Is the Neutral Condition Relevant to Study Musical Emotion in Patients?

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STUDIES CARRIED OUT IN NONMUSICAL DOMAINS provide evidence that abnormal responses to emotionally neutral stimuli are associated with medial temporal lobe (MTL) dysfunction at the level of the amygdala. In this investigation, we propose that music will be an adequate candidate to examine the role of MTL structures in judging emotional neutrality. By testing 43 patients with temporal lobe lesions and 19 controls in a task involving classification of neutral, happy, sad, and distressing music, we found that the identification of neutral stimuli was selectively impaired in patients with MTL dysfunction. This finding suggests the implication of the amygdala in classifying emotionally neutral stimuli, supporting previous neuroimaging studies. We discuss the present data in relation to facial expressions and present an intriguing case of affective disturbance resulting from a head injury to emphasize the relevance of using music to assess the ability to detect neutrality in neurological and psychiatric patients.

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THE EMOTIONAL POWER OF MUSIC IN HUMAN BEINGS is striking and produces various experiences such as great stillness, fear, or intense pleasure (Sloboda, 1991; Sloboda & Juslin, 2001). This extreme emotion can be accompanied by a physiological manifestation of "shiver down the spine" or "chills" (Panksepp, 1995). Other emotional responses have also been examined by using different experimental approaches based on either categorical or dimensional judgments. According to the categorical approach, emotions are defined as belonging to discrete classes; music listening being able to induce non ambiguous basic emotions such as happiness, sadness, anger, peacefulness or fear, as demonstrated by several empirical studies in adults and infants (Cunningham & Sterling, 1988; Kastner & Crowder, 1990; Tergwogt & Van Grinsven, 1991; Vieillard, Peretz, Gosselin, Khalfa, Gagnon, & Bouchard, in press). A matching paradigm between musical excerpts and linguistic labels is typically used to assess these emotional experiences. Additional investigations have shown that specific perceptual cues such as the mode (major-minor) and the tempo (rapid-slow) of the music can be associated with specific emotional responses such as happiness or sadness (Dalla Bella, Peretz, Rousseau, & Gosselin, 2001; Gagnon & Peretz, 2003; Gabrielson & Lindstrom, 2001; Gerardi & Gerken, 1995; Hevner, 1935; Kastner & Crowder, 1990). These responses may partly result from the perception of intrinsic musical structure. Other authors preferred to adopt a dimensional approach to study emotional experience. This is supposed to provide a better account for the richness and complexity of musical emotion as it allows for the continuous evolution of the music along different dimensions of emotion or scales (Bigand, Vieillard, Madurell, Marozeau, & Dacquet, 2005; Hevner, 1935; Juslin, 2001; Madsen, 1997; Russell, 1980; Schubert, 1996; Vieillard et al., in press; Wedin, 1972). Generally, the most commonly examined dimensions were arousal (i.e., from relaxing to stimulating) and valence (i.e., from negative to positive, or from unpleasant to pleasant). Although all these studies based on either categories or scales provide complementary knowledge about the emotional power of music, they share a common feature. They all focused their interest on the perception of emotional music and none of them, to our knowledge, investigated the ability to detect or to judge "neutral" musical excerpts.

In recent years, the neural basis of the emotions induced by musical listening has been revealed by neuroimaging methods (Blood & Zatorre, 2001; Blood, Zatorre, Bermudez, & Evans, 1999; Brown, Martinez, &

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Parsons, 2004; Khalfa, Schön, Anton, & Liegeois-Chauvel, 2005; Koelsch, Fritz, von Cramon, Müller, & Friederici, 2006; Menon & Levitin, 2005), electrophysiological (Altenmüller, Schürmann, Lim, & Parlitz, 2002; Baumgartner, Esslen, & Jancke, 2006; Khalfa, Peretz, Blondin, & Manon, 2002; Krumshansl, 1997; Sammler, Grigutsch, Fritz, & Koelsch, 2007; Schmidt & Trainor, 2001; Steinbeis, Koelsch, & Sloboda, 2006; Wieser & Mazzola, 1986) and lesion studies (Gosselin, Peretz, Johnsen, & Adolphs, 2007; Gosselin et al., 2005, 2006; Griffiths, Warren, Dean, & Howard, 2004; Peretz, Gagnon, & Bouchard, 1998; Peretz & Gagnon, 1999; Peretz, Blood, Penhune, & Zatorre, 2001). The existing studies suggest that structures involved in the auditory analysis of music in the superior temporal cortex (auditory areas) and in the inferior frontal lobe might work together with emotion-related brain structures (amygdala, parahippocampal cortex, insula, orbitofrontal cortex, and right somatosensory cortex) in experiencing musical emotions.

In neuropsychological studies, categorical and dimensional approaches of musical emotion have been considered either separately or in combination. Thus, categorical responses with forced choice recognition (Peretz & Gagnon, 1999; Peretz et al., 1998), dimensional responses along valence and arousal scales (Gosselin et al., 2006; Peretz et al., 2001), or a combination of both types of responses (Gosselin et al., 2005, 2007) have been used. The investigation of musical emotion experienced by brain damaged patients started with the case IR who developed a musical agnosia following a bitemporal lesion (Peretz & Gagnon, 1999; Peretz et al., 1998). Although this patient was not able to recognize familiar tunes, she succeeded in classifying them as sad or happy, indicating relatively spared emotional processing of music. Conversely, studies carried out in groups of patients after unilateral anteromesial temporal lobe resection (Gosselin et al., 2005, 2006), or case studies of patients with bilateral amygdala lesions (case SM, Gosselin et al., 2007), or more diffuse left cerebral damage including the insula and frontal lobe as well as the amygdala (Griffiths et al., 2004) have documented the reverse dissociation with normal recognition of music but a loss of affective responses to it. Thus, unilateral (Gosselin et al., 2005) or bilateral (Gosselin et al., 2007) amygdala lesions have been shown to selectively impair recognition of scary music and to a certain extent emotional arousal, but do not appear to affect recognition of peaceful or happy music. Recognition of sad music appears to be impaired after bilateral but not unilateral amygdala lesions. Furthermore, a subjective bias to judge dissonant music as pleasant instead of unpleasant has been demonstrated in patients with medial temporal resection including part of the parahippocampal cortex (Gosselin et al., 2006). In line with previous neuroimaging results (Blood et al., 1999), this finding suggests the involvement of the parahippocampal cortex in judging unpleasant emotional valence. However, the same patients had no difficulties in rating the musical excerpts along a happy-sad scale, indicating that the processing of emotional valence along two different scales (i.e., pleasant-unpleasant or happy-sad) may differ. These neuropsychological and functional brain imaging results indicate that the emotional processing of music recruits an "amodal" cerebral network that has already been described in other nonmusical domains. The specificity of musical emotion, however, remains to be clarified.

As previously discussed, music can induce basic emotions (happiness, sadness, fear) that we are able to categorize, but the ability to detect "neutrality" in music has not been investigated to date. With faces, it has been shown that neutral expressions are recognized in a similar way to other facial expressions. It was noteworthy that faces displaying small amounts of emotion were categorized as neutral. These findings indicate that there is a sharp boundary beyond which emotional expressions become too weak to have emotional signal value and are therefore perceived as neutral (Ekman, 1994; Etcoff & Magee, 1992; Young, Rowland, Calder, Etcoff, Seth, & Perrett, 1997). However, we still know very little about the neural bases underlying the processing of emotionally neutral stimuli.

As recognizing emotion is necessary for human beings, it might also be important to detect a lack of emotional salience. Since the ability to emotionally react is interpreted in terms of adaptation (Lang, Bradley, & Cuthbert, 1998), an excessive emotional reaction to a stimulus might appear inappropriate. The subjective interpretation of a stimulus as emotionally relevant or not appears to be essential for adequate social interactions. Several lines of evidence suggest that this ability can be altered by psychiatric pathology such as depression (Gur, Erwin, Gur, Zwil, Heimberg, & Kraemer, 1992; Leppänen, Milders, Bell, Terriere, & Hietanen, 2004), anxiety (Winton, Clark, & Edelmann, 1995), social phobias (Birbaumer et al., 1998), or schizophrenia (Heimberg, Gur, Erwin, Shtasel, & Gur, 1992). Several brain imaging studies have used neutral stimuli as a baseline condition particularly in the visual domain, but few of them specifically focused on the ability to recognize neutral expressions as belonging to a specific category. Although this lack of interest for neutral stimuli may represent an experimental bias in the literature, a number of fMRI studies have demonstrated a specific pattern of cerebral activation involving the amygdala during the processing of neutral faces in healthy volunteers and psychiatric patients (Breiter et al., 1996; Cooney, Atlas, Joormann, Eugene, & Gotlib, 2006; Kesler-West et al., 2001; Pessoa, Mckenna, Gutierrez, & Ungerleider, 2002; Somerville, Kim, Johnstone, Alexander, & Whalen, 2004; Thomas et al., 2001). These findings suggest that this structure is involved in the processing of both emotional and neutral stimuli, leading Cooney and his colleagues (2006) to question the use of neutral stimuli as a baseline condition to study emotion. According to these authors, neutral stimuli require the processing of ambiguous social information that deserves further examination.

In the musical domain, no previous studies have examined the processing of neutral stimuli. It might appear counterintuitive to study emotional processing of stimuli that are supposed to be nonemotional. It is even more paradoxical to use musical stimuli to examine neutral judgments, given that music is considered to be the language of emotion. Thus, one needs to define the term "neutral" to shed some light on the relevance of studying emotional processing of neutral stimuli in music. For this purpose, the terms "neutral" and "nonemotional" must be distinguished. Music, like facial expressions, is never nonemotional *per se*. However, it can be judged "neutral" when insufficient cues are available to promote a specific emotion. Thus, "neutral" does not mean "nothing," but "a few." In other words, the simultaneous presence of "a few" different emotional cues within a neutral stimulus makes it ambivalent. "Neutral" appears to belong to an ambiguous boundary at the junction of emotions, but it cannot be reduced to the absolute absence of emotion.

We propose that music, with its intrinsic emotional component, will be an adequate candidate to study the ability to form a "neutral" judgment. To better understand the role of the temporal lobe structures in emotional processing, we used neutral musical stimuli as an emotional category. We compared explicit classification of neutral with happy, sad, and distressing music in patients with temporal lobe lesions and normal volunteers. In particular, we explored the role of the amygdala by comparing patients with temporal lobe epilepsy with or without involvement of medial temporal lobe regions, including the amygdala. Given that previous neuroimaging studies have demonstrated that the processing of neutral faces involved the amygdala, we predicted that patients with medial temporal lobe lesions including the amygdala will be more impaired in processing neutral than emotional (distressing, happy, and sad) stimuli than patients with damage limited to the lateral temporal cortex and normal control participants. In addition, we also predicted that patients with medial temporal lobe lesions involving the amygdala would be particularly impaired in labeling distressing musical excerpts compared with the other emotions.

Method

Participants

Forty-four patients with temporal lobe epilepsy took part in this study. All patients had pharmacological intractable epilepsy and were seen during pre ($n = 26$) or postsurgical ($n = 17$) evaluation at La Salpêtrière Hospital (Paris). Patients tested during the presurgical evaluation were divided into three groups. Two groups presented with unilateral temporal lobe epilepsy with ($n = 16$) or without ($n = 6$) hippocampal sclerosis. The third group was composed of patients with bilateral temporal lobe epilepsy ($n = 4$) demonstrated by bilateral electroencephalographic abnormalities. This latter group of patients, as well as those with unilateral hippocampal sclerosis, clearly showed medial temporal lobe abnormalities. The presence or the absence of hippocampal sclerosis was determined by a neuroradiologist from MRI scans. Patients tested during the postsurgical evaluation had undergone a unilateral antero-medial temporal lobe resection for the relief of medically uncontrolled seizures. All of these patients underwent an antero-medial temporal lobe resection, including the whole amygdala as well as various amounts of the hippocampus and surrounding cortices (entorhinal, perirhinal and parahippocampal cortex) (see Figure 1 in color plate section). With the exception of one right temporal lobe patient, the excision also included the temporal pole. However, the removal never encroached into the superior temporal gyrus. Patients tested before surgery presented with pharmacologically uncontrolled seizures and were all enrolled in the program of epilepsy surgery, whereas patients tested after surgery were all seizure free at the time of testing. They all gave written informed consent before testing in accordance with the Declaration of Helsinki.

None of the patients showed extra-temporal lesions, or apparent neurological deficits, such as aphasia or hemiplegia. In all the patients, full scale IQ was greater than 70 and language was lateralized to the left hemisphere as determined by clinical data or the intracarotid amobarbital procedure (Wada & Rasmussen, 1960). A group of right-handed normal volunteers ($n = 19$) with no neurological or psychiatric problems were selected

TABLE 1. Demographic Information for Patients with Temporal Lobe Lesions and Normal Controls.

Group	Sex Male/Female	Mean Age in Years (range)	Mean Education in Years (range)	Full Scale IQ WAIS-R
Normal Controls	7/12	32 (19-53)	13 (9-16)	
Presurgical cases				
No Hippocampal Sclerosis (Left: 3 ; Right: 3)	5/1	31 (19-40)	14 (11-17)	100 (81-109)
Unil Hippocampal Sclerosis (Left: 9 ; Right: 7)	6/10	37 (16-51)	11 (7-14)	89 (75-110)
Bilateral Temporal Lobe Epilepsy	3/1	41 (30-49)	12 (12-14)	87 (72-101)
Postsurgical cases				
Unil Temporal Lobe Resection (Left: 9; Right: 8)	10/7	36 (20-50)	13 (11-18)	95 (80-114)

to match the patients as closely as possible in terms of age, sex and education. All participants had either limited or no formal musical experience. The characteristics of the participants are summarized in Table 1. Preliminary analyses showed no significant difference between the groups in terms of age, $F(4, 57) = 0.76$, $p > .05$, or level of education, $F(4, 57) = 2.26$, $p > .05$. There was also no difference between patient groups in full scale IQ, $F(3, 39) = 2.72$, $p > .05$.

Stimuli

Twenty-eight musical excerpts were composed for this study by Eric Jahyer with the intention of inducing distressing, happy, sad, or neutral emotion. The Boss DR-5: Dr Rhythm composition program was used. There were 7 polyphonic excerpts for each intended emotion. The musical excerpts were conventional in that they followed the rules of the Western tonal system using different musical styles proposed by the program (rock, bluegrass, swing pop). The average duration of the excerpts was 23.3 s ($SD = 6.4$ s). The happy excerpts were played at an average tempo (metronome marking) of 124 (range = 107-149), the sad excepts at an average tempo of 114 (range = 89-152), the distressing excerpts at an average tempo of 106 (range = 89-120) and the neutral excerpts at an average tempo of 112 (range = 100-120). An example of stimuli for each emotion category can be heard on our web site at http://nca.recherche.univ-lille3.fr/index.php?page=auditory-examples. Two other excerpts served as examples. Pilot studies were carried out in 40 normal volunteers to select 28 stimuli that were correctly classified by at least 70% of the participants, confirming that all the musical excerpts induced the intended emotion. The selected MIDI files were digitally recorded onto compact disks and presented to the participants over two loudspeakers.

Procedure

Participants were presented with the two examples followed by the 28 stimuli presented in random order. They were instructed to choose one of four labels (distressing, happy, sad, and neutral) that they felt best corresponded to each musical excerpt using a forced choice classification paradigm. Recognition accuracy was measured by the overall percentage of correctly categorized stimuli.

Results

Preliminary analyses were carried out to test the effect of lateralization of temporal lobe dysfunction on the mean correct classification of emotional and neutral stimuli obtained in pre and postoperative cases. Since we found no effect of laterality and no interaction with emotion, we systematically pooled patients with right or left sided temporal lobe damage in the following analysis. We also verified that sex had no effect or interaction with any variables of interest, and therefore grouped males and females together.

Classification of Emotional and Neutral Music

The main result of this study is shown in Figure 2, which displays the overall percentage of correctly categorized emotional vs. neutral stimuli (where emotional refers to sad, happy, and distressing music) for each

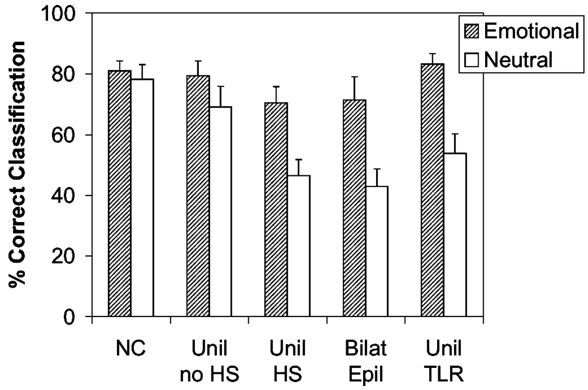

FIGURE 2. Mean percentage of correct classification of emotional and neutral musical excerpts as a function of group (Unil HS = unilateral temporal lobe epilepsy with hippocampal sclerosis; Unil No HS = unilateral temporal lobe epilepsy with no hippocampal sclerosis; Bilat Epil = bilateral temporal lobe epilepsy; Unil TLR = unilateral temporal lobe resection; NC = normal controls). Bars correspond to the standard error of the mean.

group of participants. Inspection of the data suggests that patients with unilateral hippocampal sclerosis, unilateral temporal lobe removal, or bilateral temporal lobe epilepsy were impaired in recognizing neutral but not emotional stimuli as compared to normal control participants and to patients with no hippocampal sclerosis. This was supported by statistical analyses. A two-way analysis of variance with one repeated measure (emotional vs neutral) was carried out on the mean percentage of correctly categorized emotions by the five groups of participants. The results showed a significant Group × Emotion interaction, $F(4, 57) = 5.09$, $p = .001$. Posthoc tests by Newman Keuls comparisons demonstrated that neutral stimuli were less accurately classified than emotional ones by all patient groups ($p < .005$) except patients without hippocampal sclerosis whose performance was in keeping with normal control participants. This latter group correctly recognized 81% of emotional and 78% of neutral stimuli.

Given the small number of patients, especially in two patient groups (patients without hippocampal sclerosis and patients with bilateral epilepsy), we carried out nonparametric analyses of the data to verify the validity of the parametric tests. A Kruskal-Wallis analysis of ranks was performed on the percentage of correctly classified emotional and neutral stimuli. This yielded no significant differences for the emotional condition, $H = 6.03$, $p = .20$, but a highly significant group difference for the neutral condition, $H = 20.18$, $p < .001$. Pairwise comparisons between groups carried out via Mann-Whitney test showed that all patient groups, except those without hippocampal sclerosis, performed significantly less accurately in the neutral condition than normal control participants. Within group comparisons were also carried out via Wilcoxon tests. Although no significant differences between emotional and neutral conditions were found for the normal control participants, $Z = 0.43$, $p = .67$, and patients without hippocampal sclerosis, $Z = 1.62$, $p = .11$, we obtained significant differences between the two conditions for patients with unilateral hippocampal sclerosis, $Z = 3.30$, $p < .001$, bilateral temporal lobe epilepsy, $Z = 1.83$, $p = .06$, and unilateral temporal lobe resection, $Z = 3.26$, $p = .001$, confirming results previously reported with parametric analysis.

Error Analysis of Neutral Stimuli

In order to better characterize the deficit displayed by the patients in classifying neutral stimuli, their erroneous responses were further examined. A two-way analysis of variance with one repeated measure (Error: distressing, sad, and happy) was carried out on the proportion of false classification of neutral stimuli by the five groups of participants (Figure 3). The results demonstrated an effect of Error, $F(2, 114) = 36.47$, $p < .001$]. All the participants tended to choose 'happy' significantly more frequently than 'sad' or 'distressing' labels (*ps* < .001), suggesting that they had a positive bias when exposed to ambiguous neutral music. However, there was no effect of Group, $F(4, 57) = 1.13$, $p = .35$, or a Group × Error interaction, $F(8, 114) < 1$, $p = .50$. Nonparametric analyses using the Kruskal-Wallis test were performed on the percentage of distressing, happy, and sad responses given to neutral stimuli by the different groups of participants. These analyses yielded

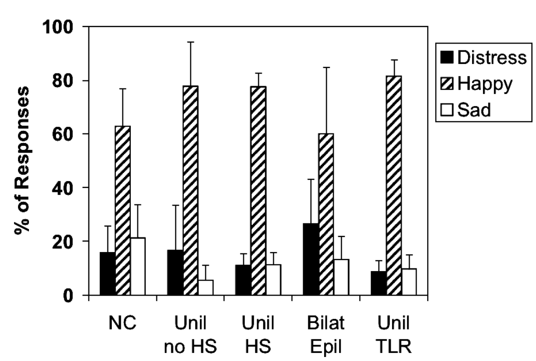

FIGURE 3. Mean percentage of distressing, happy, and sad labels given in response to neutral stimuli as a function of group (Unil HS = unilateral temporal lobe epilepsy with hippocampal sclerosis; Unil No HS = unilateral temporal lobe epilepsy with no hippocampal sclerosis; Bilat Epil = bilateral temporal lobe epilepsy; Unil TLR = unilateral temporal lobe resection, NC = normal controls. Bars correspond to the standard error of the mean.

no significant differences between groups for distressing, $H = 1.64$, $p = .80$, happy, $H = 2.69$, $p = .61$, and sad responses, $H = 1.20$, $p = .88$.

Given that we previously demonstrated that emotional responses to unpleasant music correlate with damage to the parahippocampal cortex (Gosselin et al., 2006), we tested the existence of a subjective bias towards positive affect in patients who had undergone a substantial resection of the parahippocampal cortex as compared to patients who had undergone a nonsignificant resection of this region and normal control participants. Volumetric cerebral measurements led to the identification of 7 patients (3 right and 4 left temporal lobe lesion) in our postoperative patient group with a significant resection of the parahippocampal cortex (for details of the methodology, see Noulhiane, Samson, Clémenceau, Dormont, Baulac, & Hasboun, 2006); that is, with a remaining volume being two standard deviations below the mean of normal controls. The other 7 patients (3 right and 4 left temporal lobe lesion) had relatively preserved parahippocampal cortex. The nonparametric analysis of the percentage of distressing, happy, and sad responses given to neutral stimuli showed no significant differences between groups for distressing, $H = 3.18$, $p = .20$, happy, $H = 2.19$, $p = .34$, and sad responses, $H = .73$, $p = .69$. These findings suggest that significant resection of the parahippocampal cortex did not induce a subjective bias towards positive affect in the present study.

Performance of Emotional Stimuli

To determine whether the different patient groups differed from normal control participants in recognizing the three emotions (distressing, sad, and happy), a two-way analysis of variance with one repeated measure (Emotions) was carried out on the mean percentage of correct classifications obtained by the five groups of participants. There was no significant effect of Emotion, $F(2, 114) < 1$, $p = .40$, or of Group, $F(4, 57) = 2.00$, $p = .10$, as well as no Emotion × Group interaction, $F(8, 114) = 1.62$, $p = .13$. The data are displayed in Table 2. Nonparametric analyses (Kruskal-Wallis analysis of ranks) revealed slightly different results. As previously reported, the results showed no significant group difference for distressing, $H = 5.43$, $p = .25$, and happy, $H = 2.93$, $p = .57$, music, but a significant group difference was obtained for sad music, $H = 11.10$, $p < .05$. Pairwise comparisons between groups carried out via Mann Whitney U tests showed that patients with unilateral hippocampal sclerosis performed worse than normal control participants, $U = 89.5$, $p < .05$, and patients with no hippocampal sclerosis, $U = 13.0$, $p < .01$. Moreover, patients with bilateral epilepsy performed worse than patients with no hippocampal sclerosis, $U = 2.0$, $p < .05$.

TABLE 2. Mean Percentage of Correct Responses as a Function of the Three Intended Emotions.

	Mean Percent Correct		
Group	Distress	Happiness	Sadness
Normal Controls ($n = 19$)	83.5 (4.0)	80.5 (4.6)	78.9 (3.7)
No Hippocampal Sclerosis ($n = 6$)	85.7 (7.4)	76.2 (4.8)	90.5 (4.8)
Unilateral Hippocampal Sclerosis ($n = 16$)	74.1 (6.8)	77.5 (5.0)	59.5 (7.1)
Bilateral Temporal Lobe Epilepsy ($n = 4$)	67.9 (12.2)	75.0 (10.7)	71.4 (0.0)
Unilateral Temporal Lobe Resection ($n = 17$)	87.4 (5.2)	84.9 (3.7)	77.3 (6.5)

Note: Standard errors of the mean are shown in parentheses.

Discussion

This is the first study to date to demonstrate that patients with medial temporal lobe dysfunction have difficulty processing neutral emotion in music. In particular, we found that identification of neutral stimuli was selectively impaired in patients with medial temporal lobe lesions as indicated by the presence of hippocampal sclerosis or the removal of unilateral temporal lobe structures. In contrast, patients without hippocampal sclerosis had no difficulty in identifying neutral stimuli and their performance was in keeping with that of normal controls. This finding suggests that recognition of music composed with the intention to be emotionally neutral can be disrupted by unilateral or bilateral medial temporal lobe damage. In other words, patients with temporal lobe lesions that involve medial structures are not able to accurately perceive emotionally neutral stimuli.

Before we discuss the results in further detail, we should first point out that the impaired recognition of neutral stimuli does not appear to be explained by task difficulty. Indeed, healthy participants classified neutral music as accurately as happy, sad, or distressing music, suggesting that neutral stimuli are not more difficult to recognize than emotional stimuli. Moreover, most patients correctly categorized happy, sad, or distressing music. This is important as it implies that the disproportionate impairment in the recognition of neutral stimuli cannot be explained by a general degradation in performance.

Our findings did not support our prediction that patients with medial temporal lobe lesions would be impaired in labeling distressing music. This is surprising given previous findings of impaired recognition of scary music in patients with either right and/or left temporal lobe lesions (Gosselin et al., 2005, 2007). Since 7 out of the 17 postoperative patients of the present study also participated in Gosselin et al.'s study (2005), we compared the results of these patients in the two tasks. Except for one patient who was impaired in both studies, most of the patients who poorly recognized scary music in Gosselin et al.'s study succeeded in the present one. We therefore believe that the discrepancy between the results of these two studies can be explained by methodological differences. In the present study, we used a forced choice recognition paradigm that allowed the participant to select only one single emotion among four alternatives. In Gosselin et al.'s study, the participants were free to choose as many labels as they wished and were able to provide graded judgments for each. It appears that this methodology provides a more sensitive measure in that it enables detailed quantification of emotional judgments and ambivalent responses that is not possible with a forced choice recognition paradigm. Nevertheless, the data obtained with happy music are in agreement with previous findings obtained with temporal lobe patients. This result suggests that processing positive emotional valence (i.e., happiness) does not depend on the integrity of medial temporal lobe function. Finally, a deficit in classifying sad music was only documented in patients with hippocampal sclerosis who were tested during presurgical evaluation. In addition to their medial temporal lobe dysfunction, these patients, as opposed to postoperative cases who were seizure free, had medically intractable seizures associated with very active epileptic networks. This epileptic activity frequently extends to cerebral regions that are highly connected to the temporal lobe such as the frontal and the contralateral temporal lobe areas. Since difficulties in classifying sad music have only been reported in a patient with bilateral amygdala lesions (case SM, Gosselin et al., 2007), it seems possible that the deficit in labeling sad music can be associated with the presence of a bilateral medial temporal lobe dysfunction in patients with uncontrolled epileptic seizures.

Error analysis showed that patients who experienced difficulties in recognizing neutral stimuli tended to label neutral stimuli as happy. This subjective bias that shows a tendency towards positive emotions was not specific to patients since all participants, including normal controls, displayed this pattern of response. A tendency in favor of a positive bias has already been noted in patients with medial temporal lobe removal including part of the parahippocampal cortex. These patients judged musical dissonance as pleasant while most individuals considered it unpleasant (Gosselin et al., 2006). Inspection of our postoperative data demonstrated that the removal of the parahippocampal cortex did not affect the distribution of errors given to neutral stimuli. It seems therefore problematic to propose a similar interpretation for the present results. Moreover, the emotional rating based on pleasantness judgments is very different from the categorization task used in the present study. Therefore, it is difficult to conclude that the subjective bias towards positive affect reported in these studies reflects a common mechanism.

In the visual domain, an alternative interpretation of the deficit in identifying neutral faces has been suggested. Some authors have proposed that the inherent uncertainty of neutral emotional stimuli requires the processing of contextual information that were not necessarily useful to recognize primary emotions (Russell & Fehr, 1987; Somerville et al., 2004). Thus, primary facial expressions such as happy or surprise might served as "anchors" for neutral faces, the latter being rated more negatively when presented with positive than with negative expressions. Therefore, we can suggest that assessing neutrality requires the ability to use the appropriate contextual information, which might have been impaired in our patients given the role of the hippocampus to process contextual information (see Chun & Phelps, 1999).

The most likely neural locus underlying the false attribution of emotional meaning to neutral stimuli reported in the present study seems to be the amygdala. This structure was damaged in all patients who showed impaired performance in classifying neutral stimuli. This hypothesis has found further support in neuroimaging studies showing that processing of neutral faces is associated to amygdala activation (Breiter et al., 1996 ; Cooney et al., 2006; Kesler-West et al., 2001; Pessoa et al., 2002; Somerville et al., 2004; Thomas et al., 2001). Using fMRI, Cooney et al. demonstrated that the misassignment of affective meaning to neutral stimuli obtained in patients with anxiety disorder was related to an abnormal activation of the amygdala. In keeping with the notion that processing of neutral stimuli requires the integrity of the amygdala, Leppänen et al. (2004) reported that depressed patients, in whom elevated tonic levels of activity in the amygdala have been noted, did not perceive completely expressionless faces as neutral. Instead, the faces may elicit emotion-related responses confirming early findings (Gur et al., 1992). Although these studies concerned patients with different pathologies, they all provide evidence that excessive meaning or abnormal responses to emotionally neutral stimuli is associated with amygdala dysfunction. Another hypothesis proposed by Somerville et al. is that amygdala responses to neutral faces are correlated with anxiety state. As personality states were not systematically measured in previous studies, this interpretation requires further investigation.

Unlike studies in psychiatric patients, processing of neutral stimuli has rarely been investigated in patients with brain lesions. In our own clinical practice, one of us (N.E) tested such a patient with the present paradigm. TG is a typical nonmusician with good intellectual, memory, and perceptual abilities. He showed a selective impairment of emotional processing after a severe left-sided head injury that damaged the periamygdala region, the anterior temporal pole, the post insula, as well as the orbitofrontal cortex. His disturbed affective processing has been well documented in the visual and olfactory domains (see Soussignan, Ehrle, Henry, Schaal, & Bakchine, 2005, for a detailed account of his neuroanatomical, neurophysiological, and neuropsychological profile). However, this patient also exhibited significant difficulties in classifying emotions of musical excerpts. He was completely unable to classify neutral stimuli (0% correct classification), but surprisingly, his classification of the other emotional stimuli was errorless. Interestingly, he reported that he experienced no emotion at all during musical listening. He explained that he was able to classify the excerpts according to cultural associations, assigning happiness, distress, and sadness to excerpts that sound like cartoon credits, thrillers, and romantic serials, respectively. It seems that music acquired a power of representation through associative processes that remain unaffected in this patient. The relative sparing of the representation of emotion in this patient contrasted with an impaired experience of emotion that was documented using neutral stimuli. Error analysis showed that this patient tended to choose happy as frequently as sad labels in responses to neutral music, demonstrating no specific subjective bias. Since his cerebral lesion was not limited to the amygdala, his emotional deficit cannot be solely attributed to dysfunction of this structure. This case illustrates that neutral stimuli can be used to further characterize affective disorders in neurological patients.

To summarize, the results of our investigation suggest that medial temporal lobe structures are involved in processing neutral stimuli. In support of previous neuroimaging and electrophysiological studies, this ability seems to be mediated by the amygdala. Although this study does not provide definite evidence for this association, it does demonstrate the relevance of using music to assess subjective emotional responses in brain damaged patients. Music is an attractive and universal medium that can be easily manipulated. We have shown that music is also an appropriate candidate to study the ability to detect neutrality. This specific category can be conceptualized as ambiguous. The adequate labeling of neutral musical stimuli involves emotional judgment associated to reduced part of affect. Difficulties in processing basic emotions as well as inappropriate emotional reaction to neutral stimuli, as demonstrated here, might reflect misinterpretation of emotional cues. However, the types of musical cues that convey neutrality to the listener remain to be clarified to establish the threshold below which a slightly emotional stimuli is considered neutral. Assessment of such difficulties is required to better understand affective disturbances. The ability to detect the lack of emotional salience assessed with music emphasizes the relevance of including neutral stimuli to explore social and emotional disorders in neuropsychology.

Author Note

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