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Risk of depression enhances auditory Pitch discrimination in the brain as indexed by the mismatch negativity

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HIGHLIGHTS

- Mismatch negativity amplitudes (MMNs) to slide and pitch deviants are enhanced in individuals with risk of depression.
- MMN to pitch is larger for deviants in a musical major mode context than minor one.
- The relation between MMNs to pitch deviants and depression level is influenced by musicianship.

ABSTRACT

Objective: Depression is a state of aversion to activity and low mood that affects behaviour, thoughts, feelings and sense of well-being. Moreover, the individual depression trait is associated with altered auditory cortex activation and appraisal of the affective content of sounds.
Methods: Mismatch negativity responses (MMNs) to acoustic feature changes (pitch, timbre, location, intensity, slide and rhythm) inserted in a musical sequence played in major or minor mode were recorded using magnetoencephalography (MEG) in 88 subclinical participants with depression risk.
Results: We found correlations between MMNs to slide and pitch and the level of depression risk reported by participants, indicating that higher MMNs correspond to higher risk of depression. Furthermore we found significantly higher MMN amplitudes to mistuned pitches within a major context compared to MMNs to pitch changes in a minor context.
Conclusions: The brains of individuals with depression risk are more responsive to mistuned and fast pitch stimulus changes, even at a pre-attentive level.
Significance: Considering the altered appraisal of affective contents of sounds in depression and the relevance of spectral pitch features for those contents in music and speech, we propose that individuals with subclinical depression risk are more tuned to tracking sudden pitch changes.

1. Introduction

Depression is a state of aversion to activity and low mood that affects behaviour, thoughts, feelings and individual sense of well-being (Schnaas, 2003). A depressed mood is characterized by anxiety, sadness, anger and empty, hopeless, guilty, restless feelings (Rottenberg, 2005). If depressed mood occurs frequently, becoming a stable pathological state, it can lead to major depressive disorder (MDD). Moreover, differently from a non pathological sad state, depressed mood is characterized by the intensity and pervasiveness of the pain during patients activities, causing social and emotional limitations in their lives (Gotlib and Hammen, 2009).

Perception in several sensory domains is affected by a sad, depressed mood, according to the phenomenon that has been called ‘congruency bias’, a cognitive bias that arise when individuals accept the most immediate answer, frequently congruent to their states, without testing other hypotheses. (Byron, 1990). For instance, individuals affected by major depression tend to respond to visual and auditory unpleasant stimuli, such as faces, voices and musical excerpts, in a stronger way in comparison to the healthy ones (Gollan et al., 2008). Human speech and music are built on

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some similar features such as pitch, time and silence (Juslin and Sloboda, 2013). These characteristics vary according to the individual mood and can represent significant cues to depression (France and Shiavi, 2000). For instance, depressed individuals show a speech characterised by monotony, constant speech with few changes of pitch (Darby and Hollien, 1977; Hollien, 1980) and silent pauses (Pope et al., 1970).

In the auditory domain, the impact of depression has been suggested by several studies. Michael et al. (2004), in an fMRI study, reported a significantly lower activation of the auditory cortex in people affected by major depressive disorder (MDD) in comparison to healthy ones. Also Tollkötter et al. (2006) argued that major depression disorder may imply an impaired auditory processing. Specifically they found out that depressed patients did not show a clear N1 m component in response to vowels and sine tones. Moreover, Christ et al. (2008) stated that major depression was associated with cortical dysfunctions such as impaired auditory processing of non-speech stimuli. They revealed that during stimulation by sine tones, patients affected by depression exhibited a multimodal recruitment of brain areas to sound processing and as such, the medial frontal cortex and areas of the secondary visual system (e.g. lingualis, cuneus) were involved. In addition to these findings it is remarkably acknowledged that serious major depressed patients exhibit deficits and difficulties in interpersonal communication, that is based also on both sounds production and perception (Chandrasekaran et al., 2014).

In an fMRI study Osuch et al. (2009) explored basic brain processes occurring when listening to enjoyable music in both depressed and healthy participants. Results showed that listening to the favorite music caused larger activation in control participants than in depressed patients in nucleus accumbens, ventral striatum and medial orbital frontal cortex, entailing an alteration in the brain of depressed patients when listening to their favorite and pleasant music. Depressed patients reported less interest in rewards from their favorite music in comparison to healthy controls.

Automatic discrimination of auditory stimuli of patients affected by depression disorders has also been investigated, reporting varied results. A reliable index of automatic auditory discrimination is the mismatch negativity (MMN) of an event-related potential (ERP), measured with electroencephalography (EEG) or magnetoencephalography (MEG) (Näätänen et al., 1978). The MMN is typically elicited with the oddball paradigm, as a response to an infrequent stimulus deviating from a sequence of coherent, repetitive stimuli in one or more physical features such as location, pitch, rhythm, intensity, timbre of sound source or in abstract features such as simple auditory rules (Näätänen, 1992; Näätänen et al., 2011). Furthermore MMN is affected in depression; Lepistö et al. (2004), for example, reported shorter MMNs latencies generated by deviant syllables in depressed children compared to the control group, without finding any amplitude differences. Higher MMNs amplitudes were observed in depressed patients in response to sound frequency deviants (Kahkonen et al., 2007).

Other research, in contrast, showed lower MMN responses in people affected by depression disorders. For example, Naismith et al. (2012) discovered reduced MMN amplitudes in depressed people compared to healthy ones when induced through an auditory two-tone passive oddball paradigm. In another ERP study related to the emotional prosody, Pang et al. (2014) assessed the emotional voice processing in major depressed patients presenting prosodies that involved meaningless syllables such as "dada" pronounced with angry, happy, sad, or neutral tones. They discovered that sad MMNs were not present in major depressed patients, whereas the angry and happy MMN components resulted similar when compared to the healthy group.

However, in all those studies the experimental sessions were very long potentially causing fatigue and also habituation, which by themselves might explain the discrepant findings.

Thus, a fast paradigm, called multi-feature (also known as "Optimal" paradigm), for obtaining MMN responses comparable to those obtained in the classical oddball paradigm, was introduced by Näätänen et al. (2004). It consists of various kinds of acoustic changes that are presented within the same sequence of sounds and that are alternating regularly with the repetitive and rarely occurred standard sound, while in the oddball paradigms deviants are presented more rarely (typically for a maximum of 20%). In order to obtain acoustic stimuli related to a more realistic musical context, Vuust et al. (2011) created the musical multi-feature paradigm, inserting six different feature changes in a four-tone pattern called the Alberti Bass, an a commonly used accompaniment in the Western music. This enables several MMN components related to various auditory attributes to be independently induced yielding the experimental duration to be less than 20 min (Vuust et al., 2012). Recently, Mu et al. (2016), using the musical multi-feature paradigm, found enhanced MMN amplitudes to the timbre deviant in patients affected by major depressive disorder as compared to a healthy control group. Even if the study utilized a relatively small subject sample, it suggests that MMNs can index music-related dysfunctions in depressed patients. It remains to be studied whether a risk of depression in individuals that are otherwise healthy can alone affect automatic discrimination of musical features, consequently altering neural mechanisms for perception of music and expressive sounds in general. Previous literature conceptualized the risk of depression as an enhanced probability to develop depressive disorders, presenting some correlated neural abnormalities (Carlson et al., 2015; Joormann et al., 2012; Troy et al., 2010).

In the present study, we wanted to investigate whether a subclinical risk of depression in individuals that are otherwise healthy affects the automatic discrimination of changes in the basic features of musical sounds within a musical context. In order to assess the participants' risk of depression we used the Montgomery–Åsberg Depression Rating Scale (MADRS) and the Depression subscale of the Hospital Anxiety and Depression Scale (HADS-D), two questionnaires developed to assess the severity of depressive episodes in patients as well as to discriminate depressed participants from individuals with absence of symptoms or risk of depression (Gabryelewicz et al., 2004; Leentjens et al., 2000; Montgomery and Asberg, 1979; Whelan-Goodinson et al., 2009). These scales are short and easy to administer. They are diagnostic tools, that are used by nurses and doctors in hospitals in order to reveal any signs of depression in adult individuals. Hence, MADRS and HADS-D allow for studying subclinical populations characterized by a high level of depression risk. To investigate discrimination of auditory stimuli relevant to emotional expression in individuals with subclinical risk of depression we used the musical multi-feature paradigm capitalizing from its inclusion of 4-tone patterns, half of which are in the major mode, the other half in the minor mode. Major and minor are well-known cues for emotional expression and the best predictor for valence assessment in melodies (Costa et al., 2004). Music in major is perceived as happy and bright, whereas musical excerpts within the minor scale are perceived as more sad, subdued, dark, wistful, and contemplative (Bonetti and Costa, 2017; Bonetti and Costa, 2016; Bowling et al., 2010; Cooke, 1959; Costa et al., 2000; Costa, 2012; Lahdelma and Eerola, 2016; Parncutt, 2014). We expected larger MMN amplitudes to deviants of musical multi-feature paradigm in participants with higher pronounced risk of depression. Furthermore, we predicted the emotional context provided by the major and minor stimuli to modulate the MMN amplitude differently.