

Original Article

Being moved by listening to unfamiliar sad music induces reward-related hormonal changes in empathic listeners

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Many people enjoy sad music, and the appeal for tragedy is widespread among the consumers of film and literature. The underlying mechanisms of such aesthetic experiences are not well understood. We tested whether pleasure induced by sad, unfamiliar instrumental music is explained with a homeostatic or a reward theory, each of which is associated with opposite patterns of changes in the key hormones. Sixty-two women listened to sad music (or nothing) while serum was collected for subsequent measurement of prolactin (PRL) and oxytocin (OT) and stress marker (cortisol and adrenocorticotrophic hormone) concentrations. Two groups of participants were recruited on the basis of low and high trait empathy. In the high empathy group, PRL and OT levels were significantly lower with music compared with no music. And compared to the low empathy group, the high empathy individuals reported an increase of positive mood and higher ratings of being moved with music. None of the stress markers showed any changes across the conditions or the groups. These hormonal changes, inconsistent with the homeostatic theory proposed by Huron, exhibit a pattern expected of general reward. Our findings illuminate how unfamiliar and low arousal music may give rise to pleasurable experiences.

Keywords: being moved; music; sadness; prolactin; oxytocin; cortisol

Introduction

Deriving immense pleasure from listening to personally relevant music is a germane experience for millions of people. Some of these experiences have seemingly puzzling components, such as lack of familiarity or negative or somber emotional content. Such experiences offer an intriguing window into the way music—and art in general—is able to capitalize on our mental and physiological processes aimed to deal with interpersonal interactions and loss. Here, we explore how music may harness mechanisms involved in homeostasis and reward.

Often, strong emotional experiences associated with sad music are linked to personal memories triggered by the music.¹ They are also heav-

ily related to personally meaningful lyrics,² shaped by attitudes,³ and connected to the brain's reward system.⁴ However, there are multiple challenges in linking these experiences to the music itself, since external reasons, such as memories and lyrics, provide the most obvious explanations for the experiences.⁵ Past research has demonstrated that previously unfamiliar sad instrumental music may elicit highly pleasurable experiences in some listeners, whereas others find such music merely relaxing.⁶ The key difference here seems to be that enjoyment is linked to the ability to empathize with fictional events and expression conveyed by music. This has been recently conceptualized as the Pleasurable Compassion Theory,⁷ which draws from

empirical studies involving sad music^{3,8,9} that have identified that the enjoyment of sad music is linked with the feeling of being moved rather than actually liking the sadness expressed. This enjoyment, in turn, is more common for people who score high on empathy, whereas those low on empathy tend to focus on negative aspects of the experience.

What might be the mechanism that underpins this distinct and paradoxical feeling of being moved by unfamiliar sad music? This question has parallels in other forms of art, such as film and literature.^{10,11} Several explanations have been offered that range from misattribution of the emotion¹² to the enjoyment of beauty,¹³ mood repair,¹⁴ nostalgia,¹⁵ and reassessing one's values in life.¹⁶ An integrated review of mechanisms across biological, psychological, and cultural explanations has suggested that none of the existing reasons alone are sufficient to fully explain the experiences,¹⁷ and biological substrates have only rarely been probed despite theoretical proposals^{18,19} and the focus on reward mechanisms and intense emotions involved in music listening.^{20,21}

Our primary research aim is to test whether the feeling of being moved induced by unfamiliar sad music can produce a distinct hormonal response in listeners. More specifically, we explore whether the pattern of hormonal responses is either consistent with a conjectured homeostatic response to a social loss that leads to reward at a distal stage, or with an alternative explanation related to the brain's reward system at a proximal stage. Moreover, we hypothesize that the capacity to empathically engage with fictional events, such as music, may modulate the theorized response,⁷ allowing us to selectively observe the predicted pattern of responses.

The first conjecture relates to the homeostatic theory, put forward by Huron.¹⁸ According to this theory, increased prolactin (PRL) levels are assumed to reflect the homeostatic function that mitigates the negative effects of social distress and loss that a serious tragedy—or its simulated version in the case of fiction and music—is able to trigger. The homeostatic theory predicts an increase in PRL levels in response to various stressors,²² and an increase in oxytocin (OT) levels linked to its anxiolytic functions.²³ This increase in PRL at the proximal stage will eventually lead to reward at a distal stage when the effects of this homeostatic

adjustment are experienced without any actual loss. Administration of OT has been shown to act as an anxiolytic and to reduce stress and anxiety.^{24,25} However, the impact of experimentally induced emotion on OT levels is less clear; elevated OT levels have been observed after negative emotion induction in some studies,^{26,27} but a decrease has been reported in others.^{28,29} The homeostatic theory also predicts increased cortisol and adrenocorticotrophic hormone (ACTH) levels as part of the engagement of the hypothalamic–pituitary–adrenocortical (HPA) axis triggered by stress or negative emotions. Increases in stress-related hormones (cortisol or interleukin-6) have been observed in studies where negative emotions have been induced through social rejection,³⁰ laboratory-based social stress,³¹ unpleasant pictures,³² or stressful or unpleasant music.^{33,34} However, a recent empirical test of the homeostatic theory conducted by Huron and colleagues³⁵ found no change in PRL levels associated with sad music exposure. This study utilized an additional (nonmusical) negative emotion induction procedure, used self-selected music that may have brought additional confounds (autobiographical memories, familiarity, and arousal differences), and had both men and women as participants, introducing differences in PRL secretion³⁶ and emotional contagion,³⁷ all of which may have contributed to the null results.

Another putative explanation for the enjoyable aspects involved in experiencing negative emotions with art is provided by the reward theory. Psychological reward and its biochemical correlates are known to originate from the dopaminergic system³⁸ that is involved in a host of functionalities and responses involved in prediction and anticipation. The striatal dopaminergic system is engaged by rewarding activities at a proximal stage,³⁹ including listening to intensely pleasurable music.⁴⁰ Recently, it was found that music-induced pleasure was up- and downregulated, respectively, by exciting or inhibiting the dorsolateral prefrontal cortex with transcranial magnetic stimulation (TMS)²⁰ in line with the finding that TMS of the prefrontal cortex induces striatal dopamine release.⁴¹ Furthermore, a recent study⁴² found that an orally administered dopamine precursor increased (and a dopamine antagonist decreased) the hedonic experience induced by music, consistent with dopamine as causally related to music-induced pleasure. The

hormonal markers linked to reward are complex; first, the release of PRL is tightly controlled by the dopaminergic system, and dopamine is known to inhibit endogenous PRL release.^{43,44} This suggests that any pleasurable activity producing dopamine would decrease PRL levels. Curiously, this pattern of increased dopamine and decreased PRL levels has been reported in rodents after exposure to classical music,^{45,46} which is in line with the reward theory if we side with the assertion that rats actually enjoy music—or are at least able to derive positive effects from it, as suggested by a recent meta-analysis.⁴⁷ OT, another complex neuropeptide involved in social and rewarding behaviors,⁴⁸ is now assumed to interact with the dopaminergic system by enhancing attention toward social stimuli and, therefore, increasing their rewarding potential.^{49,50} It is likely that these complex couplings of the systems and the focus of the studies, the past research using emotion manipulations to trace changes in OT levels have yielded mixed patterns of results; some studies have recorded decreased OT levels after positive emotion induction by films,²⁷ while other studies have reported increased levels of OT after positive emotion manipulations using other means, such as being comforted after stress,⁵¹ or behaving in synchrony with a partner.⁵²

The two theories are supported by scattered evidence, and as they provide opposite predictions for the key hormones in relation to the valence of the triggering emotion, it is no surprise that the evidence is mixed. For instance, the increased levels of endogenous PRL have been reported after positive emotion induction using films²⁷ and pleasant pictures,³² which is inconsistent with both theories. If we adopt an influential theory by Kemp and Guastella,⁵³ regarding how hormonal correlates are connected to social interaction, conflicts relating to positively versus negatively valenced triggers dissipate. This account proposes that the hormonal responses are not really driven by the nominal valence of the emotion induced, but by the motivational direction as in approach and withdrawal motivation,⁵⁴ a scheme that successfully integrates diverse neural processes involved in emotions. More importantly, this scheme puts a strong emphasis on empathy that drives the interpretation of emotional triggers in terms of the approach-withdrawal scheme. In Kemp and Guastella's framework, "empathy is an approach-

related affective state regardless of whether the stimulus to which empathy is directed is negative or positive" (p. 225).⁵³ This explanation may reconcile the inconsistent outcomes of the homeostatic and reward theories as empathic engagement is associated with exogenously administered OT. However, studies involving empathy and sad emotion, tracing endogenous OT levels, have recorded decreases in OT levels after negative emotion induction. For instance, Barraza and Zak⁵⁵ observed decreased OT levels after an emotion manipulation with a sad video only when empathy was primed with a perspective-taking task, whereas the video without the task led to an increase in OT. A similar reversal of OT levels has been reported when trait empathy has been one of the distinctions between the clinical and control groups; decreased OT levels have been observed after an empathy-eliciting sad film clip viewed by normal participants, but increased OT levels were recorded in schizophrenic patients, who scored significantly lower in trait empathy compared with the normal group.⁵⁶

In sum, we have two contrasting predictions regarding hormonal levels in response to listening to sad music. The homeostatic theory predicts that sad music induces negative emotions and distress that is sufficient to engage the HPA system and trigger an increase in peptide (PRL and OT) and stress (cortisol and ACTH) hormones at a proximal stage. The pleasure comes through at a distal stage via a reward mechanism triggered through the homeostatic adjustment to the loss, which is excessive with respect to the actual loss. The reward theory, on the other hand, simply accounts for the pleasurable experience with an associated decrease in peptide hormones (PRL and OT) due to an interaction with the reward system at a proximal stage (dopamine inhibition) and posits no changes in stress-related markers (there are no distal stages involved). Moreover, a third position emphasizes empathic engagement with the emotional event in terms of approach-avoidance, which predicts either an increase or a decrease in OT levels depending on trait empathy (i.e., an increase in OT levels after emotion manipulation when no particular empathic engagement takes place and a decrease in OT levels by those scoring high on empathy in an empathy-eliciting task). Recent studies focused on pleasure derived from listening to sad music have shown that trait empathy is a strong

mediator of experienced pleasure.^{6,7} This phenomenon enables a design that capitalizes on the individual differences in reactivity to unfamiliar sad music by contrasting the participants' trait empathy levels. We predict that participants scoring high on empathy will experience a stronger positive mood and feelings of being moved after listening to unfamiliar sad music, as well as hormonal patterns consistent with the reward theory, whereas those that score low on empathy will exhibit the pattern predicted by the homeostatic theory, similar to studies showing OT increases after exposure to sad film clips.^{55,56}

Methods

The study protocol was approved by the Medical Ethics Board of the Hospital District of Southwest Finland (medical ethics approval, ETMK 58/1801/2016). The setup mirrors partially the study by Eerola and colleagues,⁶ where emotion induction was carried out using unfamiliar sad instrumental music that induced a pleasurable experience in highly empathic participants and boredom in participants scoring low in empathy selected from a nationally representative sample. The same musical stimulus (as well as two additional ones), similar behavioral measures, and psychophysiological measures (electrodermal activity (EDA) and heart rate variability (HRV)) were used in the present study, but additionally, blood samples drawn at baseline and after each of the two experimental conditions were collected.

Participants

Participants were recruited initially from local colleges using an online survey targeted toward women between the ages of 18 and 39. Exclusion criteria for the study were pregnancy, mental health issues, medical operations, endocrine disorders, medication, smoking, and drug or alcohol abuse. The sample size was estimated on the basis of the previous studies involving PRL (expected $n = 39$ per group;²⁷ expected $n = 7\text{--}10$ per group³²) and OT (expected $n = 54$;⁵² expected $n = 7\text{--}47$ per group⁵⁵), using power analysis with a significance level of 0.05 to obtain a power of 0.80 with the past effect sizes. This aggregated estimate suggested $n = 34$ as the average group size, and we decided to target 35 participants per group. From the 300 candidates who responded, 70 participants were invited, half representing low

and half representing high capacity for being moved by sad music. The capacity for being moved by sad music was predicted on the basis of a previous study,⁶ using the lowest and highest 25 quantiles in an aggregate measure comprising the Emotional Contagion Scale (ECS)³⁷ and the fantasy subscale of the Interpersonal Reactivity Index (IRI).⁵⁷ Eight participants failed to give repeated blood samples during the experiment. Table 1 summarizes the background variables across the groups and highlights the main differences concerning empathy (the IRI and ECS) and emotional reactivity (the musical sophistication index (MSI)-Emotions and the Toronto Alexithymia Scale (TAS), defined below).

Stimulus selection

The musical manipulation consisted of a sequence of three 6- to 8-min tracks validated to induce pleasurable sadness and feelings of being moved in past studies.^{6,58,59} These tracks were the Piano concerto no. 23, 2nd movement by W. A. Mozart, performed by François-Xavier Roth and Les Siècles; *Discovery of the Camp* by Michael Kamen; and *Oblivion* by Astor Piazzola, performed by Stjepan Hauser and the Zagreb Philharmonic Orchestra.

Procedures

Participants were seated in a comfortable chair in a private room. A qualified nurse inserted an intravenous catheter into the nondominant arm. This was followed by a 20-min adaptation period⁶⁰ followed by the baseline measures (blood samples and self-reported mood). This was followed by the first condition, either music or silence detailed below, each lasting 20 min, after which the second set of measures were taken. The second 20-min manipulation, either silence or music, whichever they had not previously gone through, was followed by the third set of identical measures. The duration of the conditions was optimized for capturing hormonal changes in plasma samples; plasma PRL has been shown to peak 15 min after a stressor,⁶¹ while OT has a 15-min half-life.⁶² To control for the diurnal variation of hormones, each experimental session took place between 2:00 and 6:00 p.m. Blood samples were centrifuged at 3000 g at 4 °C for 45 min, and plasma samples were stored at -80 °C.

During the experiment, the participants' current mood was assessed using the Profile of Mood States questionnaire (POMS, 24-item version),⁶³ supplemented with two mood descriptors relevant

Table 1. Participant background measures across the high and low empathy groups (means and standard errors)

	High empathy 32	Low empathy 30	Statistics
<i>N</i>			
Age	24.2 (0.88)	24.9 (0.90)	$t = -0.54, P = 0.590$
IRI-Fantasy	32.5 (0.58)	24.7 (0.60)	$t = 9.34, P \leq 0.001$
ECS	64.2 (0.66)	50.8 (0.68)	$t = 14.18, P = 0 < 0.001$
BDI	3.8 (0.70)	3.9 (0.73)	$t = -0.12, P = 0.909$
TAS	50 (1.34)	55 (1.38)	$t = -2.64, P = 0.011$
GAD	10 (0.52)	9.6 (0.53)	$t = 0.58, P = 0.564$
GHQ	22.2 (0.53)	22.9 (0.54)	$t = -0.90, P = 0.371$
MSI-General	4.2 (0.17)	3.6 (0.17)	$t = 2.25, P = 0.028$
MSI-Engagement	7.8 (0.64)	7.0 (0.66)	$t = 0.94, P = 0.353$
MSI-Perceptual	5.2 (0.14)	4.8 (0.14)	$t = 1.63, P = 0.108$
MSI-Training	3.4 (0.33)	2.8 (0.34)	$t = 1.22, P = 0.227$
MSI-Singing	4.2 (0.17)	3.5 (0.18)	$t = 2.79, P = 0.007$
MSI-Emotions	5.6 (0.10)	5.9 (0.11)	$t = 4.22, P < 0.001$
ASM	97.3 (2.05)	91.0 (2.12)	$t = 2.13, P = 0.037$

ASM, Attitudes toward Sad Music; BDI, Beck Depression Inventory; ECS, Emotional Contagion Scale; GAD, generalized anxiety disorder; GHQ, General Health Questionnaire; IRI, Interpersonal Reactivity Index; MSI, musical sophistication scale; TAS, Toronto Alexithymia Scale.

for the design, *being moved* and *sadness*. The mood measurements were taken after baseline and each experimental condition. In addition, after the music condition, participants reported their emotional experiences using visual analog scales (0–100) for felt pleasure, being moved, anxiousness, relaxation, and sadness. They also rated how much they liked the music and how familiar they were with it. Participants received 50 EUR in compensation for travel expenses.

Several background measures were collected from all participants: the ECS,³⁷ IRI,⁵⁷ Beck Depression Inventory (BDI),⁶⁴ TAS,⁶⁵ a measure of generalized anxiety disorder (GAD),⁶⁶ Goldsmith MSI (Gold-MSI),⁶⁷ the Attitudes toward Sad Music Scale (ASM),³ and the General Health Questionnaire (GHQ).⁶⁸ Participants also reported the number of days since menstruation and whether they relied on hormonal contraception.

Data analysis

Hormonal assays. OT was assayed from 1 mL of blood plasma drawn into chilled EDTA tubes, centrifuged at 4 °C and transferred to plastic tubes, and stored at −80 °C. OT concentration was assessed using enzyme-linked immunosorbent assay (ELISA) kits (Ab133050, Abcam) following manual procedure. The detection threshold of the OT assay was 15.625 pg/mL. The intra-assay coefficient of variation was 17.31%. Mean accuracy was measured on three concentration values and was 90% with 18% CV at 1000 pg/mL, 105% with 5% CV at 125 pg/mL, and 15.625 with 133% CV at 15.625 pg/mL. PRL was determined from 1 mL of serum using a two-site sandwich immunoassay using the chemiluminometric method (ADVIA Centaur[®] by Siemens AG). The coefficient of variation of the method ranged from 3.1% to 6.6%, with PRL levels from 3.3 to 118 ng/mL. Cortisol was assayed from 1 mL serum samples analyzed with the IMMULITE[®] 2000 (Siemens AG) automated chemiluminescent enzyme immunoassay with 8.2% CV at 3.3 µg/dL. ACTH was assayed from 2 mL of plasma drawn into chilled EDTA tubes and analyzed with the IMMULITE 2000 (Siemens AG) automated chemiluminescent immunoassay analyzer with 10.0% CV at 24 pg/mL. C-reactive protein was assayed from 1 mL serum using an immunoturbidimetric assay with ADVIA 2400 (Siemens AG). The intra-assay variations ranged from 4.9% to 7.8%, depending on the level (2.25–49.96 mg/L). This marker of inflammation was collected to screen for acute inflammation, although it has also been used as an index of depressive symptoms and negative moods.⁶⁹

Psychophysiological indices. EDA and electrocardiogram (ECG) signals were continuously measured during the experiment. EDA was measured

from the distal phalanges of the index and middle fingers, and the ECG signal was captured using electrodes placed on the lower chest and neck using a NeXus-10 MKII system with BioTrace software (Mind Media BV, Netherlands). For both measures, the sampling rate was 256 Hz, and the signals were filtered with a low-pass filter (a first-order filter with a 5-Hz cutoff). One tonic (mean tonic activity) and three phasic components (the number of significant phasic responses, $nSCR$; the sum of the amplitudes of the phasic driver peaks, $AmpSum$; and time integral of the phasic driver, $iSCR$) were extracted using the Ledalab toolbox for MatLab.⁷⁰ HRV indices were derived from the ECG signal after extracting R peaks from the signal using stationary wavelet transforms,⁷¹ and visually inspecting the tachograms and removing artifacts. The standard measure of variability (standard deviation of all normal-to-normal R-R intervals, $SDNN$), and the power of normalized low frequency (LF , 0.04–0.15 Hz) and high frequency (HF , 0.15–0.40 Hz) spectral components were estimated with wavelet transforms using the RHRV library.⁷² The ratio of LF and HF frequencies was also calculated (LF/HF). All indices were extracted from epochs of equal duration (10 min), with each epoch starting 4 min after the beginning of the condition.

Analysis operations. Psychophysiological and hormonal measures were log-transformed before the analyses. Self-report measures, psychophysiological and hormonal measures were adjusted for baseline levels by calculating the percentage change from the baseline to keep the units comparable. After the baseline adjustment, hormonal and psychophysiological measures were checked for outliers, and all values above 1.5 IQR were constrained to 1.5 IQR. In the case of the hormonal variables, a maximum of 8 (6.4%) and in the case of the psychophysiological variables, a maximum of 7 (5.6%) values were constrained in this way. Analyses were carried out using generalized linear mixed models with two fixed effects (condition and empathy) and two random effects (participant and session), unless the data came from a single session (self-reported emotions) where a normal between-subjects t -test was conducted. We also added a number of covariates to the analyses to determine the impact of age, menstruation phase, musical sophistication, mood, and the use of hormonal

contraception on the outcome measures, although they did not interact with the main variables of interest (see Tables S1–S4, online only).

Code and data availability. All data and analysis code are available at Github: <https://tuomaseerola.github.io/sad-music-hormones/>.

Results

There were no differences between the empathy groups in self-reports of negative moods at baseline ($t(1,60) = 0.83$, $P = 0.41$), nor after silence ($t(115) = -0.97$, $P = 0.336$) or music ($t(115) = 0.46$, $P = 0.65$). For positive mood, no baseline difference was observed between the two groups ($t(1,60) = 0.46$, $P = 0.65$). However, after the music condition, the high empathy (HE) group gave significantly higher ratings of positive mood ($M = 3.09$, expressed as the relative change from baseline, $SE = 4.76$) than the low empathy (LE) group ($M = -9.73$, $SE = 3.74$; $t(114) = 2.56$, $P = 0.012$), and the increase in positive mood was significant within the HE ($t(60) = 2.92$, $P = 0.005$) but not in the LE group ($t(60) = 0.14$, $P = 0.889$), as illustrated in Figure 1A. The ratings of emotions felt during the music condition showed significant differences between different emotion scales ($t(246) = 3.90$, $P = 0.00012$). Two out of the three most highly rated emotion scales showed significant differences across the empathy groups, namely, feeling relaxed ($M = 79.4$, $SE = 3.10$, and $M = 62.6$, $SE = 4.74$ for the HE and LE groups, respectively; $t(272) = 2.87$, $P = 0.0044$), and being moved ($M = 67.2$, $SE = 3.70$, $M = 52.3$, $SE = 4.60$, for the HE and LE groups; $t(272) = 2.54$, $P = 0.0117$). However, there was no significant difference in the ratings of pleasantness ($M = 84.8$, $SE = 2.58$ for the HE group; $M = 75.6$, $SE = 3.05$ for the LE group, $t(272) = 1.56$, $P = 0.119$). This replicates previous findings,⁶ where participants with high trait empathy have consistently reported stronger feelings of being moved than those with LE.

Turning to peptide hormones and stress markers, there were no significant differences between the groups at baseline ($t(60) < 1.47$, P 's > 0.147). PRL exhibited decreased levels from the baseline for all groups and conditions. The HE group exhibited significantly lower levels of PRL in the music condition ($M = -7.76$, $SE = 1.20$, expressed

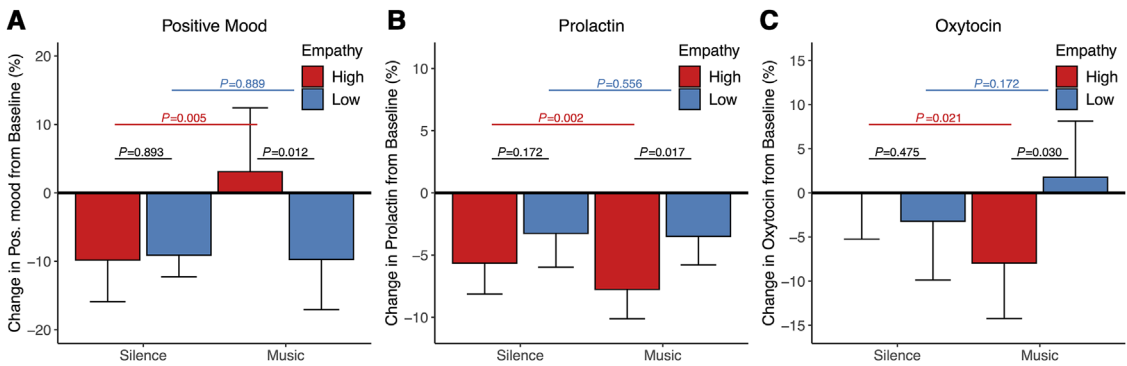


Figure 1. The percentage change with respect to baseline for positive mood (A), prolactin (B), and oxytocin (C) for the high (red) and low (blue) empathy groups. All values are represented as the average change across the groups ($N = 32$ and $N = 30$). The black bars represent the standard error of the mean.

as a relative change from the baseline) than in silence ($M = -5.65$, $SE = 1.27$, $t(60) = 3.17$, $P = 0.0024$), whereas for the LE group, the levels were comparable across the two conditions (music $M = -3.50$, $SE = 1.17$; silence $M = -3.26$, $SE = 1.39$; $t(60) = 0.592$, $P = 0.556$). There was no difference in PRL levels between the groups in the silence condition ($t = 1.38$, $P = 0.172$), but there was a significant difference in the music condition ($t = 2.45$, $P = 0.0166$). OT showed a similar pattern; in the HE group, the music condition ($M = -7.94$, $SE = 3.21$) exhibited significantly lower levels of OT than silence ($M = -0.06$, $SE = 2.64$, $t = 2.37$, $P = 0.0211$), while the LE group showed an increase in OT from silence ($M = -3.22$, $SE = 3.39$) to music ($M = 1.77$, $SE = 3.24$), although this difference failed to reach statistical significance ($t = 1.381$, $P = 0.1724$). A comparison of the relative change in OT between the groups revealed a significant difference only in the music condition ($t = 2.21$, $P = 0.0297$), with the LE group exhibiting higher relative OT levels. During silence, the levels were comparable in both groups ($t = 0.72$, $P = 0.475$). The stress markers (cortisol and ACTH) failed to exhibit any significant differences between the conditions and empathy groups (for cortisol, all t 's < 1.54 , P 's > 0.128 ; for ACTH, all t 's < 0.5 , P 's > 0.66). Figure 1 displays the relative change from baseline in the main predictors across participant groups and conditions (a full breakdown of all variables is given in Table S1, online only). Ancillary analyses explored the use of hormonal contraception ($n = 28$) and the phase of the menstruation cycle based on participants' self-reported days since men-

strual onset (cycle day 1), and the musical sophistication index as covariates, which yielded the identical patterns of results (see Tables S2–S4, online only).

Psychophysiological responses exhibited an interaction between condition and empathy: Two out of three indicators of phasic EDA, the *area of the phasic driver* and the *number of significant phasic peaks*, showed significantly lower relative values in the music condition compared with silence in the LE group (both t 's > 2.30 , P 's < 0.05), but such changes were not observed in the HE group ($t(54) < 0.77$, $P > 0.42$). The tonic skin conductance level showed no differences between conditions or groups (t 's < 1.1 , P 's > 0.27). Indicators of HRV exhibited a pattern similar to phasic EDA, with all measures (SDNN, LF, HF, and LF/HF) showing significant decreases in the music condition compared with silence in the LE group (t 's > 2.1 , P 's < 0.035), but no changes in the HE group (all P 's > 0.51).

In sum, the hormone measurements (PRL and OT) were consistently lower in the music condition compared with silence in the HE group, but this change is absent in the LE group. Both measures are also significantly different between the two groups in the music condition only. None of the stress hormones showed any significant changes between the conditions or groups. The self-reports demonstrate that the HE group had a more positive mood after the music condition than the LE group, and the reporting of emotions after the music condition also indicated that HE participants felt more moved and relaxed during music listening. However, decreases in EDA and HRV suggested that the LE group was

more relaxed during the music listening condition than in silence, but such differences were not evident in the HE group. Taken together, the pattern of results is consistent with the reward theory in HE participants, whereas the homeostatic theory did not receive support from the HPA system markers or the theorized increases in the peptide hormone levels in either group of participants.

Discussion

This is the first evidence of subtle experimenter-selected music induced changes in peripherally measured neuropeptides as opposed to studies involving stress reactions to music^{33,73,74} or neurochemical indicators of reward in response to self-selected music involving strong emotions involved in rare situations where listeners experience chills to their favorite music.^{20,40} The self-reports of felt emotions replicate the findings of an earlier study⁶ involving the same stimuli, exhibiting similar emotional differences related to empathy. The hormonal changes observed in the present study are consistent with the reward theory, where the enjoyment of sad music is related to triggering of the dopaminergic system in those that engage empathically with the music and are being moved by it (i.e., the HE group). The activation of the dopaminergic reward system is known to rapidly inhibit the continuous secretion of PRL,⁴⁴ which may explain the consistent low levels of PRL in those who reported higher levels of positive mood and enjoyment (i.e., the HE group). The findings are also partially consistent with a prior emotion induction study using sad and happy music, which showed decreases in PRL levels only after listening to happy music, but not after sad music.³⁵ This complementary evidence from two different designs addressing the same theory provides converging evidence that the homeostatic theory is incorrect. Moreover, the decreased levels of OT are also consistent with the interpretation that emphasizes the approach-avoidance perspective and social interpretation of the trigger; decreased levels of OT have previously been observed after viewing empathy-eliciting films or films paired with empathic engagement,^{55,56} whereas increased OT is associated with psychological and physical stressors.⁷⁵ Thus, the hormonal results are in line with the reward theory and the notion that empathic engagement modulates the emotional interpretation of this experience.

We have established that merely listening to unfamiliar instrumental sad music can cause notable changes in neuropeptides at the peripheral level in certain types of listeners. These changes are interpreted to support the reward theory, although direct evidence is missing since dopamine cannot be assessed from blood samples. Dopamine has been shown to increase during intense music-induced pleasure; more specifically, Salimpoor and colleagues⁴⁰ observed increased dopamine levels in the right nucleus accumbens through positron emission tomography. The reports how music-induced reward can be modified by the stimulation or inhibition of the frontostriatal circuits and by pharmacological manipulation of dopamine levels provide direct causal evidence of how dopaminergic system modulates the hedonic experiences related to intense musical pleasure and reveals the neural architecture involved in this process in more detail.^{20,42} Our findings do not provide any additional insights into the circuitry involved in these processes, but broaden the scope of such reward processes from the intensely pleasant experiences to those that can be experienced in the context of unfamiliar, low-arousal music. Moreover, the empathy-related differential reactivity in hormonal and emotional measures is an important building block in the process, and consistent with past results obtained with self-reports,^{6,8} psychophysiology,⁷⁶ and neural responses.⁴ This differential neuropeptide reactivity related to different trait empathy levels may be linked to genotypes related to dopamine transporters and receptors that have been implicated in dopaminergic functionality associated with trait empathy,⁷⁷ as well as genotypes related to OT receptors.⁷⁸ However, these observations relate mainly to social interactions and positive emotions,⁷⁹ although the jury is still out on whether these associations hold.⁸⁰ Music may nevertheless provide an elegant and ecologically valid means of unraveling the social and emotional contribution of empathy on experiencing positive emotions. The findings further our understanding of how affective processes capitalize on the reward system and are influenced by individual differences, such as trait empathy. Further research that focusses on other emotional concepts, individual differences, or gender would be good alternatives for follow-up investigations, as the current study focused on a one type of emotion (pleasant

experience induced through sad music), maximized the group differences in empathy in lieu of other potential individual differences, and only focused on young women. It would also be important to seek a causal understanding of how the reward system contributes to the experience of music-related pleasure by inhibiting the effects of dopamine using an antagonist, such as naltrexone or risperidone, as done by Ferreri *et al.*,⁴² but in a context of less arousing and less familiar music. In order to design better therapeutic interventions involving music, it would be crucial to establish whether the enjoyment of these experiences could be modified by empathy or compassion training,^{81,82} and whether such experiences are able to help individuals suffering from anhedonia and depression linked to dopaminergic impairments.

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Author contributions

T.E. contributed to the experiment design and stimulus selection, analyzed and interpreted the obtained data, and played the main role in writing the manuscript. J.K.V. assisted in data collection, experiment design, and writing. H.K. contributed to the experiment design and data analysis. H-R.P., V.P., and K.S. contributed to collection of data and writing.

Supporting information

Additional supporting information may be found in the online version of this article.

Table S1. Means and standard errors of all hormone markers.

Table S2. Summary of the phase of the menstrual cycles in participants.

Table S3. Contraception and menstruation—impact on prolactin.

Table S4. Contraception and menstruation—impact on oxytocin.

Competing interests

The authors declare no competing interests.

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