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Emotional Reactions to Music in Dementia Patients and Healthy Controls: Differential Responding Depends on the Mechanism

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Abstract

Music is frequently regarded as a unique way to connect with dementia patients. Yet little is known about how persons with dementia respond emotionally to music. Are their responses different from those of healthy listeners? If so, why? The present study makes a first attempt to tackle these issues in a Portuguese context, with a focus on psychological mechanisms. In Experiment 1, featuring 20 young and healthy adults, we found that musical excerpts which have previously been shown to activate specific emotion induction mechanisms (brain stem reflex, contagion, episodic memory, musical expectancy) in Sweden were valid and yielded predicted emotions also in Portugal, as indexed by self-reported feelings, psychophysiology, and post hoc mechanism indices. In Experiment 2, we used the same stimuli to compare the responses of 20 elderly listeners diagnosed with Alzheimer's disease (AD) with those of 20 healthy listeners. We controlled for cognitive functioning (Mini-Mental State Examination) and depression (Geriatric Depression Scale). Our predictions about how mechanisms would be differentially affected by decline in brain regions associated with AD received support in that AD patients reported significantly lower levels of (a) sadness in the contagion condition, (b) happiness and nostalgia in the episodic memory condition, and (c) anxiety in the musical expectancy condition. By contrast, no significant difference in reported surprise was found in the brain stem reflex condition. Implications for musical interventions aimed at dementia are discussed, highlighting the key role that basic research may play in developing applications.

Keywords

Brain, dementia, emotion, mechanism, music listening

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Literature

Researchers in music psychology have increasingly been urged to focus on applications and to consider the social benefits of their research (for an early example, see Sloboda, 2005). However, it has also been suggested that basic research can play a crucial role in maximizing such benefits (e.g., Juslin, 2011). This is because only a deep theoretical understanding of the causal mechanisms underlying the effects of interest will enable practitioners to develop truly effective interventions. In this article, we highlight the role that music psychology could play in tackling one of the greatest global challenges of our time: dementia. More specifically, we present empirical data which illustrate how basic research and theories of music and emotion could

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have important implications for applications of music in dementia care.

The Challenge of Dementia Disorders

Dementia refers to a broad category of progressive and irreversible brain diseases that cause a long-term and often gradual decline in general cognitive functioning, severe enough to affect daily functioning (Ferri et al., 2009). The patient may suffer from a deterioration of the ability to think and remember, as well as problems with language, motivation, emotions, and motor behavior.[1] People with dementia often experience decreased quality of life, due to social isolation, loss of self-esteem, changing family relationships, and a declining ability to perform daily activities (Górska et al., 2018).

Dementia is the most frequent form of pathological aging, with 46 million people living with dementia worldwide (Batsch & Mittelman, 2012). Roughly 10% of people will develop the disorder at some point in their lives (Loy et al., 2014), and due to the world's aging population, Alzheimer's Disease International has projected that more than 131 million people in the world will have the disease in 2050. Thus, dementia presents one of the greatest social, economic, and health challenges of our time.

Dementia has no cure. Pharmaceutical approaches have been developed to ameliorate symptoms and increase quality of life (Wollen, 2010), but due to limited benefits and a high rate of adverse side-effects, non-pharmacological interventions are increasingly regarded as desirable. Thus, for instance, the European Collaboration on Dementia Project recommends that dementia treatment combines pharmacological and non-pharmacological approaches (https://www.alzheimer-europe.org/Research/European-Collaboration-on-Dementia).

Music and Dementia

One problem with most non-pharmacological approaches outlined so far is that they tend to be costly and require specially trained staff for their implementation. Could music offer a viable alternative? Surprisingly, perhaps, in view of the generally steep decline of memory processes in dementia disease, dementia patients can show a surprisingly robust musical memory (e.g., Baird & Samson, 2015).[2] They might be able to correctly perceive pitches and melodies, recognize familiar songs, and recall familiar lyrics (Särkämö et al., 2012).

Music listening seems promising as an intervention, since it is easy to administer, has few secondary effects (compared to prescription drugs), and is relatively inexpensive. Music can also be tailored to personal taste and be flexibly consumed in a great variety of contexts (Västfjäll et al., 2012). Musical interventions could be particularly suitable in dementia care because findings show that music already serves crucial functions for older people: they use music to regulate moods, reduce loneliness, and evoke memories, contributing to their sense of self-identity, social belonging, and agency (e.g., Creech et al., 2013; Hays & Minichiello, 2005; Laukka, 2007).

Studies indicate that music can be enjoyed by dementia patients, even at later stages when communication skills may be lost (Baird & Samson, 2015). Indeed, even in the very final stage, patients seem to respond differently to music than to other sensory stimuli (e.g., visual, tactile; Särkämö et al., 2012). This could explain why music is becoming one of the most common non-pharmacological approaches to relieve symptoms (Garrido et al., 2017).

Broadly speaking, there are two general types of musical intervention: *music therapy*, (implemented by a trained music therapist and following an established protocol) and *other music-based interventions* (comprising musical activities implemented by nursing staff, the patients themselves, or family caregivers). Both types may involve *active* (playing, singing) and *receptive* (listening) approaches (Särkämö, 2018).

Benefits of Music Listening

In this article, we present findings of particular relevance to the use of music in non-therapeutic settings with a receptive approach. Some advantages of using pre-recorded music outside of formal music therapy settings are the relative ease of access and affordability of such interventions.

Several studies have indicated that mere music listening may have significant benefits (for an overview, see Garrido et al., 2017). For instance, musical interventions could reduce agitation, anxiety, depression, and behavioral symptoms (e.g., apathy) relative to a control group (Clément et al., 2012; Holmes et al., 2006; Narme et al., 2014; Sakamoto et al., 2013; Sung et al., 2006). A recent Cochrane review found that the evidence is strongest regarding reduction of depression and behavior problems (van der Steen et al., 2017).

Musical interventions do not show universally positive results, however. Some studies obtained no significant benefits of musical activities on symptoms as compared with control conditions or standard care (e.g., Narme et al., 2014; Raglio et al., 2015), while others found that a decrease in agitation in some patients was offset by an increase in agitation in others (Garland et al., 2007). All of this suggests the need to achieve more consistent effects.

The Role of Emotions

It has been suggested that the positive effects of music on dementia symptoms may be driven by the pleasantness of the activity rather than by the music itself (Ferreri et al., 2019). Even short-term improvements in cognitive functioning as a result of listening to music may be mediated by the music's effect on emotions and arousal (Särkämö, 2018). For example, El Haj, Postal, and Allain (2012) observed better autobiographical memories after exposure to patient-selected music than after a piece of music chosen by the experimenter. Significantly, self-selected music produced more intense emotional responses with predominately positive valence. Considering that many uses of music in dementia care focus on emotion, Ferreri et al. (2019) note that "while the impact of music on emotion and well-being is important for normal aging, it becomes crucial in pathological aging" (p. 635).

We define *emotions* here as

> relatively brief, intense, and rapidly changing reactions to potentially important events (subjective challenges or opportunities) in the external or internal environment—often of a social nature—which involve a number of subcomponents (cognitive changes, subjective feelings, expressive behavior, and action tendencies) that are more or less 'synchronized' during an emotional episode. (Juslin, 2011, p. 114)

Moreover, we distinguish between *perceiving* an emotion expressed in the music and actually *feeling* the emotion (e.g., Gabrielsson, 2002). This distinction matters, because different psychological processes—and, hence, different neural substrates—may be involved, depending on the type of process (Juslin & Sakka, 2019).

Researchers have investigated how dementia patients *perceive* emotions in music, with mixed results (Drapeau et al., 2009; Gosselin et al., 2005, 2007; Hsieh et al., 2012; Kerer et al., 2014; Omar et al., 2010). However, despite acknowledgement that music may influence listeners' subjective well-being and health through the emotions it evokes (Chin & Rickard, 2013; Västfjäll et al., 2012), few studies have explored how emotional *reactions* to music in dementia patients may differ from those of healthy listeners.[3]

Narme et al. (2014) confirmed the value of a musical intervention in influencing the emotions of patients with mild-to-moderate dementia—as measured by facial expressions, mood ratings, and content discourse. However, the authors did not consider the underlying mechanisms of these reactions. We argue that such mechanisms hold the key to explaining the mixed findings and individual differences in previous studies, because it is precisely at the mechanistic level that individual differences tend to emerge (Juslin, 2019, p. 396).

Underlying Mechanisms: A Theoretical Framework

To understand emotional reactions to music in dementia patients, we need a theoretical framework that describes the mechanisms mediating between musical features and emotional reactions, and that offers predictions about the brain regions associated with each mechanism. The term *mechanism* usually refers to the causal process through which an outcome is brought into being. This entails a functional (or psychological) description of what the brain is "doing" in principle (e.g., retrieving a specific memory). The second author has developed the most extensive theoretical framework for music and emotions to date (Juslin, 2019). The theory proposes eight induction mechanisms (in addition to cognitive goal appraisal), which developed gradually and in a specific order during evolution, from mere reflexes to complex judgments:

– *Brainstem reflex*: a hardwired attention response to subjectively "extreme" values of simple acoustic features (e.g., inducing *arousal* by means of volume, speed, or sensory dissonance).
– *Rhythmic entrainment*: a gradual synchronization of an internal body rhythm, such as heart rate, with an external rhythm in the music (e.g., evoking *calm* with a slow, rhythmic lullaby).
– *Evaluative conditioning*: a regular pairing of a song with other positive or negative stimuli, leading to an association (e.g., evoking a positive feeling of *safety* via familiar connotations).
– *Contagion*: an internal "mimicry" of the voice-like emotional expression of the music via so-called "mirror neurons" (e.g., evoking *joy* with a fast and high-pitched song in major key).
– *Visual imagery*: inner images of an emotional character conjured up by the listener through metaphorical mapping of the music (e.g., inducing *relaxation* by means of 'new age' music).
– *Episodic memory*: a conscious recollection of a particular event from the listener's past that is cued by the music (e.g., arousing *nostalgia* with a personally significant melodic theme).
– *Musical expectancy*: a response to the unfolding of the syntactic structure of the music and its expected/unexpected notes (e.g., evoking *anxiety* via phrases without a clear tonal center).
– *Aesthetic judgment*: a subjective evaluation of the aesthetic value of the music based on an individual set of weighted criteria (e.g., evoking *pleasure* and *awe* with a beautiful sonata).

A web-survey study featuring 668 participants from six countries showed that all of the above mechanisms occur, to varying degrees, across cultures, and that collectively, they may account for a wide range of emotions (Juslin et al., 2016). By synthesizing theory and results from different domains outside music, Juslin (2013, 2019; Juslin & Västfjäll, 2008) was able to develop predictions about the characteristic of each mechanism—such as their information focus, mental representations, cultural impact, emotions induced, and key brain regions. The latter predictions are of special importance when it comes to understanding how mechanisms might be differentially affected by the decline of specific brain regions in dementia.

Brain Atrophy in Dementia

There are at least 100 different types of dementia, and the symptoms differ depending on the type (Milne, 2010). One may thus expect patients with different types of dementia to respond differently to music. In this study, we focus on the most common form of dementia, namely Alzheimer's Disease (AD), which makes up about 50–70% of all cases.

According to the amyloid-cascade hypothesis of AD, a disruption of balance between production and clearance of amyloid precursor protein leads to the development of amyloid-beta plaques and intracellular accumulations of a modified tau protein called neurofibrillary tangles. These pathologies in turn cause neurodegeneration as well as progressive cognitive impairment (Benzinger et al., 2013; Hardy & Higgins, 1992).

However, studies show that the atrophy is not constant all over the brain (Benzinger et al., 2013; La Joie et al., 2012). In the initial stages of AD, structural damage is found mainly in the temporal and parietal lobes (in particular the entorhinal cortex and hippocampus), the orbitofrontal cortex, the precuneus, and other neocortical areas (e.g., Frisoni et al., 2010). In contrast, the primary sensory, motor, and anterior cingulate cortices are largely spared (e.g., Braak & Braak, 1997; Cuingnet et al., 2011; Frisoni et al., 2007, 2010; Hoesen et al., 2000; Lehmann et al., 2013; Singh et al., 2006; Thompson et al., 2003, 2007; Villain et al., 2012). One crucial domain of impairment is memory. Early on, AD impairs episodic memory, with more variable damage of semantic memory, and relative preservation of procedural memory (e.g., Jacobsen et al., 2015). Based on such findings, one can develop predictions about how AD patients might react differently to music from healthy controls.

The Present Study

The aim of this study is to make a first attempt to explore whether and how AD patients may differ from healthy controls in their emotional reactions to music, with a particular focus on mechanisms. Imaging studies suggest that music listening may engage auditory, cognitive, emotional, and motor functions, and that musical functions can be relatively preserved in AD (Warren et al., 2003). It has thus been argued that music-induced emotions and memories are preserved, even in more advanced stages of dementia (Särkämö, 2018).

However, in view of the theoretical framework outlined above, we will argue that this may not actually be true in a general sense, regardless of the emotion-induction mechanism. We submit that dementia might influence emotional responses differently, depending on the psychological process underlying the response. Dementia tends to affect some brain regions more than others, and because different mechanisms involve different brain regions, we can expect dementia to influence some mechanisms (and their emotions) more than others.

Emotion-induction mechanisms—like many other psychological processes—cannot be observed directly, but have to be inferred from behavioral output in systematic experiments. Hence, we manipulated mechanisms in two experiments. The first (the manipulation check) aimed to validate stimuli previously tested in Sweden in a Portuguese context, with a sample of young, healthy adults. The second experiment (the comparison) aimed to examine whether emotional reactions to music of AD patients differ from those of healthy controls of a similar age, and also whether such differences depend on the target mechanism.

Ethics Statement

This study was carried out in accordance with the recommendations in Guidelines for Good Clinical Practice (https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice) and the ethical principles stated in the Declaration of Helsinki (World Medical Association, 2001) as well as by the Portuguese National Committee for Data Protection, and the clinical boards of the two health care facilities involved, as part of a written agreement in force between M-iti Madeira and the respective institutions (and also in accordance with Portuguese law). All participants provided written informed consent; they were informed about the purpose of the study, the task, the procedure, possible risks or benefits, matters of confidentiality, their right to withdraw from the study at any time without penalties or loss of benefits, and so forth. The research study protocol was approved by the National Committee for Data Protection, and by the participating health care facilities.

Experiment 1: The Manipulation Check

In order to compare the emotional responses of AD patients with those of controls, we first need to have an experimental paradigm, featuring musical stimuli that reliably activate mechanisms in a selective manner. Four mechanisms (brain stem reflex, contagion, episodic memory, and musical expectancy) have been tested in experiments (Juslin et al., 2014, 2015) showing that responses to music may be successfully predicted, based on theoretically based manipulations of specific mechanisms. However, studies so far have been limited to a single culture (Sweden), wherefore it is unclear whether the same paradigm would be effective in a different culture.

The aim of Experiment 1 was thus two-fold. First, by replicating previous results in a novel cultural context (Portugal), we wanted to confirm that the experimental stimuli would be suitable for the dementia comparison in Experiment 2. Second, by including a sample of young participants, the data could help us to control for effects of age per se. (Experiment 2 featured only elderly participants with or without an AD diagnosis.[4]) All three groups could not be run in the same experiment, because the manipulation check required the use of self-report indices for mechanisms in order to validate the paradigm, and those were regarded as too complex to use with dementia patients (cf. Banovic et al., 2018).

In Experiment 1, we manipulated four target mechanisms, and the "default predictions" of each condition were as follows. The *brain stem reflex* mechanism is triggered by extreme features (e.g., high sound level, quick attack, and sharp timbre) that occur locally and cannot be predicted from the syntax of the music (Juslin, 2013). Consistent with an "early" reaction that occurs before any elaborate classification of the sounding event has taken place (Simons, 1996) and with previous studies conducted in Sweden (Juslin et al., 2014, 2015), we expected the brain stem reflex condition to arouse primarily *surprise-astonishment* in listeners.

The *contagion* mechanism is thought to be activated by a moving emotional expression in the music, which is "mimicked" internally by the listener (Juslin, 2001). This effect will be particularly strong if the music features a voice-like lead part—either a real voice or a musical instrument reminiscent of the human voice (Juslin, 2019). The contagion condition featured a piece of music with a cello timbre and a sad expression (Juslin & Laukka, 2003, pp. 792–995). Consistent with "matching" sad responses found in previous studies using this piece (Juslin et al., 2014, 2015), we expected the contagion condition to arouse primarily *sadness-melancholy* in listeners.

The episodic memory mechanism is thought to be activated by salient musical features associated with emotional events that the listener can remember (Baumgartner, 1992; Cady et al., 2008; Janata et al., 2007; Juslin & Laukka, 2004; Juslin et al., 2008, 2011, 2014, 2015, 2016). To evoke music-associated episodic memories, without having to encode them during the experiment, we used a piece assumed to be highly familiar to the present sample due to its frequent occurrence in social events (e.g., weddings). Consistent with previous experiments (Juslin et al., 2015), we expected the episodic memory condition to arouse primarily *happiness-elation* and *nostalgia-longing* in listeners.

The *musical expectancy* mechanism is believed to be activated by unexpected melodic, harmonic, or rhythmic sequences (Huron, 2006; Meyer, 1956). Thus, in order to activate this mechanism, and more specifically to confound listeners' musical expectations, we selected a piece which would deliberately violate listeners' expectation about its continuation over time. Consistent with previous studies, which show that pieces corresponding to this characteristic may arouse anxiety (Juslin et al., 2014, 2015), we thus predicted that the musical expectancy condition would induce primarily *anxiety-nervousness* in listeners.

In order to detect felt—as opposed to perceived—emotions, it is advisable to measure multiple emotion components (e.g., Lundqvist et al., 2009). Hence, we relied on converging evidence from self-reported feelings, "post hoc" self-reports of mechanisms (*MecScale*), and psychophysiological measures. We also used a "control" condition, in the form of a "neutral" musical stimulus, to help rule out alternative explanations. To our knowledge, this is the first attempt to replicate the experimental BRECVEMA paradigm in a non-Swedish context.

Method

Participants. Twenty university students, 10 males and 10 females, 18–33 years old ($M = 24.10$, $SD = 4.19$), were recruited by means of posters and advertisements throughout Madeira University. A total of 25% of the students played a musical instrument and 15% had received music education. All participants were native Portuguese speakers. None of them reported a hearing problem. They received no compensation for their anonymous and voluntary participation.

Design. The experiment used a within-subjects design, with target-mechanism as independent variable (five levels: brain stem reflex, contagion, episodic memory, musical expectancy, and neutral condition) and self-reported feelings (nine scales), mechanism impressions (*MecScale*), autonomic activity (skin conductance level), and facial electromyography (zygomaticus and corrugator muscles) as dependent variables. An additional "baseline" condition was featured in the psychophysiological analyses.

Musical Material. We featured five instrumental musical pieces, which have previously been validated in in Sweden. (More complete descriptions of each stimulus may be found in Juslin et al., 2014, 2015.) The five pieces were selected so as to "isolate" the effects of individual mechanisms as much as possible so that no mechanisms other than those targeted in a given condition would diffuse the effect of the target mechanism. To facilitate a selective activation of non-memory mechanisms, we chose classical pieces likely to be unfamiliar to the listeners (as checked by asking them to rate their familiarity with each piece and report any music-evoked memories). Conversely, the memory condition featured a piece that was likely to be highly familiar.

Brain stem reflex. To obtain a startle response, we used a section called *Infernal Dance of all Kashchei's Subjects* from *The Firebird*, a ballet and orchestral concert work composed by Igor Stravinsky in 1910 (performed by the Berlin Radio Symphony Orchestra, conducted by Lorin Maazel). The excerpt, which was previously used by Juslin et al. (2015), starts with a loud drum and brass chord, which is repeated intermittently, five times. The sound level of the excerpt was carefully calibrated, so as to produce a reliable response (length: 30 s).

Contagion. To produce emotional contagion, we used the piece *Prayer* from *Jewish Life No. 1*, written by Ernest Bloch in 1924 (performed by Jay Bacal, using the Vienna Symphonic Library). This lyrical and expressive piece, composed for cello and piano and marked *andante moderato*, expresses *sadness* (e.g., using slow tempo, low pitch, legato articulation, and minor mode) and was previously validated in Juslin et al. (2014, 2015) (length: 50 s).

Episodic memory. To evoke emotional episodic memories, we used the piece *Wedding March in C major*, from *Suite of Incidental Music* (Op. 61) to William Shakespeare's play *A Midsummer Night's Dream*, written by Felix Mendelssohn-Bartholdy in 1842 (performed by Margareta Lindgren on a church pipe organ). This piece is a commonly used wedding march in Portugal, and was previously tested in Juslin et al. (2015) (length: 56 s).

Musical expectancy. To manipulate listeners' expectancies, we used the piece *Lyric Suite, Three Pieces for String Orchestra, Part III: Adagio Appassionato*, written by Alban Berg in 1926 (performed by Wiener Philharmoniker, conducted by Claudio Abbado). The composition loosely follows Arnold Schoenberg's 12-tone practice (which abandons harmonically conceived tonality) and displays a low degree of key clarity (length: 70 s).

Control condition. As a supposedly "neutral" stimulus, we included an unknown piece with the title "minimalist music," composed by the alias *Mihangeliago* and downloaded from the Internet. The piece was chosen because it did not seem to feature any type of information deemed necessary to induce an emotion through one of the mechanisms in the BRECVEMA framework. Previous findings have confirmed that the piece does not generally tend to evoke emotions (Juslin et al., 2015; Sakka & Juslin, 2018). It may be described as moderately slow, soft, and monotonous (stimulus length: 59 s).

Measures

Self-reports. We measured the subjective feeling component of the listeners' affective responses by means of ratings on seven emotion scales, which covered all four quadrants of the *circumplex* model in terms of valence and arousal (cf. Russell, 1980). Included were the five scales featured in our predictions (i.e., *happiness-elation, sadness-melancholy, surprise-astonishment, anxiety-nervousness, nostalgia-longing*), as well as two additional scales with contrasting levels of arousal (*boredom-indifference* and *anger-irritation*) which would serve as "controls." (Only the control condition was expected to produce *boredom* and none of the conditions was expected to evoke *anger*.) In addition to these emotions, the participants also rated their *familiarity* with the music and their *liking* for the music. All ratings were made on a scale from 0 (*not at all*) to 4 (*a lot*).[5]

As part of the "manipulation check" in Experiment 1, we also collected subjective data on the induction mechanisms that might have occurred, using *MecScale* (Juslin et al., 2014). The scale consists of eight items (in Appendix), each targeting one of the mechanisms in the BRECVEMA framework. The notion is that although many processes are implicit in nature, they may co-occur with subjective impressions that can be reported by listeners. Self-reports of mechanisms cannot be taken as "veridical," but the *MecScale* items have been found to be highly predictive of both target-mechanism conditions (Juslin et al., 2014) and felt emotions (Juslin et al., 2015) in previous research. Listeners in this experiment were asked to respond to each of the eight questions with a simple *yes* or *no* answer.

Psychophysiology. To enhance the validity of our emotion inferences, we also obtained psychophysiological indices. The goal was to distinguish *felt* emotions from mere *perception*, and to support the self-reports. Physiological indices are not related to emotions in any simple way (Larsen et al., 2008). However, it is feasible to link such measures to broader dimensions of arousal and valence (for an example in a musical context, see Juslin et al., 2015).

Skin conductance is highly reflective of autonomic arousal (Andreassi, 2007) and facial muscle activity is a reliable indicator of emotional valence. Zygomaticus muscles (used when smiling) are correlated with positive affect, whereas corrugator muscles (used when frowning) are correlated with negative affect (Cacioppo et al., 1986).

All indices were obtained using the Biosignalsplux 8 Channel Hub (PLUX Wireless Biosignals, S.A., Lisboa, Portugal) and the OpenSignals software. Skin conductance level (SCL) was measured by means of electrodes that were placed on the palmar surface of the non-dominant hand, at the thenar and the hypothenar eminences (Fowles et al., 1981). SCL was recorded in microSiemens (μmho).

Facial electromyography (EMG) measures electrical signals involved in indirect facial muscle movements and is capable of detecting muscle contractions in response to emotional stimuli even when no obvious facial expression is observed (Tassinary et al., 2007). Bipolar facial EMG recordings were made from the left corrugator and zygomatic muscle regions in accordance with Fridlund and Cacioppo's (1986) guidelines. Before attaching self-adhesive disposable electrodes, we cleansed the participant's skin to reduce interelectrode impedance. Facial activity was measured in microvolts (μV) and analyzed using the maximum voluntary contraction. The raw EMG data were filtered, using a filter between 28 and 250 Hz, in order to increase signal-to-noise ratio. Mean values for SCL and EMG were calculated for baseline and experimental conditions. The baseline recordings were obtained prior to the listening test during relaxation under silent conditions.

Procedure. The participants read the instructions and gave written informed consent before the test began. Listeners were tested individually in a single session. Tests were conducted in a quiet, familiar place (a private office or private room). Participants were instructed that they would listen to five pieces of music, and that after each piece they would be required to report their emotional experience of

Table 1. Correlations (r_{pb}) between emotion ratings and target mechanism conditions in study 1.

Emotion Scale	Mechanism condition				
	Control	Brain stem	Contagion	Expectancy	Memory
Happiness-Elation	-.071	.033	-.175	-.320	**.532***
Sadness-Melancholy	-.250	-.325*	**.683***	.049	-.157
Surprise-Astonishment	-.324*	**.730***	-.285	.125	-.246
Nostalgia-Longing	-.171	-.214	**.406***	-.235	.214
Anxiety-Nervousness	-.140	.160	-.319	**.359***	-.060
Anger-Irritation	.123	.153	-.200	.006	-.082
Boredom-Indifference	**.646***	-.210	-.235	-.088	-.113
Liking	-.313	.083	.241	-.174	.162
Familiarity	-.273	-.071	-.242	-.164	**.750***

Note. Values show point-biserial correlations (r_{pb}) between listener's emotion ratings (coded continuously) and target-mechanism conditions (coded dichotomously). Correlations that are both statistically significant and positive in direction are shown in boldface. (Alpha level was Bonferroni-adjusted from $\alpha = .05$ to $\alpha = .0011$.)
* $p < .0011$
$N = 100$

the music on rating scales. They were also informed that they would be fitted with electrodes so that we could conduct physiological measurements, and that rings and watches should be removed.

First, the participants relaxed during silence, until a stable baseline was recorded. Then, the listening test began. After each stimulus, the listeners rated felt emotions and then relaxed again for a while before the next piece was played. It was emphasized that they should report what they *felt*, not what the music expressed. The participants listened to the music through a pair of high-quality loudspeakers (Creative Inspire T3300). Stimulus administration and data collection were handled using the free online platform eSurv. Stimulus order was randomized for each listener, whereas sound level and order of rating scales were held constant. A session lasted about 45 minutes.

Results and discussion

Emotion ratings. In order to check whether the target-mechanism conditions evoked predicted emotions in the normal sample of young adults, we computed point-biserial correlations (r_{pb}) between listeners' ratings of the seven emotions as well as *liking* and *familiarity* (coded continuously) and target-mechanism conditions (coded dichotomously).

Table 1 shows the results. Correlations that are both statistically significant and positive in direction are shown in boldface. Due to the large number of tests performed ($n = 45$), alpha level was Bonferroni-adjusted from $\alpha = .05$ to $\alpha = .0011$. Most of the results given in Table 1 were as expected. Thus, for example, the control condition evoked *boredom-indifference*; the brain stem condition evoked *surprise-astonishment*; the contagion condition evoked *sadness-melancholy*; the expectancy condition evoked *anxiety-nervousness*; and the memory condition evoked *happiness-elation*. The memory condition also showed a tendency to evoke *nostalgia-longing*—but this trend did not remain significant after Bonferroni correction. *Liking* was not significantly correlated with any of the mechanism conditions, and only the memory condition correlated significantly with *familiarity* (as intended).

In addition to the expected findings, the contagion condition tended to induce *nostalgia-longing*; that is, a non-intended emotion. This tendency is consistent with previous evaluations of the same paradigm in Sweden (Juslin et al., 2015), where sadness-inducing music tended to evoke nostalgia as well (see also Taruffi & Koelsch, 2014). However, the correlation between *sadness-melancholy* and the contagion condition was significantly stronger ($p = .005$) than the one between *nostalgia-longing* and the contagion condition—as tested using the r-to-Fisher-Z transformation in the Statistica software.

Mechanism items. In order to further support the conclusion that the four conditions "triggered" the intended mechanisms, we computed the Spearman's rho (ρ) correlations between the target-mechanism conditions and the eight items featured in *MecScale* (all variables coded dichotomously). Table 2 shows the results. Correlations that are both statistically significant and positive in direction are shown in boldface. Alpha level was Bonferroni-adjusted, from $\alpha = .05$ to $\alpha = .00128$, due to the large number of tests ($n = 40$). To the degree that *MecScale* has predictive value, we would expect only four of the 40 correlations to be both significant and positive in direction: those correlations that involve items corresponding to the four target mechanisms. All other correlations should ideally be negative and/or non-significant.

As may be seen in Table 2, only three out of 40 correlations diverged from this pattern. Thus, significant and positive correlations between mechanism conditions and corresponding *MecScale* items were obtained for all four mechanisms. By contrast, the control condition was not positively correlated with any of the items.

Table 2. Correlations (ρ) between *MecScale* items and target mechanism conditions in the pre-test.

	Mechanism condition				
Scale item	Control	Brain stem	Contagion	Expectancy	Memory
Brain stem	-.182	**.787***	-.296	-.068	-.239
Entrainment	-.320*	**.397***	-.264	-.154	**.342***
Memory	-.154	-.209	-.099	-.099	**.562***
Conditioning	-.161	-.161	.191	-.010	.141
Visual imagery	-.124	-.227	.031	-.072	**.391***
Contagion	-.434*	-.333*	**.475***	.071	.222
Expectancy	-.065	-.011	-.227	**.638***	-.335*
Appraisal	-.331*	.120	-.030	.070	.170

Note. Values show Spearman's rho (ρ) correlations between responses to the *MecScale* items (coded dichotomously) and target-mechanism conditions (coded dichotomously). Correlations that are both statistically significant and positive in direction are shown in boldface. The alpha level was Bonferroni-adjusted from $\alpha = .05$ to $\alpha = .00128$.
* $p < .00128$
$N = 100$

There were also a few additional correlations, which highlights the difficulty of clearly separating different mechanisms when using "real" pieces of music. Note that both the brain stem condition and the memory condition were (moderately) correlated with the entrainment item. In addition, the memory condition was correlated with the visual imagery item. This is to be expected, because episodic memories are commonly represented in the form of images (Tulving, 2002).

However, the target effects were stronger. For the brain stem condition, the correlation with the brain stem item was significantly larger than the one with the entrainment item ($p < .001$), and for the memory condition, the correlation with the memory item was significantly larger than the correlation with the entrainment item ($p = .027$). The difference between the correlations that involved the memory and visual imagery items, respectively, did not reach significance ($p = .061$).

Psychophysiological Measures. To evaluate the manipulation of target mechanism on psychophysiology, we carried out one ANOVA with *mechanism* as within-subjects factor (six levels: baseline, control, brain stem reflex, contagion, episodic memory, and musical expectancy) for each physiological measure. All data were z-transformed prior to analyses. The results showed that *mechanism* produced a highly significant overall effect on skin conductance level ($F_{5,95} = 23.771$, $MS = 11.116$, $p < .001$), EMG zygomaticus ($F_{5,95} = 8.347$, $MS = 6.104$, $p < .001$), and EMG corrugator ($F_{5,95} = 4.017$, $MS = 3.490$, $p < .001$). The effect was largest for skin conductance ($\eta^2 = .556$), followed by EMG zygomaticus ($\eta^2 = .305$), and EMG corrugator ($\eta^2 = .175$).

Figure 1 presents means and standard errors for each of the psychophysiological indices. Starting with skin conductance level (upper panel), it can be seen that all sounding conditions yielded a higher level than baseline (relaxation). One can also tentatively distinguish between conditions that evoked emotions high in arousal (above the mean) such as *surprise* (brainstem reflex), *happiness* (episodic memory), and *anxiety* (musical expectancy), and conditions that evoked emotions low in arousal (below the mean), such as *sadness* (contagion) and *boredom* (control) (cf. Table 1 above). Post hoc tests (Tukey's HSD) confirmed that target-mechanism conditions yielded higher skin conductance level than baseline (all ps < .001). Moreover, the brain stem condition yielded significantly higher skin conductance level than both the control condition ($p = .005$) and the contagion condition ($p = .002$); as did also the memory condition (control, $p = .036$; contagion, $p = .013$). Remaining differences were not significant.

Moving on to the facial EMG zygomaticus data, inspection of Figure 1 (middle panel) suggests that all sounding conditions produced more zygomaticus activity than the baseline condition, and that the conditions that involved predictions for neutral (Brain stem reflex → *surprise*) or mainly positive emotions (Episodic memory → *happiness, nostalgia*) produced much zygomaticus muscle activity (consistent with a positively valenced response), whereas the conditions that involved predictions for mainly negative emotions (contagion → *sadness*, musical expectancy → *anxiety*) produced less zygomaticus muscle activity (consistent with a negatively valenced response). Post hoc tests revealed that all mechanism conditions yielded more zygomaticus muscle activity than the baseline condition (ps = .0137–.0001). However, none of the remaining contrasts were significant.

Finally, with respect to the EMG corrugator data, the lower panel of Figure 1 shows that all sounding conditions produced more corrugator muscle activity than baseline. Furthermore, the results suggest that target-mechanism conditions that aimed to evoke no emotion (control) or mainly positive emotions (episodic memory) produced less corrugator muscle activity than mechanism conditions that aimed to arouse neutral (brain stem reflex) or negative (contagion, expectancy) emotions. Post hoc tests indicated

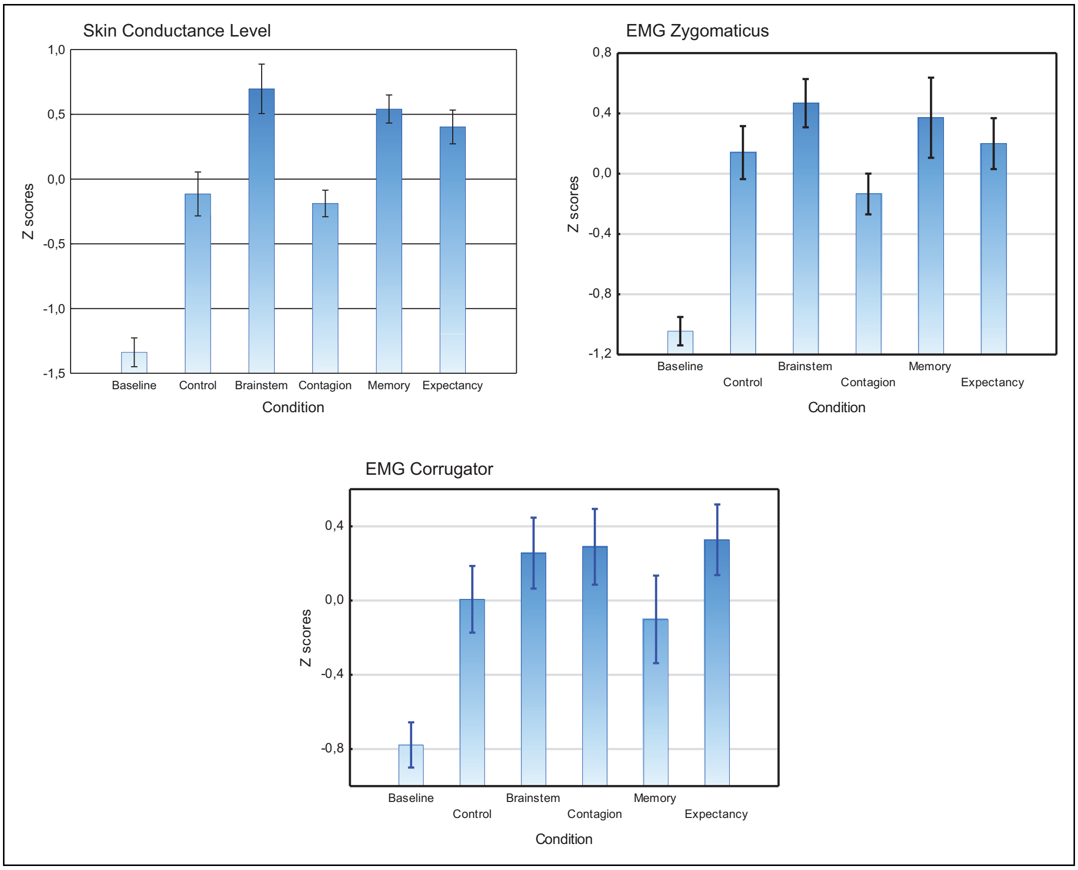

Figure 1. Means and standard errors of psychophysiological indices as a function of condition.

that the brain stem, contagion, and expectancy conditions produced significantly more corrugator muscle activity than baseline ($ps = .0041–.0089$), whereas the control and memory conditions did not differ significantly from baseline. Remaining contrasts were not significant.

In summary, then, the manipulation-check data showed that the stimuli activated target mechanisms and induced emotions largely as intended. The self-report data offered relatively strong support, whereas the psychophysiological data offered modest support suggesting that all target mechanism conditions were more emotion-evoking than baseline. The differences in psychophysiological patterns that occurred between conditions were generally consistent with the emotion ratings in terms of arousal and valence.

Experiment 2: The Comparison

Experiment 1 confirmed that the target-mechanism stimuli used in previous research in Sweden are valid also in a Portuguese context. This paved the way for the second experiment, which aimed to compare the emotional responses of AD patients with those of controls of the same age. We used the same stimuli and measures as in Experiment 1, except that mechanism indices (*MecScale*) were not included. Because AD is usually associated with a higher rate of depression than other types of dementia (Garrido et al., 2017), we measured depression levels in participants to rule out that differences between the groups would reflect depression per se (Sakka & Juslin, 2018), as opposed to cognitive impairments associated with AD.

Underlying mechanisms cannot be observed directly; rather, they must be inferred from behavioral output. We expected to find that listeners with AD differ from controls in terms of the quality and quantity of emotions aroused by musical stimuli, mainly because of cognitive impairments due to brain atrophy. Moreover, because different mechanisms involve different neural substrates, the precise nature of the differences between AD patients and controls was expected to vary depending on the mechanism (i.e., an interaction). Taking into account brain studies as well as our own hypotheses about brain regions involved in each mechanism (for a recent review, see Juslin & Sakka, 2019), we could formulate a prediction about whether the responses of AD patients would differ or not from those of controls for each mechanism.

Brain stem reflexes are quick, automatic and "hard-wired" reactions to extreme acoustic features in the music (Juslin, 2019). They involve the reticulospinal tract, which travels from the reticular formation of the brain stem, and the intralaminar nuclei of the thalamus (Davis, 1984; Kinomura et al., 1996). Alarm signals to auditory events in the form of startle reflexes may be emitted as early as at the level of the inferior colliculus (Brandao et al., 1993). Since AD patients display pathological changes (Braun & Van Eldik, 2018) as well as a significant total volume reduction in the brain stem (Lee et al., 2015) compared with controls, one could perhaps expect impaired auditory processing. However, as observed by Dugger et al. (2011), the inferior colliculus is *not* affected consistently by AD until the later stages. The brain stem reflex condition is expected to arouse mainly *surprise-astonishment* in listeners (Experiment 1). Based on the relative sparing of brain areas associated with this mechanism, we predicted that self-reported levels of *surprise-astonishment* by AD patients in this condition would *not* differ significantly from those of healthy controls.

Emotional contagion from music will tend to include brain regions for the perception of emotions from the voice, including right-lateralized inferior frontal regions (the frontal gyrus) and the basal ganglia (Adolphs et al., 2002; George et al., 1996; Schirmer & Kotz, 2006), and also so-called "mirror neurons" in pre-motor regions, particularly areas involved in perceiving emotional vocalizations (Paquette et al., 2018; Warren et al., 2006). Recent findings show that shape changes of the basal ganglia take place as AD progresses (Cho et al., 2014). Aβ plaques have also been found in the frontal gyrus (Nicoll et al., 2003). Impairment of these brain areas might severely affect the contagion mechanism. The contagion stimulus is normally expected to arouse *sadness-melancholy* in listeners (Experiment 1). However, given the above findings, we predicted that AD patients would report significantly lower levels of *sadness-melancholy* in this condition than would controls.

Episodic memory is usually divided into different stages (e.g., encoding, retrieval). The conscious experience of recollecting an episodic memory involves the medial temporal lobe, particularly the hippocampus (Nyberg et al., 1996) and the medial pre-frontal cortex (Gilboa, 2004; for similar findings in music, see Janata, 2009). Additional areas linked with episodic memory retrieval are the precuneus (Wagner et al., 2005), the entorhinal cortex (Haist et al., 2001), and the amygdala (for emotional memories; cf. Dolcos et al., 2005). Evidence shows that most of these areas are affected early by AD (Frisoni et al., 2010). Further, even though memory for familiar music seems to be relatively spared (Cuddy et al., 2012, 2015; Kerer et al., 2013), it remains unclear whether episodic memories associated with familiar music are also spared. The episodic memory condition is usually expected to arouse *happiness-elation* and *nostalgia-longing* in listeners (Experiment 1); however, because AD patients show early episodic memory impairment, we predicted that they would report significantly lower levels of *happiness-elation* and *nostalgia-longing* in the memory condition than would controls.

Musical expectancy involves a response to the unfolding of the syntactical structure of the music, and its expected or unexpected continuation (see Meyer, 1956), akin to a syntax in language. Lesion studies show that parts of the left perisylvian cortex are involved in various aspects of syntactical processing (Brown et al., 2000). Data suggest that parts of Broca's area increase their activity when sentences increase in syntactical complexity (Caplan et al., 1998; Stromswold et al., 1996; for music, see Maess et al., 2001). Musical expectancy also involves monitoring of conflicts between expected and actual sequences. This could recruit parts of the anterior cingulate (Botvinick et al., 2004) or orbitofrontal cortices (Koelsch, 2014). A number of studies have found that the perisylvian cortex and Broca's area become gradually impaired in AD (e.g., Tanzi et al., 1987, 1988; Thompson et al., 2001; Wasco et al., 1993), whereas the anterior cingulate cortex is spared until very late stages (Brun & Englund, 1981). As far as we know, only a single study of music to date has explored expectations generated in AD patients while listening to music. Clark et al. (2016) found that patients showed a significant deficit in labeling of melodies as finished or unfinished. The musical expectancy condition is normally expected to arouse *anxiety-nervousness* in listeners (cf. Experiment 1); however, based on the studies outlined above, we predicted that AD listeners would report significantly lower levels of *anxiety-nervousness* in this condition than would controls.

Method

Participants. The experiment featured 40 participants spread across two groups. The dementia group, consisting of individuals diagnosed with possible or probable AD, included 13 females and 7 males, aged 68–87, $M = 76.15$, $SD = 6.37$. The control group, consisting of age-matched volunteers without the diagnosis, featured 15 females and 5 males, aged 65–86, $M = 71.3$, $SD = 5.80$. Mean age for the complete sample = 73.70, $SD = 6.50$. One participant in each group played a musical instrument; two in the control group and one in the dementia group had received formal music education. Statistical tests (a Mann-Whitney U test for age and chi-square tests for gender, musical training, and music education) revealed no significant differences between the groups regarding background variables. All participants were native Portuguese speakers, and they received no compensation for their anonymous and voluntary participation.

The AD patients were recruited at two health care facilities in Portugal.[6] An agreement was signed between M-iti Madeira/University of Madeira and the institutions, in which it is stated that the parties will collaborate to advance research in neurorehabilitation in patients. We presented our study to the clinical boards of both institutions, and asked them to recruit persons diagnosed with mild to moderate stage AD; we were informed about the number of persons they were able to recruit, and that an accredited staff member would be available at all times, in case something unexpected should happen.

The following exclusion criteria were used to select the AD participants: none of them should have (additional) conditions known to lead to cognitive deficits, such as head trauma, stroke, or alcoholism; they should not have any hearing problem or be unable to comprehend task instructions. Prior to the experiment, all patients were diagnostically assessed by a team of physicians and nurses. Dementia severity was classified as level 1 (*mild*) or 2 (*moderate*), as specified by the Clinical Dementia Rating Scale (CDR, Morris, 1993), though these data were, unfortunately, classified. However, we measured cognitive impairments as part of this study (described below). All patients were taking anti-dementia medication at the time of the study.

Design. We used a mixed factorial design with *group* as between-subjects independent variable (two levels: AD patients, controls), and *mechanism* condition as within-subjects independent variable (five levels: brain stem reflex, contagion, episodic memory, musical expectancy, and control). (Notably, AD is formally a quasi-experimental variable, because it is not possible to randomly distribute participants across the two conditions.) An additional baseline condition was included in the psychophysiological analyses. Self-reported feelings, autonomic activity (skin conductance level), and facial electromyography (zygomaticus and corrugator muscles) were the dependent variables. Moreover, we controlled for level of depression and cognitive impairment via psychometric tests.

Musical Material. We used the same stimuli as in Experiment 1.

Measures

Self-reports. To measure feelings, we used the same terms as in Experiment 1, although all ratings were made on a scale from 0 (*not at all*) to 2 (*a lot*), in order to simplify the task for AD patients in particular.

Psychophysiology. We used the same measures as in Experiment 1.

Psychometric Tests. To assess cognitive impairment, we used a Portuguese translation (Guerreiro et al., 1994) of the Mini-Mental State Examination (MMSE; Folstein et al., 1975). This is a widely used 30-point questionnaire featuring tests of attention, orientation, memory, language, and visual–spatial skills. The MMSE has been shown to have validity and reliability for the diagnosis and longitudinal assessment of AD (Mitchell, 2013). Any test score of 24 or more (out of 30) indicates "normal" cognition. Below this, scores indicate *mild* (19–23 points), *moderate* (10–18 points), or *severe* ($\leq$ 9 points) cognitive impairment (Pangman et al., 2000).

Depression affects a large number of elderly people, and is also a significant aspect of the symptomatology of AD (Espiritu et al., 2001). Hence, we used the Geriatric Depression Scale (GDS) to assess level of depression (Yesavage et al., 1982). The GDS is a 30-item self-report questionnaire, for which a test score of 0–9 is interpreted as "normal," 10–19 as "mildly depressed," and 20–30 as "severely depressed." In addition to accurately detecting depression in people whose cognition is intact, the GDS may be used to screen for depression in people whose MMSE scores are at 15 or above (Jongenelis et al., 2005).

Procedure. The procedure was the same as in Experiment 1, except that AD patients were always tested in the company of accredited staff at their health care facility. (No additional support was required to complete measures.) Whenever deemed necessary, we obtained a signature on the consent form from the legal representative.

Results and Discussion

Analysis of the overall test scores from the MMSE revealed a significant difference between the two experimental groups. As expected, the dementia group showed lower scores (M = 18.00, SD = 3.89) than the control group (M = 28.20, SD = 1.74; t_{38} = -10.702, p < .001, d = 1.711). By contrast, the dementia group did not show significantly different overall scores on the GDS (M = 6.65, SD = 4.73) from the control group (M = 6.85, SD = 5.36; t_{38} = 0.125, p = .901, d = 0.040). The results confirm that it is meaningful to compare the two experimental groups with regard to their emotional responses.

Emotion Ratings. Our theoretical predictions imply that the effect of dementia on emotional responses to music will differ depending on the induction mechanism responsible for the emotion. Hence, the effect of main interest is the interaction between target-mechanism condition and listener group. Figure 2 shows means and standard errors for each rating scale as a function of target-mechanism condition and group. As may be seen, the overall trends are largely as expected. Thus, for instance, the memory condition induced the most *happiness-elation*, the contagion condition induced the most *sadness-melancholy*, the brain stem condition induced the most *surprise-astonishment*, the episodic memory condition induced the most *nostalgia-longing*, and the expectancy condition induced the most *anxiety-nervousness*.

As regards the additional scales that we included for control purposes, it may be seen in Figure 2 that none of the target-mechanism conditions induced *anger-irritation*, and that only the control condition induced *boredom-indifference*. The control condition was the least liked of all conditions, and only the episodic memory condition received high ratings of *familiarity*.

However, the results in Figure 2 also suggest some interaction between mechanism and group, which we wished to investigate further. Since the overall trends on the scales

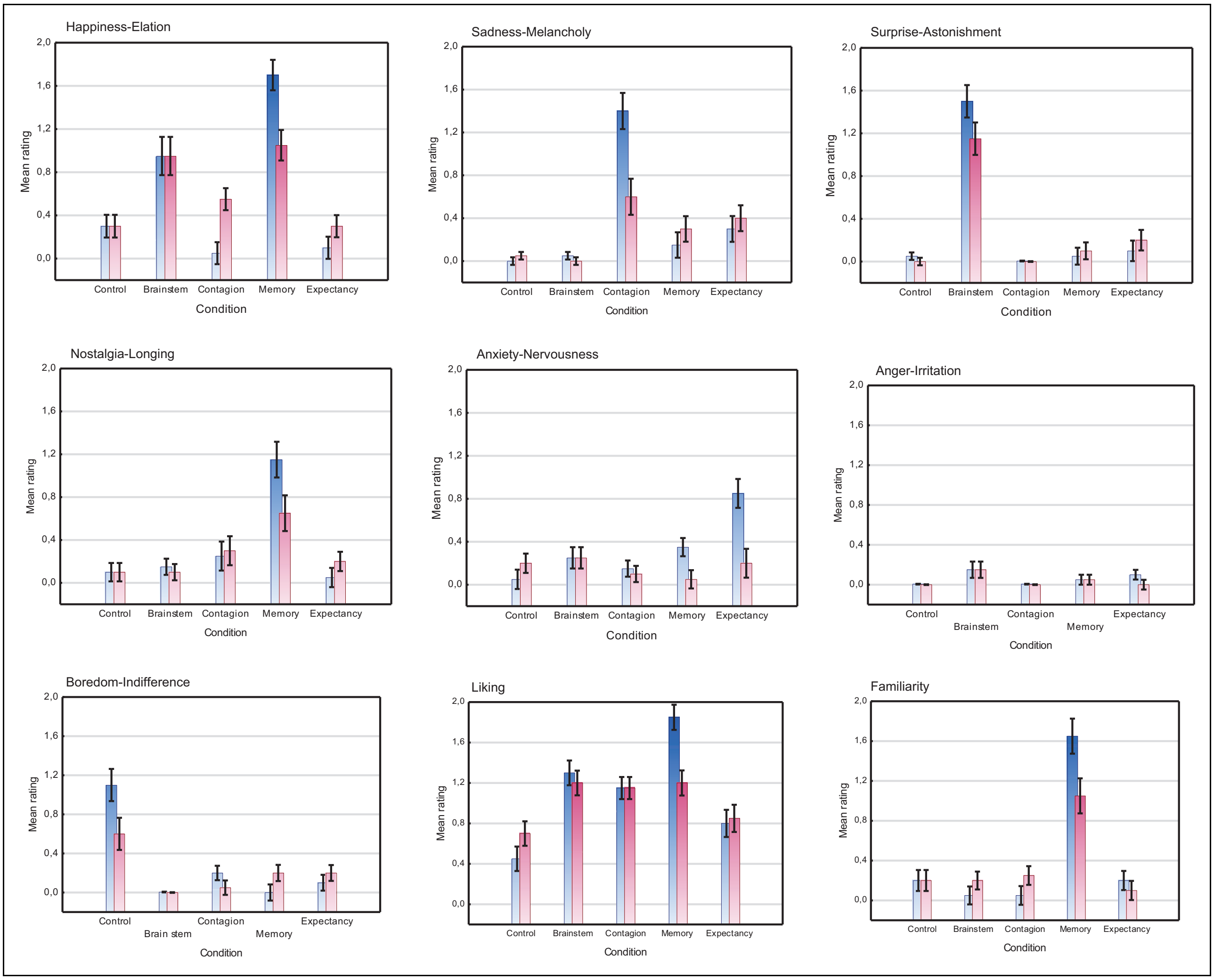

Figure 2. Means and standard errors of ratings as a function of condition and experimental group (blue bars = healthy controls; red bars = dementia patients).

featured for control purposes were mostly similar to those in the manipulation check (cf. Study 1), we focused our statistical tests on the five rating scales for which we had formulated predictions. Hence, we conducted one two-way, mixed ANOVA for each emotion scale, with *mechanism* as within-groups factor (five levels: control, brain stem reflex, contagion, episodic memory, and musical expectancy) and *group* as between-groups factor (two levels: dementia patients, healthy controls).

A summary of the results is shown in Table 3. As may be seen, there was a significant main effect of *mechanism* on all five scales, with the largest effect occurring on the *surprise-astonishment* scale and the smallest on the *anxiety-nervousness* scale. By contrast, there was no significant effect of *group* on any of the scales. Most importantly, there was a significant interaction between *mechanism* and *group* for four of the five scales (i.e., *happiness-elation, sadness-melancholy, nostalgia-longing, anxiety-nervousness*), which suggests that the effect of dementia on these emotions differed, depending on the mechanism condition. Conversely, there was no significant interaction for *surprise-astonishment*. Careful inspection of Figure 2 does suggest less of an interactive effect for this scale.

In order to test our predictions, we conducted planned comparisons (t tests, independent samples) of the mean ratings of the groups for the relevant mechanisms and rating scales. The results were in accordance with our predictions. In the contagion condition, dementia patients reported significantly less *sadness-melancholy* (M = 0.60, SD = 0.82) than controls (M = 1.40, SD = 0.68; t_{38} = -3.355, p = .002, d = 0.944). They also reported more *happiness-elation* (M = 0.55, SD = 0.60) in this condition than controls (M = 0.05, SD = 0.22; t_{38} = 3.468, p = .001, d = 0.968). In the episodic memory condition, dementia patients reported less *happiness-elation* (M = 1.05, SD = 0.76) than controls (M = 1.70, SD = 0.47; t_{38} = -3.255, p = .002, d = 0.922), and less *nostalgia-longing* (M = 0.65, SD = 0.88) than controls (M = 1.15, SD = 0.59;

Table 3. Summary of analyses of variance for listeners' ratings on five emotion scales.

Scale	*MS*	*F*	*p*	eta-squared
Happiness-Elation				
Mechanism	10.600	32.962	<.001*	.465
Group	.005	.013	.909	.001
Mechanism x Group	1.780	5.535	<.001*	.127
Sadness-Melancholy				
Mechanism	6.463	27.922	<.001*	.424
Group	0.605	2.283	.139	.057
Mechanism x Group	1.543	6.665	<.001*	.149
Surprise-Astonishment				
Mechanism	12.867	92.185	<.001*	.708
Group	0.130	0.546	.464	.014
Mechanism x Group	0.311	2.230	.068	.055
Nostalgia-Longing				
Mechanism	4.618	18.373	<.001*	.326
Group	0.245	0.719	.402	.019
Mechanism x Group	0.633	2.517	.044*	.062
Anxiety-Nervousness				
Mechanism	1.093	5.591	<.001*	.128
Group	1.445	7.273	.010	.161
Mechanism x Group	0.983	5.028	<.001*	.117

Note. For *Mechanism* and *Mechanism x Group*, $df = 4$ (effect) and 152 (error). For *Group*, $df = 1$ (effect) and 38 (error).
* $p < .05$

t_{38} = -2.122, p = .040, d = 0.643). In the expectancy condition, dementia patients reported less *anxiety-nervousness* (M = 0.20, SD = 0.52) than controls (M = 0.85, SD = 0.67; t_{38} = -3.417, p = .001, d = 0.957). By contrast, we observed no significant difference in reported *surprise-astonishment* between dementia patients (M = 1.15, SD = 0.75) and controls (M = 1.50, SD = 0.61; t_{38} = -1.629, p = .112, d = 0.504) in the brain stem condition.

Psychophysiological Measures. To evaluate the manipulation of target mechanism on psychophysiology, we carried out one ANOVA with *mechanism* as within-subjects factor (six levels: baseline, control, brain stem reflex, contagion, episodic memory, and musical expectancy) and *group* as between-subjects factor (two levels: dementia patients, healthy controls) for each physiological measure.

The results indicated that *mechanism* produced a highly significant main effect on skin conductance level ($F_{5,190}$ = 71.968, MS = 30.815, p < .001), EMG zygomaticus ($F_{5,190}$ = 15.481, MS = 12.897, p < .001) and EMG corrugator ($F_{5,190}$ = 5.116, MS = 5.583, p < .001); again, the effect was largest for skin conductance level (η^2 = .654), followed by EMG zygomaticus (η^2 = .298), and EMG corrugator (η^2 = .119). In addition, the main effect on EMG zygomaticus was qualified by a highly significant interaction between *mechanism* and *group*, $F_{5,190}$ = 4.136, MS = 3.445, p = .0014, η^2 = .098, which suggests that the effect of mechanism condition on EMG zygomaticus activity varied depending on the group. There were no significant main effects of *group* for any of the indices.

Figure 3 shows means and standard errors for the three psychophysiological indices, as a function of mechanism and group. Regardless of the index, there was hardly any difference between groups in baseline. In the mechanism conditions, the results tentatively suggest that the largest difference between the groups with respect to specific conditions occurred for the indices that are mostly reflective of emotional valence (EMG zygomaticus, EMG corrugator) rather than autonomic arousal (SCL).

Planned comparisons (t tests) confirmed that the only significant contrasts between the groups occurred for the facial EMG results. Starting with EMG zygomaticus (middle panel), results indicated that dementia patients showed less activity in the brain stem condition (M = 0.469, SD = 0.889) than did controls (M = 1.326, SD = 0.801), t_{38} = -3.201, p = .003, d = 0.910. Furthermore, dementia patients showed more zygomaticus activity in the contagion condition (M = -0.158, SD = 0.484) than did controls (M = -0.652, SD = 0.338), t_{38} = 3.737, p < .001, d = 1.024; they further showed more zygomaticus activity in the expectancy condition (M = 0.477, SD = 0.959) than did controls (M = -0.233, SD = 0.778), t_{38} = 2.570, p = .014, d = 0.760. With regard to EMG corrugator (bottom panel), dementia patients showed more corrugator activity in the memory condition (M = 0.065, SD = 0.917) than did healthy controls (M = -0.481, SD = 0.718), t_{38} = 2.097, p = .043, d = 0.636. Remaining contrasts were not significant.

In summary, the results were largely in accordance with our predictions: We obtained a significant difference in self-reported emotion between dementia patients and healthy controls for three target-mechanisms (contagion → *sadness*; episodic memory → *happiness, nostalgia*; expectancy → *anxiety*), but not for brain stem reflex (→ *surprise*). The significant interaction effects and the absence of a main effect of group show that these results do not simply reflect an overall "response bias" in the dementia group (e.g., responding with more sadness overall): the emotional responses *do* depend on the target-mechanism condition (e.g., responding with less sadness in the contagion condition, but *not* in the other conditions). Psychophysiological indices offered partial support: significant main effects of mechanism on all measures, and a lack of main effects of group, show that stimuli evoked emotions successfully in both groups. Tendencies toward interactions between target mechanism conditions and group were mainly confined to the valence-sensitive measures, in particular EMG zygomaticus activity.

General Discussion

In this study, we made a first attempt to examine whether and how emotional responses to music in AD patients differ from those of healthy controls. In Experiment 1, we replicated previous findings in Sweden by showing that theoretically based manipulations of four target mechanisms

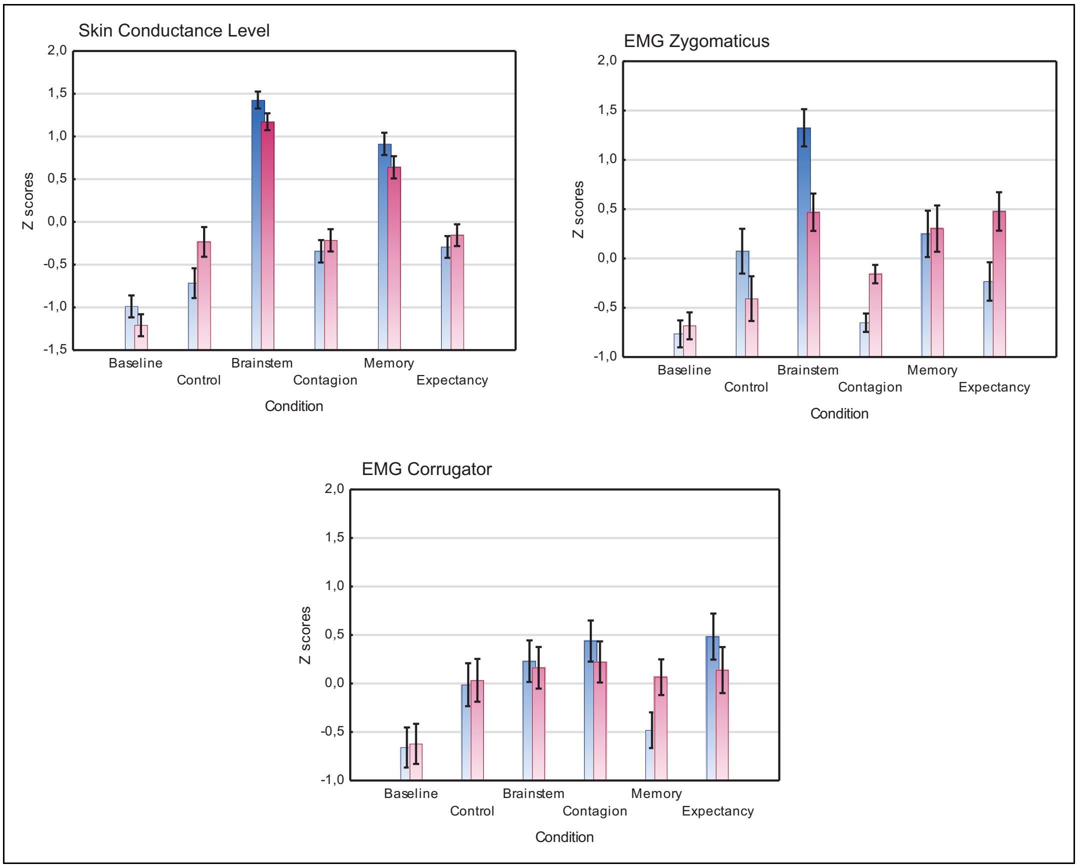

Figure 3. Means and standard errors of psychophysiological indices as a function of condition and experimental group (blue bars = healthy controls; red bars = dementia patients).

produced predicted emotions in a sample of young listeners from another culture (Portugal), as suggested by self-reports of feelings and mechanisms, and psychophysiological measures. In Experiment 2, we used the same paradigm to show that differences in emotional reactions between AD patients and healthy controls of a similar age depend on the mechanism—as shown by significant interactions between target mechanism and group for the contagion, episodic memory, and musical expectancy mechanisms—though not for the brain stem reflex mechanism, whose primary neural substrate (i.e., the inferior colliculus) seems largely spared until later stages of AD (Dugger et al., 2011). The results for the controls were very similar to those of the younger participants in Experiment 1 except that the results for *nostalgia-longing* and episodic memory were even more in line with the predictions.

However, there were also some unexpected results, mainly for the psychophysiological results in Experiment 2. We did not find any statistically significant interaction between SCL (indexing autonomic arousal) and group. Tendencies towards interactions were more evident in the indices reflective of emotional valence (EMG zygomaticus and EMG corrugator). Our results are consistent with the findings from a previous study, which found no differences in arousal between AD patients and healthy controls when listening to music (Irish et al., 2006).

The EMG data were mostly consistent with the self-reported feelings. When responses in the dementia group differed from those of healthy controls, they did so by showing trends in the "wrong" direction, compared to expected effects for healthy listeners. For instance, AD patients showed higher levels of zygomaticus muscle activity than controls in the contagion condition (aimed to induce sadness) and the expectancy condition (aimed to induce anxiety).

In principle, these results could be interpreted in two ways. One possible explanation is that dementia listeners smiled more because they actually felt less sadness and anxiety than controls, as the self-reports suggested (confirming our predictions). Another possibility is that their muscle activity was related to liking (e.g., Witvliet & Vrana, 2007): AD patients might have liked the piece, despite feeling little or no emotion, consistent with some independence between "emotion" and "preference" (Juslin et al., 2010, pp. 634-637). However, there were no differences between the two groups in rated liking of the contagion and expectancy conditions (Figure 2), which renders the latter explanation less plausible.

A more peculiar result regarding the EMG data was that AD patients showed a weaker zygomaticus muscle reaction in the brain stem reflex condition than controls, despite the fact that they reported a similar level of surprise and showed a similar level of SCL. Zygomaticus muscle activity in the brain stem reflex condition may reflect “cross-talk” from other muscles of the middle and lower facial regions during a startle response (e.g., Juslin et al., 2014). One possible explanation for the present finding could be that dementia patients showed a “muted” motor response; that is, that their brain stem mechanism was properly activated and that they felt surprise, but that the startle was reduced due to poor muscle coordination and slow motor response in dementia (Buchman & Bennett, 2011; Yan & Zhou, 2009). (This tendency could have been exacerbated by medication.) Some decrease in the startle magnitude is found even with normal aging (Ellwanger et al., 2003). Another explanation might be that differences in zygomaticus activity are caused by early impairment of brain stem structures, apart from the inferior colliculus, which may be required for the unimpeded expression of a startle response (e.g., parts of the reticulospinal tract; see Boulis et al., 1990).

There are a number of limitations of this study which should be kept in mind. First, our listener samples were relatively small, which limits statistical power and calls for replication. Second, we manipulated only four of the mechanisms in the BRECVEMA framework, and it seems possible that other mechanisms are also differentially affected by dementia. Third, we included only a single piece to represent each target mechanism—unlike some earlier studies (see Juslin et al., 2015)—which means that artefactual results due to specific songs cannot be completely ruled out. Fourth, the psychophysiological measures were limited to three indices, and this may have prevented us from detecting more subtle differences between the groups.

Most importantly, our sample featured only two levels of AD, mild and moderate, and we did not manage to recruit an equal number of patients for each level. It appears plausible that there are differences between mild and moderate AD for some of the mechanisms. This highlights the need to use larger samples in future studies so that various stages of dementia can be contrasted regarding specific mechanisms. Research has shown that the effectiveness of musical interventions tends to decrease with severity of impairment (Holmes et al., 2006), and each mechanism may show a unique developmental trajectory regarding impairments.

Interest in the use of pre-recorded music in non-therapist-led interventions and musical programs is increasing (e.g., Garrido et al., 2017), and many of the uses of music in dementia care involve a focus on emotions, for instance to address problems such as apathy, anxiety, or aggressiveness (Ferreri et al., 2019). Thus, a key aim for research may be to induce beneficial emotions in dementia patients in as systematic manner as possible. Detailed knowledge about mechanisms may play a crucial role in optimizing a musical intervention (Bradt, 2018; Juslin, 2011, 2019), by helping the practitioners to adapt the intervention to each patient’s needs and cognitive resources (e.g., with regard to music preference and stage of dementia).

Researchers in the present domain seem to agree about the importance of understanding underlying mechanisms (Baird et al., 2019; Brancatisano & Thompson, 2019; Garrido, 2019; Ghilain et al., 2019). Yet little is known about how, exactly, emotional reactions to music are affected by dementia in its different stages, or how they might depend on the mechanism. To our knowledge, this is the first study to apply the BRECVEMA framework to a sample of AD patients and to manipulate mechanisms in order to understand how brain atrophy in dementia could influence emotional responses. Regardless of its limitations, the present study provides some preliminary data that may help to explain mixed findings and individual differences in previous research. First, the interventions thus far could have included stimuli that activated distinct mechanisms, only some of which were successful. Second, musical preferences play a key role in interventions (Garrido et al., 2017), and this factor also happens to be related to mechanisms: preferred music is likely to be more familiar to the listener, and familiarity will enable a greater number of mechanisms to be activated (e.g., memory-based mechanisms).

Practitioners might thus be able to achieve more consistent outcomes in their musical interventions, if they are able to control for mechanism and familiarity (Juslin, 2011, 2019). But how may findings such as these be translated into protocols and procedures in dementia care? One approach may be to design interventions in such a way as to target those emotion induction mechanisms most likely to be responsive based on brain scans showing the nature of damage in each patient. Mechanisms that remain preserved might constitute a solid basis for targeted musical interventions. (It should be acknowledged, though, that the practicality of this approach may vary a lot, depending on treatment routines and resources available in specific countries.)

The exploitation of our findings in such interventions would require a very controlled and timely use of induction mechanisms, beyond passive music listening. Interactive media may be an ideal candidate for delivering such controlled musical stimuli in accordance with patients’ needs. Virtual environments have been reported to be effective tools for delivering personalized cognitive stimulation therapies in different neurological conditions (Maggio et al., 2019), and some studies showed enhanced efficacy when compared to traditional paper-and-pencil programs (Faria et al., 2016, 2020). Moreover, it has been found that people with dementia can effectively use interactive technologies when designed adequately (Ferreira et al., 2020).

We believe that incorporating mechanism manipulations in a virtual reality cognitive stimulation platform may increase intervention efficacy, while at the same time making the intervention more accessible and affordable (a computer program tends to be less costly to implement than are interventions by a music therapist). For this reason, we are planning to extend with our findings an existing tool called *Musiquence*, designed to exploit music and reminiscence cognitive-stimulation strategies in gaming contexts for people with dementia (Ferreira et al., 2019). Further study of how various emotion mechanisms are differentially affected by dementia—taking the different stages of the disease into account—would seem to be a promising avenue of research in order to develop such musical interventions.

Contribution

GB researched literature and conceived the study. GB, PJ and SB were involved in study design. GB and SB obtained ethical approval. GB and PJ worked on stimulus selection and performed data analyses. GB wrote the first draft of the manuscript, PJ the second draft. All authors reviewed and approved the final version.

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Notes

1. We will use the term patient (from the Latin word patiens; suffering) to refer to individuals who suffer from dementia. This use is in accordance with the American Psychological Association's (2018) resolution, which recommends that the term patient is used to describe all individuals diagnosed with mental health, behavioral health, and/or a medical disease, disorder, or problem, at all venues where health care services and/or health-related research endeavors take place. Patient might also be the term preferred by those receiving health care services (Deber et al., 2005).
2. This is perhaps because the brain regions involved (e.g., the caudal anterior cingulate cortex and the ventral pre-supplementary motor areas) are commonly spared in the early stages of the disease (Jacobsen et al., 2015).
3. This is similar to how listeners suffering from depression react differently to some music, compared to controls (Garrido & Schubert, 2015; Sakka & Juslin, 2018).
4. A lack of difference in response between the two groups might be due to either both groups showing similar (normal) age changes or both groups responding in the same way as young adults. Experiment 1 could help to disambiguate such a result.
5. Notably, we used a slightly smaller number of emotion scales than in previous studies (e.g., Juslin et al., 2015, 2016). This was done mainly to reduce the "cognitive load" of the rating task for AD patients who would use the same rating scales in Experiment 2.
6. One of the facilities was a health care center and the other was a day care center.

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Appendix: Mechanisms Items (*MecScale*)

1. Did the music feature an event that startled you?
   Yes ☐ No ☐

2. Did the music have a strong and captivating pulse/rhythm?
   Yes ☐ No ☐

3. Did the music evoke a memory of an event from your life?
   Yes ☐ No ☐

   If *yes*, the memory was:
   Negative ☐ Positive ☐ Mixed ☐

4. Did the music evoke more general associations?
   Yes ☐ No ☐

   If *yes*, the association was:
   Negative ☐ Positive ☐ Mixed ☐

5. Did the music evoke images while you were listening?
   Yes ☐ No ☐

6. Were you touched by the emotional expression of the music?
   Yes ☐ No ☐

7. Was it difficult to guess how the music (e.g., melody) would continue over time?
   Yes ☐ No ☐

8. Did you find the music aesthetically valuable?
   Yes ☐ No ☐