). Research focusing on patient assessments has signaled two main outcomes from psychedelic therapy: a shift from feeling disconnected from the world to feeling connected with oneself and others, and a shift from emotional avoidance to acceptance (Watts et al., 2017).

Music is often used as an adjuvant to PAT, functioning as a vital mediating factor for meaningful emotional and imaginary experience and self-exploration during the sessions through the elicitation of anthropomorphic, transportative, synaesthetic, and material sensations (Barrett, Preller, & Kaelen, 2018; Bonny & Pahnke, 1972; Moore, 2013; O'Callaghan et al., 2020). It has been found to act synergistically with the drug, as evidenced by multiple experiments. One of these was Helen Bonny's research program on music in psychedelic psychotherapy (using LSD) in the 1970s. When the program came to an end, she explored the extent to which music could stimulate imagery without drug administration, thus developing what has since become known as the Bonny Method of Guided Imagery and Music (McKinney & Honig,

Table 1. Main Outcomes of Music Listening and the Use of Psychedelics.

Music listening:
- the tendency to listen to music can be very strong but is essentially non-addictive
- music affects the body and the brain by triggering neuroendocrine reactions to the sound up to the production of endogenous opiates or related substances
- music may engage the hedonic systems of the brain, triggering pleasure, reward, and the experience of (positive) emotions
- music can facilitate peak experiences, sustained positive behavioral changes, personality adaptations, and positive clinical outcomes
- music listening can prompt visceral reactions, mood regulation, and motivation through dopaminergic activity within the reward circuit
- music can modulate physiological arousal and homeostatic regulation through mediation of the autonomic nervous system
- the musical experience may span the continuum from hedonic pleasure to eudaimonic enjoyment
- there are adaptive and maladaptive ways to cope with music

Use of psychedelics:
- psychedelics are inherently pathogenic, bypassing adaptive information processing systems with a danger of addiction
- psychedelics affect the body and the brain by triggering neurochemical and neuroendocrine release, which can affect higher cortical brain functioning
- psychedelics affect emotions, generating empathogenic sensations of care, love, and connection to others and the natural world
- psychedelics can have clinical benefits by stimulating emotional release and acceptance, inducing peak experiences, and facilitating autobiographical insight and connections with oneself and others
- psychedelics produce significant changes in perception, mood, and cognitive processes
- psychedelics may improve adaptation, relieve symptoms of mental disorders, and induce pleasure
- there are adaptive and maladaptive ways of using psychedelics

2017). In both cases, music complements the aims of psychedelic therapy by providing continuity within an experience of timelessness and structure while patients relinquish control and enter their inner worlds, enabling emotional release and peak experiences with a characterizing sense of unity, transcendence, reverence, wonder, meaningfulness, and ineffability (Bonny & Pahnke, 1972).

Psychedelics modulate the musical experience

Experiences triggered by psychedelics and music deploy several corresponding brain mechanisms that rely on common neurobiological and neurochemical processes (see Table 1 for an overview). Both activate neural areas that are involved in emotion, autobiographical memory, mental imagery, and self-referential processing. Moreover, psychedelics have the potential for enhancing auditory perception (Barrett, Preller, Herdener et al., 2018; Luo et al., 2016; Tang & Trussell, 2015), particularly via serotonin 5-HT2A signaling. This supports increases in emotionality, connectedness, and meaningfulness in response to music, as commonly observed after the administration of LSD and other psychedelics (Barrett, Preller, Herdener et al., 2018).

Music and psychedelics thus seem to influence each other in the sense that music acts upon the overall subjective experience triggered by the substance, while the experience itself also enhances the processing of acoustic features and music-evoked emotions. The presence of musical stimuli has even been found to be more important than the intensity of the substance consumed for predicting the reduction of depression (Kaelen et al., 2018) and the overall efficacy of music in psychedelic therapy was stressed also by the patients themselves (Barrett, Preller, & Kaelen, 2018; Belser et al., 2017; Watts et al., 2017). In psychedelic contexts, music listening seems to facilitate the experience by (1) encouraging the relinquishment of control, (2) facilitating emotional arousal and release, (3) triggering peak and spiritual experiences, (4) directing and structuring the experience, and (5) stimulating imagination (Bonny & Pahnke, 1972).

Music listening during a psychedelic trip seems to enhance emotional sensations related to transcendence, wonder, tenderness, power, nostalgia, and joyful activation (Kaelen et al., 2015), and has been found to promote mainly positive sensations that are associated, in turn, with effective therapeutic outcomes (Gabrielsson & Wik, 2003; Garcia-Romeu et al., 2014; Griffiths et al., 2006; Maslow, 1964; MacLean et al., 2011). Music listening thus seems to add considerably to the beneficial effects of psychedelics, enhancing mental imagery, emotion processing, meaning formation, and openness (Kaelen et al., 2016, 2018).

Empirical support for these claims has been provided by research on music-evoked emotions following LSD administration, demonstrating that music can facilitate peak experiences (Griffiths et al., 2006), sustained positive behavioral changes (Griffiths et al., 2011) and personality adaptations (MacLean et al., 2011), and constructive clinical outcomes (Griffiths et al., 2016; Johnson et al., 2014; Ross et al., 2016). In addition, LSD seems to influence the perception of distinct acoustic features, for example by altering the way the brain processes timbre (Kaelen et al., 2017). Besides these psychological effects, interactions between the effects of music and psychedelics were also shown to affect the state of neural networks (e.g., the default mode, the somatomotor network, and the visual network), revealing distinct brain states characterized by a specific pattern of cortical activity in specific networks (Adamska & Finc, 2022).

Interacting with timbral complexity, a significant degree of decoupling has been found to take place under the influence of LSD between the right precuneus (a hub highly connected to the inferior and superior frontal gyrus, but less so to the auditory regions), the right auditory cortex, and the right inferior temporal gyrus. The precuneus plays an important role in self-referential cognition and emotion regulation (Buckner et al., 2008; Cavanna & Trimble, 2006; Schilbach et al., 2012) but seems to exhibit a considerable degree of desynchronization after psychedelic intake (Carhart-Harris et al., 2016; Muthukumaraswamy et al., 2013; Riba et al., 2002), with observable effects such as ego dissolution and increased emotional lability (Carhart-Harris et al., 2016; Lebedev et al., 2015; Tagliazucchi et al., 2014, 2016). It seems that decreases in precuneus-auditory/inferior frontal gyrus coupling reflect a reduced regulatory influence of the precuneus on emotion processing, which may facilitate the intensification of emotional responses to music (Kaelen, 2017).

Music listening under the influence of psychedelics has also been shown to alter brain entropy, resulting in a transformative experience or the experience of an altered sense of self, as well as long-term changes in personality and behavior (Carhart-Harris et al., 2014; Lebedev et al., 2016). Although many aspects of the mechanisms behind these changes require further investigation, there is some evidence for a temporal dysregulation of emotion-regulating brain mechanisms (Carhart-Harris et al., 2012, 2016; Muthukumaraswamy et al., 2013; Tagliazucchi et al., 2016), which could explain the enhanced responsiveness to emotionally evocative stimuli, expressed through reduced feelings of control, ego dissolution, enhanced suggestibility, and reduced emotional inhibition. Enhanced receptivity to music can thus be seen as a trigger activating emotions, thoughts, and memories with personal salience and therapeutic relevance (see Kaelen, Giribaldi, Raine et al., 2018 for an overview).

It remains to be tested, though, whether resonance maximization could improve therapeutic outcomes such as those focusing on personality traits (e.g., openness to experience, absorption, suggestibility) or if music preferences could serve as predictive indicators for the (non)supportive effect of music (Kaelen et al., 2018). It is also important to emphasize the relevance of the preparation phase of psychedelic treatment as well as securing a safe and welcoming environment, commonly referred to as set and setting (Horton et al., 2021; Strickland et al., 2020). In this case, set can be described as the mindset or psychological state of the individual, including the participant's own background and state, previous encounters, personality, mood, expectations, and motivations. The setting or treatment setup, on the contrary, refers to the (supportive or non-supportive) environmental context in which the drug is taken (Carhart-Harris et al., 2018; Nutt, 2012).

Music as a psychedelic resonator

Recent research on music processing has seen a paradigm shift by regarding the aesthetic experience from a biological perspective while relying heavily on neuroscience and evolutionary biology (Reybrouck et al., 2022). To what extent, then, can music act as a psychoactive trigger, prompting the release of the brain's natural opiates (e.g., endorphins, enkephalins, dynorphins) that give us the sensation of pleasure and reward? This question offers is a promising new direction for mental healthcare practice, deviating somewhat from more conventional treatments and therapies, both in terms of drug administration and underlying theoretical frameworks (Barrett, Preller, & Kaelen, 2018).

The impact of music and ways of listening

The effects of music are not merely triggered by acoustic features and human physiology. They are also mediated by the listeners' attentional choices and mental states. There is no pharmaceutical model, as such, to explain the impact of music in terms of its structure or features, as in the case of a specific drug that consistently produces a homogeneous effect, irrespective of the individual user (Sloboda, 2005). Yet, from the perspective of psychophysics and psychobiology, there seems to be evidence of cause and effect in terms of cues (e.g., sudden loud sounds) and responses (e.g., listeners' instant physical reactions, such as the startle reflex; Reybrouck & Eerola, 2017). There is less evidence to support an understanding of higher-level processing and further research is needed. Early work on the use of music in psychedelic therapy has already produced some recommendations as to the characteristics of suitable stimuli for complementing the psychedelic experience. These take the form of playlists reflecting specific recommendations including instrumentation, forward movement, phrasing and dynamics, melodic line, stability of rhythm, and overall subjective mood. These playlists mostly lack specificity, however, and still require additional empirical testing and validation (Barrett et al., 2017). In general, most of the stimuli used in therapeutic interventions to date consist of ensemble pieces, stimuli with vocals typically excluding lyrics or including them in a language unfamiliar to the patient, and the music usually comprises ethnic, neo-classical (e.g., Max Richter or Olafur Arnalds), or classical music examples (e.g., Henryk Górecki or Arvo Pärt) (Kaelen et al., 2018).

It might be tempting to generalize from these findings and to consider specific (types of) musical stimuli as having a universal eliciting power. The extent to which it might be legitimate to infer that some musical characteristics are more effective than others can also be questioned, since individually tailored selections of music have been shown generally to yield better results than standardized selections. In any case, auditory stimuli affect individual listeners for many reasons, including their acoustic features and the individual's music preferences, personality traits, and personal associations with the stimuli. It has been shown that the three most most important predictors of response to psychedelic therapy are (1) liking of the music (style and quality), (2) resonance (music matching the listener's intrinsic emotional state), and (3) openness (the listener is open to/accepts the music-evoked experience) (Kaelen et al., 2018). Liking, however, seems to have the greatest impact on overall experience perhaps because it acts as an index for the emotional utility of a musical stimulus and thus functions as a kind of gatekeeper (or filter) for its possible effects (Barrett, 2017).

The neurochemistry of musical pleasure and reward

Music liking is closely related to the experience of pleasure and reward. The relationship between sensory pleasure and enjoyment, however, is complex, although considerable progress has been made in the understanding of the neurobiology of pleasure (Berridge & Kringelbach, 2008; Kringelbach, 2009). A first step is the study of the hedonic experience, even though it focuses rather narrowly on the experience of pleasant feelings. As such, it differs from the eudaimonic experience, as discribed above. Crucial for the motivation behind both kinds of experience is the coupling of cortical with subcortical brain regions, thus engaging a general-purpose system that enables a seeking disposition for expectations regarding the availability of an environment for reward (Alcaro et al., 2007). This seeking disposition, moreover, seems to have hedonic properties irrespective of the actual attainment of the reward. Baseline-level coupling should be distinguished, however, from phasic bursts that fire in response to specific cues, such as unpredicted rewards, prediction errors, novel stimuli, and physical, affective, or motivational salience (Venkatraman et al., 2017).

Here, the neurotransmitter dopamine is important (Nadal & Skov, 2013). It co-occurs with intensely pleasurable responses to music, triggering dopamine release in the mesolimbic striatal system and the sensory regions for auditory reception (Belfi & Loui, 2020; Zatorre & Salimpoor, 2013). Ligand-based position emission tomography research obtained even more ground-breaking findings, demonstrating a functional dissociation between the anticipatory and consummatory phases of peak emotional experiences, with the former being linked with dopaminergic activity in the caudate nucleus. The anticipatory phase is highly interconnected with limbic regions mediating emotional responses, while the consummatory phase is associated with activity in the nucleus accumbens. The distinction between the two phases suggests that musical appreciation has two dimensions: wanting and liking (Salimpoor et al., 2011).

Although the studies outlined above have produced valuable findings, there is still no conclusive evidence with respect to the complex neurochemical indicators of reward. This holds especially for concentrations of hormones such as prolactin and oxytocin, and their relation to dopamine release. The release of prolactin is controlled by the dopaminergic system, but dopamine itself is known to inhibit endogenous prolactin release (Fitzgerald & Dinan, 2008; Ben-Jonathan & Hnasko, 2001). This seems to suggest that many of its known effects decrease in the case of pleasurable experiences (Eerola et al., 2021), undermining some theoretical positions on the hedonic theory of music-induced sadness (Eerola et al., 2018; Huron & Vuoskoski, 2020; Ladinig et al., 2021). Could individual listeners' profiles and their evaluative weightings solve this paradox (Reybrouck & Eerola, 2022)?

There is more agreement as to the role of the nucleus accumbens with regard to its control of the release of dopamine. It is associated with the processes of reward, pleasure, and motivation, which collectively point in the direction of basic activities for survival (Brattico & Pearce, 2013), but its underlying mechanisms are still debated (Eerola et al., 2021). The homeostatic theory, for instance, claims that hormonal changes reflect homeostatic functioning by neutralizing the negative effects of distress, with increased levels of prolactin (in response to potential stressors) and oxytocin (in relation to its anxiolytic function) (Huron, 2011; Taylor et al., 2006; van den Burg & Neumann, 2011). The reward theory, on the contrary, states that psychological reward and its corresponding neurochemical correlates originate from the dopaminergic system, which is involved in prediction and anticipation (Schultz, 2013, 2015). Release of dopamine in the nucleus accumbens is believed to be associated with peaks of autonomous nervous activity accompanying the experience of intense emotional moments, including music-induced pleasure (Ferreri et al., 2019). Music, in this view, has the ability to manipulate hedonic states by pitching into the ancient reward circuit with large interconnections between the limbic regions that mediate emotional response (Salimpoor et al., 2011).

Music as a good drug?

Although considerable progress has been made regarding our overall understanding of the neurochemistry of musical pleasure and reward, there seem to be multiple routes to hedonic happiness, either with or without eudaimonic enjoyment. So far, four categories of enjoyable feelings have been identified: eudaimonia combined with hedonic enjoyment; hedonic enjoyment without eudaimonia; eudaimonia without hedonic enjoyment; and those that are enjoyed neither hedonically nor eudaimonically (Waterman, 1990a, 1990b). To generalize, it could be stated that mechanisms involved in fundamental pleasures share some overlap with those involved in higher-order pleasures, in the sense that they all draw on the same neurobiological dispositions for sensory pleasure (Berridge & Kringelbach, 2008).

Might some ways of listening be preferable to others because they are adaptive rather than maladaptive (see above)? The pursuit of music can be an appealing endeavor, even if music consumption can resemble addictive behavior; thus music may be conceptualized as a "good drug" (McFerran & Saarikallio, 2014, p. 94). If fueled by a tendency to strive for excessive contact with the enjoyable trigger, the analogy relies on the mechanism of medium maximization (Hsee et al., 2003), where the individual loses sight of the end by focusing on the means (Jayawickreme et al., 2012). This entails the danger of reducing hedonic happiness to mere hedonism, or the pursuit of pleasure for its own sake.

Addiction should also not merely be considered in a negative sense. It can also be defined more positively, with the runner's high as a typical example of a positive redefinition of the term (Glasser, 1976). In this view, music exerts powerful psychological effects through a wide range of sensory, emotional, cognitive, and motor channels, which may reflect the dynamics of coping with the sonic world. This search for effects can become addictive, in the sense that it becomes a search for overabundance.

Should the broad search for effects still be considered as addiction in its strictest sense (see Cockrill et al., 2011 for in-depth discussion)? This question can be addressed in two ways. First, there is the search for stimuli that have the potential for inducing relaxation as well as euphoria and peak experiences. To the extent that music can cause endorphins and adrenaline to be released in the blood to anesthesize or to pump up the listener (Billings, 2000; Blood et al., 1999), it may lead to the phenomenon of overabundance with the looming danger of addictive behavior. Nevertheless music can also induce rapid and potent changes in mood and level of arousal, and reduce negative states and craving tendencies (Donovan, 1988; Florentine et al., 1998).

A second, more promising approach, is to define addiction in terms of its costs and benefits (see below), and pain and pleasure. A distinction should be made here between music as a stressor, such that it exceeds the boundaries of optimal stimulation zones (e.g., critical range of loudness, spectral configuration of the sounds, overmodulation of the signal) or disrupts homeostatic level settings (Reybrouck et al., 2021, 2022). Listeners may enjoy stimuli that cause discomfort and have a negative impact on their health (McFerran & Saarikallio, 2014; Welch & Fremaux, 2017a, 2017b), resulting in hearing-threshold shifts (Kujawa & Liberman, 2006) and other complaints that are commonly categorized under the umbrella term of vibroacoustical diseases (Alves-Pereira & Castelo Branco, 2007; Castelo Branco & Alves-Pereira, 2004). There is, however, a whole gamut of music that is enjoyable within the optimal zone of stimulation, to the extent that it may function as an elicitor of neurochemical release. As such, some music might be regarded as an endogenously generated psychoactive trigger, as well as a resonator. The extent to which music can be considered a "good drug," however, requires some caution. There are some commonalities between drug abuse and compulsive music listening (e.g., medium maximization), but drugs typically hijack the reward and motivational systems rather than simply evoking their responses. Yet it is possible to conceive of a continuum between hijacking and evoking, with the differences between them relating to degree rather than quality. Harmful addiction to music, such that its costs are greater than its benefits, has been evidenced by observed markers of psychopathology, cases of happiness overdrive, mania, dysfunctional behavior, and poorer clinical functioning (Gruber et al., 2011), in particular when individuals listen to extremely loud music. Listening is less compulsive than most typical addictive behaviors and music listeners are unlikely to suffer from withdrawal symptoms if they cease listening. Positive addiction to music remains ill-defined and needs to be operationalized. The term *addiction* could be broadened and its negative connotations weakened, much as the distinction between distress and eustress has broadened and weakened the negative connotations of the term *stress*. We make this argument because the addictive power of music is only as effective as listeners allow it to be. Their individual attitudes to music listening and their beliefs about it should be considered, in terms of both its intra- and interpersonal effects.

Conclusion

In this article, we have focused on the psychoactive effects of music. We started with the mechanisms that underlie listening to music and moved on, via the transition from merely coping, rather than seeking pleasure and reward, to the higher-level mechanisms that underlie engaging in and making sense of fully fledged aesthetic experiences. Having elaborated on the modulatory power and effects of psychedelics we asked, finally, to what extent can music also function as a psychedelic resonator?

There is, however, a major distinction to be made between the use of psychoactive substances and music. Psychoactive substances are physical substances that directly trigger the generation and release of endogenous neurotransmitters, while music consists of pressure waves prompting similar effects albeit more indirectly. The power of music to induce such effects should be investigated by researchers in a field of study at the intersection of neuropharmacology and brain dynamics. Researchers in this field should try to find out why human beings listen to music, how they can maximize their resonance with the stimulus, and if music listening can provide a less invasive and less harmful alternative for listeners in search of peak experiences and altered states of consciousness. It is likely that future research on neuroaesthetics and the neurochemistry of musical emotions will provide further insights into many aspects of these topics that are somewhat elusive.

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