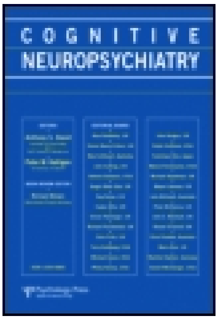

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Amelioration of psychiatric symptoms through exposure to music individually adapted to brain rhythm disorders - a randomised clinical trial on the basis of fundamental research

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Amelioration of psychiatric symptoms through exposure to music individually adapted to brain rhythm disorders – a randomised clinical trial on the basis of fundamental research

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Introduction. This pilot study examined, whether long-term exposure of psychiatric patients to music that was individually adapted to brain rhythm disorders associated with psychoticism could act to ameliorate psychiatric symptoms.
Methods. A total of 50 patients with various psychiatric diagnoses were randomised in a 1:1 ratio to listen to CDs containing either music adapted to brain rhythm anomalies associated with psychoticism – measured via a specific spectral analysis – or standard classical music. Participants were instructed to listen to the CDs over the next 18 months. Psychiatric symptoms in both groups were assessed at baseline and at 4, 8 and 18 months, using the Brief Symptom Inventory (BSI).
Results. At 18 months, patients in the experimental group showed significantly decreased BSI scores compared to control patients. Intriguingly, this effect was not only seen for symptoms of psychoticism and paranoia but also for anxiety, phobic anxiety and somatisation.
Conclusions. Exposure to the adapted music was effective in ameliorating psychotic, anxiety and phobic anxiety symptoms. Based on the theories of neuroplasticity and brain rhythms, it can be hypothesised that this intervention may be enhancing brain–rhythm synchronisation and plasticity in prefrontal–hippocampal circuits that are implicated in both psychosis/paranoia and anxiety/phobic anxiety.

Keywords: adapted music; psychosis; anxiety; brain rhythms; neuroplasticity

In the search to find effective therapies with minimal side effects to treat psychiatric disorders such as psychotic, anxiety, personality and mood disorders, the collaboration of clinical psychiatry with theoretical research fields is crucially important. It is widely accepted that such disorders involve disturbances in neurotransmitter metabolism and plasticity (Bagorda, Teuchert-Noodt, & Lehmann, 2006; Dawirs & Teuchert-Noodt, 2001; Diaz, Chappell, Christian, Anderson, & McCool, 2011; Eisch & Petrik, 2012; Inta, Lima-Ojeda, Gass, & Fusar-Poli, 2012; Revest et al., 2009) as well as in brain–rhythm synchronisation (Begic et al., 2011; Pape, Narayanan, Smid, Stork, & Seidenbecher, 2005; reviewed in Uhlhaas, Haenschel, Nikolic, & Snger, 2008). Nevertheless, effective therapies with as few side effects as possible are still required.

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New impetus has come from the field of brain rhythm and neuronal oscillation research. Since desynchronised networks are known to underlie psychiatric disorders, one area to explore is whether the use of extrinsically applied rhythms might act to influence brain oscillations. Deep transcranial brain stimulation is a promising therapeutic strategy, but there is controversy over the magnitude and durability of its effects (Bersani et al., 2012; reviewed in George et al., 2009).

Interventions using music have long existed, but they mainly involve the relationship between therapist and client (Bruscia, 1998) and are mostly viewed as a supplemental psychotherapeutic strategy (Fachner, Gold, & Erkkila, 2012; Grocke, Bloch, & Castle, 2009; Mossler, Chen, Heldal, & Gold, 2011; Silverman, 2003). Little attention has been given to the application of music as an actual physiological treatment. Some studies have reported that listening to music can reduce depression (reviewed in Chan, Wong, & Thayala, 2011) as well as anxiety and pain during surgery or cancer treatment (Gooding, Swezey, & Zwischenberger, 2012; Guetin et al., 2012). However, there has been little research into the effect of music on psychiatric symptoms like psychosis and paranoia.

Recent empirical data have suggested that an intervention for children in which rhythmically adapted music individually delivered through earphones may be effective in improving learning disorders, attention-deficit disorder, and probably also in ameliorating psychiatric symptoms (Haffelder, 2013). From a neurobiological point of view, it is conceivable that this effect might be based on the induction of neuroplastic reorganisational processes through the modulation of rhythmic brain activities. Nevertheless, to date, this concept lacks scientific evidence. This pilot study is the first to examine whether long-term exposure to music that is rhythmically adapted to brain rhythm disorders associated with psychoticism can affect psychotic and paranoid symptoms.

Methods

Trial design

A randomised controlled clinical trial with a pre- and post-test design and a two-time measurement in between time period was conducted.

Participants

Participants were recruited from three institutions in Herford and Bünde, Germany: the Psychiatric Institution at Herford Hospital, a teaching hospital attached to Hannover University, the "Klinke", a non-profit organisation for psychosocial activities and the Centre of Social Psychiatry Bünde. A total of 50 patients were enrolled, 32 (64%) women and 18 (36%) men with mean age of 48.3 years (range: 20–80 years). Patients suffered from a variety of psychiatric conditions, including psychotic, anxiety, personality and mood disorders (cf. Table 1). All failed to achieve satisfactory amelioration of their symptoms through classical psychotherapy or pharmacological interventions, and for many the illness was severe enough that they were receiving a disability pension. Diagnoses were made by experienced clinical psychiatrists according to the criteria of the International Classification of Diseases (ICD)-10 (World Health Organization, 2004).

As this was a pilot study, there were no restrictions regarding diagnosis and medication status, and all patients continued to receive treatment as usual when participating in the study, including receipt of medication. The only exclusion criterion was a score in the Brief Symptom Inventory (BSI) of less than 63, which is the threshold of clinical concern.

Table 1. Characteristics of 50 patients randomised to experimental (EG) or control group (CG).

Characteristic	EG (*n* = 25)	CG (*n* = 25)
Age[a]: years, mean (SD)	50.2 (12.3)	46.3 (10.9)
Female, *n* (%)	17 (68)	15 (60)
Unemployed, *n* (%)	18 (72)	18 (72)
On disability pension, *n* (%)	17 (68)	11 (44)
Diagnoses, *n* (%)		
Major depression	7 (28)	10 (40)
After infant brain injury	1	
With suicidal tendency	1	
With anorexia nervosa		1
With paranoid symptoms		1
Substance induced (medication addiction)	1	
Bipolar disorder	1 (4)	2 (8)
Posttraumatic stress disorder (PTBS)	4 (16)	3 (12)
With depressive symptoms	1	1
With psychotic symptoms	1	
With anorexia nervosa		1
With anxiety	1	
Anxiety disorder	2 (8)	4 (16)
With major depression	1	1
With anorexia nervosa		1
Borderline personality disorder	3 (12)	2 (8)
With depressive symptoms	1	
With PTBS and anxiety	1	
Schizophrenic psychosis	6 (24)	2 (8)
Paranoid psychosis	1 (4)	2 (8)
Occasionally psychotic symptoms	1 (4)	

[a]At start of study.

Procedures were conducted at the Centre of Social Psychiatry Bünde in Germany. The study protocol was approved by the institute's ethical committee. All patients were informed about the study at a presentation by two of the authors (G. H. and G. T.-N.) and provided informed consent prior to any intervention.

Randomisation and blinding

Participants were randomised in a 1:1 ratio to either the experimental or the control group using a computer-generated list of random numbers (see Figure 1). The trial was single-blind. Both the patients and the staff who provided the interventions were aware of group assignment, but the researcher who assessed the outcome measures was blinded.

Interventions

General remarks on the specific modulation

Both terms *intervention* and *modulation* are presently used in the context of adapted music which implies the relevant facilities for diagnostic and therapeutic applications (Haffelder, 2013). Accordingly, mental problems can be identified by diagnostic measurements utilising the electroencephalography (EEG) spectral analysis procedure in combination with an analysis of event-related potentials.

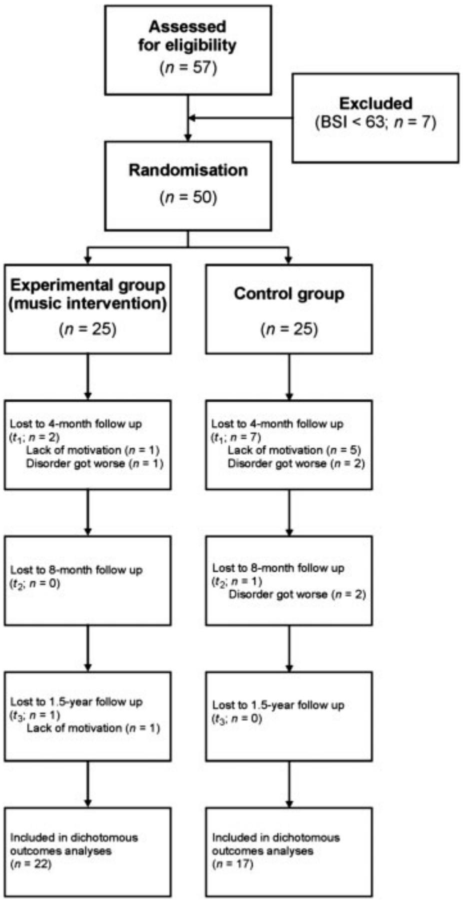

Figure 1. Flow chart of study participants.

By analogy with telecommunication, modulation is utilised, when information-carrying signals must be transmitted over some medium separating the transmitter and the receiver. The carrier is modulated with the input signal for the purpose of conveying information. The carrier operates usually at a much higher frequency than the input signals (information).

From an abstract point of view, for the therapeutic music intervention, the carrier (e.g., Mozart Piano Concerto) is modulated with input parameters (e.g., selected frequencies for the therapy, e.g., for theta waves). Then, the modulated music is transferred to CD which is the medium. The patient is the "receiver", who decodes and listens to the content of the CD.

Individual music adaption

Research on the impact of different sorts of music, composers, rhythms, instruments, tuning and frequencies on the brain has formed the basis of the individualised neuroactive music therapy used in our institute (Haffelder, 2013). Mozart has proven to be able to provide the brain with music for comfortable listening and to improve the performance in certain mental tasks, for example, spatial–temporal reasoning (Campbell, 1997; Steele et al., 1999; Tomatis, 1991). This "Mozart effect" can be intensified by playing the music composition slightly decelerated (as practiced in the days of Mozart). Furthermore, the instruments are tuned to the old French pitch of 432 Hz which corresponds to the harmonic ratio of natural body rhythms including electrical activities of the brain as measurable with EEG, metabolism, breathing, pulse, and so on.

Missing frequencies (i.e., patterns that are either completely absent or detectable only with very low amplitude) can gradually be reactivated by applying the difference tone procedure via the music as carrier and are modulated to an acoustically higher frequency range. To enhance the learning and thus the therapeutic effect, the CD also incorporates a musical anchor which can provide a variety of acoustic faults for stimulation such as sound volume changes, crackling noises, audio over-amplification, animal sounds, and so on. Also short music dropouts can help to improve the learning process and thus the therapeutic effect.

In addition to the modulation, the music was lateralised with a phase angle shift. When difficulties were encountered during spectral analytic measurements (EEG) which originated from faulty synchronous interaction of the two hemispheres, the lateralisation was compensated, that is, the correction was applied on the basis of the music carrier. The music moves from one ear to the other, accompanied from time to time by changes in volume. This helps to synchronise the two hemispheres of the brain via the corpus callosum. This lateralisation is thought to enable the brain to work efficiently and to develop new potentials for mental and creative activity.

Implementation of the music intervention

All participants were provided with CDs containing recorded music. For those randomised to the experimental group, music was individually adapted to the brain rhythms associated with each individual's psychotic symptoms detected by the pre-test EEG recording. Control patients were provided with standard classical music (Mozart, Bach, Schubert, etc.).

Patients were instructed to listen to these CDs over the next 18 months, using headphones or earphones that conveyed oscillations to the scalp. Listening was not to be done as an exclusive activity in itself but in combination with physical exercise of any type (Haffelder, 2013).

Outcome measures

Pre-test

To determine brain rhythm disorders associated with psychiatric symptoms, a special spectral analytic measurement in combination with an analysis of event-related potentials was used. This measurement was developed at the Institute for Communication and Brain Research, Stuttgart, Germany and is based on clinical EEG (Haffelder, 2013), which can be visualised by the EEG spectrogram indicating the level of activity for the individual frequencies separately for both hemispheres.

Typical rhythm disorders of the activated frequency pattern are deviations of associated, suppressed or deactivated frequencies, different resonance frequencies, dissonances, phase shifts or noises due to simultaneously activated frequencies. This is the essential information and input parameter for modulating the individually adapted music with brain rhythm frequencies from 0.5 Hz up to 30 Hz. Thereby, psychotic symptoms are mainly characterised by deviations in the theta-frequency range and decreased communication between hemispheres.

Primary and secondary outcome

Psychiatric assessments were conducted at baseline (t_0), after 4 months (t_1), 8 months (t_2) and after one and half year (t_3), with the final assessment taking place after the intervention was completed. The primary outcome was the change at each time point on the patient's psychiatric symptoms assessed by the German version of the BSI (Derogatis & Melisaratos, 1983; Derogatis & Spencer, 1982; Spitzer et al., 2011). The BSI is a short version of the Symptom Inventory List (SCL-R-9) and is a self-report questionnaire consisting of 53 items using a 5-point Likert scale ranging from "not at all" to "extremely". It covers nine symptom dimensions: somatisation, obsession-compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism as well as three global indices of distress: global severity index, positive symptom distress index and positive symptoms total, which measure the current or past levels of symptomatology, intensity of symptoms, and number of reported symptoms, respectively (Derogatis & Spencer, 1982). According to the manual, clinically significant scores are defined as a global severity index greater or equal to a t score of 63 compared with the norms for a particular population.

Two secondary outcomes were assessed. A self-report questionnaire (designated as "Q") was designed to document, whether, how often and for how long participants listened to the provided music, and whether they felt any amelioration of their symptoms through this intervention (see Supplemental Material). In addition, both participants and their treating therapists were consulted about their experience with the intervention in order to gain a subjective evaluation.

The following three criteria were established to measure success of the intervention:

(1) Decrease in BSI score below 63 (the threshold for normal).
(2) Report on the Q questionnaire of meaningful amelioration of disease symptoms, defined as an increase of at least five points on the 10-point scale.
(3) Progress or normalisation of psychological symptoms, as reported by the treating therapist.

Analyses

All data analyses were performed using Excel (Microsoft Office 2010), statistical analyses were done using SPSS statistics (v. 19, IBM). After creating dichotomous data for group comparison, they were analysed using the chi-square test for homogeneity. Significance levels were defined as follows: $p < .05$, significant (*); $p < .01$, very significant (**) and $p < .001$ highly significant (***).

Analyses were done on the per-protocol population for the following reasons: first, this pilot study was conducted to evaluate the efficacy potential of the intervention; second, there was no reason to expect any withdrawals due to adverse side effects but only due to lack of interest and motivation; and third, participants were not blinded regarding which intervention they were receiving.

Results

Three participants in the experimental group and eight in the control group left the study early due to a lack of motivation or worsening of their disorder, resulting in group Ns of

22 and 17, respectively (see Figure 1). All study completers stated on questionnaire Q that they listened to the provided music daily, and found the music to be enjoyable.

There were no significant group differences at baseline, 4 months and 8 months. At 18 months, in the experimental group, 10 of the 22 patients (45%) of the experimental group showed significantly decreased BSI scores compared to the control patients (χ^2 = 21.78, p < .001; see Figure 2A and Table 2). Analyses of the different symptom dimensions revealed significant improvements in the experimental group compared to the control group over the time period of $t_0 - t_3$ in the dimensions psychoticism (χ^2 = 5.9, p < .05), paranoid ideation (χ^2 = 5.27, p < .05), anxiety (χ^2 = 6.74, p < .01), phobic anxiety (χ^2 = 4.67, p < .05) and somatisation (χ^2 = 6.54, p < .05). No significant effects were seen for obsession-compulsion (χ^2 = 1.23, p > .05), interpersonal sensitivity (χ^2 = .1, p > .05), depression (χ^2 = .03, p > .05) and hostility (χ^2 = 2.03, p > .05; see Figure 2B–J).

No participant in either group reached any of the three success criteria at 4 months or 8 months. At 18 months, in the experimental group, 10 of the 22 patients (45%) achieved all three criteria; seven (32%) met Criterion #2 and Criterion #3, but not Criterion #1 (i.e., they did not reach the threshold of 63 in the BSI); and five (23%) did not achieve any criterion. In comparison, in the control group, none of the 17 patients achieved all three success criteria; three patients (18%) met Criterion #1 and Criterion #3 but not Criterion #2 (i.e., amelioration of disease symptoms as assessed by the questionnaire); three (18%) met Criterion #2 but no other criterion; and 11 (64%) did not meet any of the criteria (see Figure 3).

Discussion

The majority of patients in the experimental group showed an improvement in their psychiatric symptoms by the end of the treatment. Interestingly, although mainly directed to psychotic symptoms, the adapted music was not only effective for psychoticism and paranoia but also for anxiety, phobic anxiety and somatisation. This may possibly be explained by looking at the neuroanatomical and physiological mechanisms underlying these symptom complexes. We here discuss the neuroanatomical and neurophysiological commonalities and differences of the symptom complexes, and – on the basis of clinical and fundamental research – theorise on how the adapted music might be stimulating specific brain rhythms and thereby inducing reorganisational processes.

It is widely accepted that psychosis involves disturbances in the neurotransmitters dopamine, glutamate and gamma-aminobutyric acid (GABA), as documented in both animal studies (reviewed in Dawirs & Teuchert-Noodt, 2001; Weinberger & Lipska, 1995) and clinical studies (Akil et al., 1999; reviewed in Williamson & Allman, 2012). In a non-invasive animal model, gerbils (*Meriones unguiculatus*) that were reared in an environment deprived of stimulation and were further subjected to trauma in early life through administration of a single dose of methamphetamine, show a disconnection between prefrontal and limbic as it is also seen in schizophrenia. Local GABAergic interneuronal innervation, glutamatergic interconnections between cortical and subcortical areas as well as the ascending neurotransmitter systems dopamine, serotonin and norepinephrine are affected (Bagorda et al., 2006; Brummelte, Neddens, & Teuchert-Noodt, 2007; Busche, Polascheck, Lesting, Neddens, & Teuchert-Noodt, 2004; Dawirs, Teuchert-Noodt, & Czaniera, 1994; Lesting, Neddens, Busche, & Teuchert-Noodt, 2005; Witte, Bagorda, Teuchert-Noodt, & Lehmann, 2007). Interestingly, mouse strains that have been psychogenetically selected and bred for high anxiety levels show similar

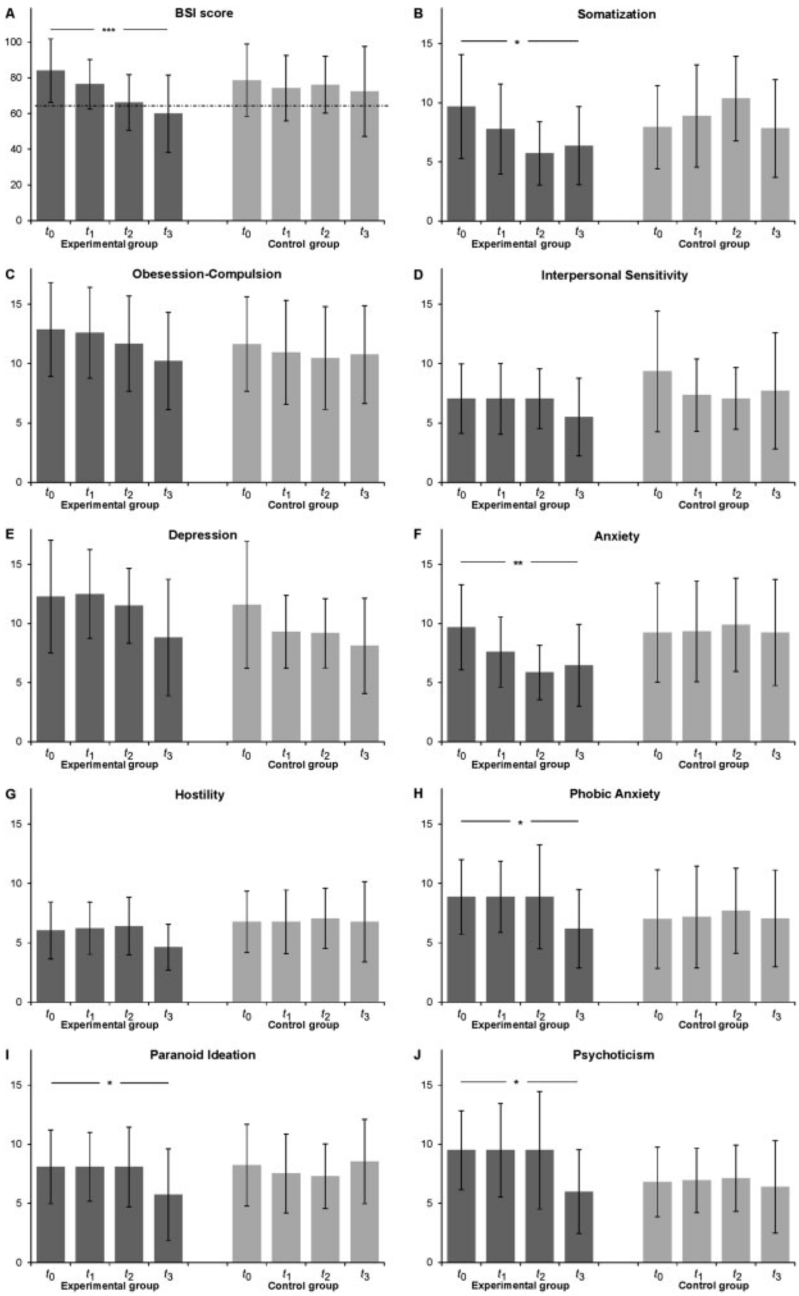

Figure 2. Change in BSI scores over time ($t_0 - t_3$) in experimental and control patients. A. BSI score total; dashed line marks BSI score of 63; B–J. BSI scores for the individual symptom dimensions. Given are means ± SD; significances calculated between experimental and control group over time $t_0 - t_3$. *$p < .05$, **$p < .01$, **$p < .001$.

Table 2. Changes in primary and secondary outcomes in the experimental (EG) and control group (CG).

	4-month follow-up		8-month follow-up		1.5-year follow-up	
Outcome	EG	CG	EG	CG	EG	CG
BSI[a] (*n*/*N* (%))	0/22 (0)	0/22 (0)	0/22 (0)	0/22 (0)	10/22 (45.5)	3/17 (17.6)
Q[b] (*n*/*N* (%))	0/22 (0)	0/22 (0)	0/22 (0)	0/22 (0)	17/22 (77.3)	0/17 (0)

[a]BSI score < 63.
[b]Amelioration of at least five steps in Q.

disconnectivity of prefrontal–amygdalar–hippocampal circuits (Browne et al., 2013; Yilmazer-Hanke, 2008).

Psychoticism and anxiety do not only have anatomical but also neurophysiological correlates. Although nearly all oscillation frequencies are involved in psycho-cognitive processes to some extent (Basar, Basar-Eroglu, Karakas, & Schurmann, 2001), the prefrontal–hippocampal circuit, which is of special interest in the context of psychoticism and anxiety, is mainly dominated by theta oscillations (4–7 Hz, Uhlhaas et al., 2008). Theta rhythms coordinate local activities in both prefrontal and hippocampal microcircuits (Buzsaki, 2002; Raghavachari et al., 2006; Tsujimoto, Shimazu, & Isomura, 2006) and ensure prefrontal–hippocampal communication (Lisman & Buzsaki, 2008; Siapas, Lubenov, & Wilson, 2005). Reasonably, with respect to both psychoticism and anxiety, theta and gamma oscillations (30–200 Hz) are of special interest. Several studies have shown that abnormal oscillations in these bands are associated with psychosis (Gordon, Williams, Haig, Wright, & Meares, 2001; Spencer et al., 2003) and thus represent the functional correlate of disconnectivity in limbo-cortical networks (reviewed in Uhlhaas et al., 2008). This is conceivable, as the synchronisation of theta and gamma waves mainly depend on glutamatergic and GABAergic interactions in the prefrontal cortex (PFC) and hippocampus, the areas and the neurotransmitters, respectively, that are severely affected in psychosis (Gonzalez-Burgos & Lewis, 2008; Spencer et al., 2003). Remarkably, coupled theta activities between PFC, hippocampus and amygdala underlie anxiety and

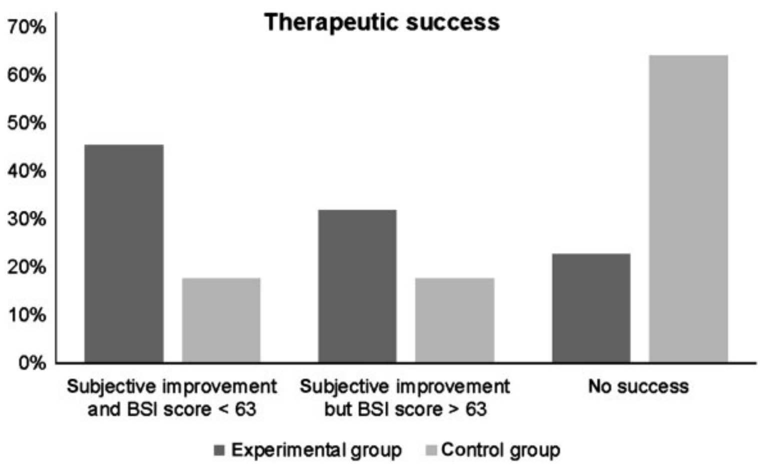

Figure 3. Therapeutic success in experimental and control patients evaluated by a decrease in BSI scores below 63, self-reported improvement (questionnaire Q), and improvement reported by the treating therapist.

fear memory consolidation (Lesting, Geiger, Narayanan, Pape, & Seidenbecher, 2011; Seidenbecher, Laxmi, Stork, & Pape, 2003). These anatomical and physiological correlates of psychoticism and anxiety may explain how the adapted music intervention was able to affect both these symptoms despite being directed towards the former.

In the case of somatisation, the other complex for which improvement was seen, although the underlying biological mechanisms of this disorder are still little understood, it is a common attendant symptom of several psychiatric disorders including psychosis, anxiety disorders and depression (reviewed in Mai, 2004; Stein & Muller, 2008). Hence, it is logical that an improvement in these symptom dimensions would be accompanied by a reduction of somatisation as well. In the current study, although none of the participants was diagnosed with an actual disorder of the somatoform category, those in the experimental group showed an improvement.

It has frequently been demonstrated that dysfunctional brain oscillations are not only due to anatomical and neurochemical disturbances; conversely, synchronised brain activity also plays a crucial role in activity-dependent self-organisation of reorganising networks (Singer, 1995; Uhlhaas et al., 2008).

We can hypothesise that the modulation of brain rhythm frequencies might enhance communication between local and distant networks, modulate neurochemical interactions and even induce neuroplastic processes to the point of reorganisation of maladaptively connected prefrontal–limbic circuits. The assumption that neuroplastic processes had been induced by the alternative music intervention gets support, as the effect of the music in the present study was not only present when participants listened to the music but also persisted in the interim and even beyond.

The hippocampus shows life-long high plastic capacities due to its innate neurogenesis and synaptogenesis. Thus, neuroplastic processes are most likely to be induced in this structure. In this context, a notable aspect is that – based on practical experience – patients were instructed to engage in exercise of any type when listening to the music. Physical exercise is known to induce plasticity in the hippocampus (Schaefers, 2012; Schaefers, Grafen, Teuchert-Noodt, & Winter, 2010; van Praag, Kempermann, & Gage, 1999) and might thereby support effects of the music intervention.

The PFC shows lower plastic capacities in adulthood, but still preserves the potential for structural adaptation, especially in the glutamatergic and GABAergic interplay which is highly affected in psychosis (Bagorda et al., 2006).

With regard to the induction of neuroplasticity by the adapted music, frequencies in the theta and gamma range are of special interest, as they are tightly linked to neuroplasticity and learning in hippocampal as well as prefrontal areas (reviewed in Fell & Axmacher, 2011; Zhang, 2011). As preference was given to theta waves and as the adapted music had long-term effect, it can be speculated that a theta–gamma phase synchronisation might have been re-induced, leading to the amelioration of psychotic and anxiety symptoms.

Although theta and gamma oscillations are of particular importance, the other frequencies may play a role as well, especially in the context of the modulation of glutamatergic, GABAergic and dopaminergic innervation patterns. Alpha waves (7–13 Hz) are generated in thalamic nuclei as a result of reciprocal interactions between excitatory and inhibitory neurons and are modulated by acetylcholine, serotonin and glutamate (Hughes et al., 2004; Lörincz, Crunelli, & Hughes, 2008). They are necessary for precise synchronisation of high frequency oscillations in the PFC and for inter-hemispheric communication (Doron, Bassett, & Gazzaniga, 2012; Foxe & Snyder, 2011) and hence might be the key target of the lateralisation effect of the adapted music. Beta waves (14–30 Hz), which are generated in distributed cortical regions and are required for distant cortico–cortical synchronisation (Kopell, Ermentrout, Whittington, & Traub, 2000), support inter-hemispheric communication (Schnitzler & Gross, 2005), which is known to be affected in psychoticism (Chaim et al., 2010; Hoptman et al., 2012). Indeed, a reduction of frontal beta synchrony has been found in schizophrenic patients (reviewed in Ferrarelli et al., 2012). Moreover, recently it has been shown that beta oscillations are tightly linked to the dopaminergic system (Sharott et al., 2005) as well as GABAergic inhibition and N-methyl-D-aspartate (NMDA) receptor activity (Traub, Bibbig, LeBeau, Buhl, & Whittington, 2004), an important glutamatergic receptor mediating long-term potentiation and neuroplasticity. Conversely, there are indications that beta oscillations might influence dopaminergic neurotransmission in the prefrontal–hippocampal circuit, which shows characteristic imbalances in psychosis and anxiety disorders (Busche et al., 2004; Dawirs et al., 1994; Diaz et al., 2011; Laruelle, Kegeles, & Abi-Dargham, 2003). Together with frequencies in the alpha and delta range (0–3 Hz), beta oscillations are involved in thalamo-frontal, intra-hemispheric and inter-hemispheric communication. Hence, stimulation of these frequencies may influence the disturbed communication found in psychoticism (Chaim et al., 2010; Florio, Fossella, Maravita, Miniussi, & Marzi, 2002; Hoptman et al., 2012). Moreover, the correlation between slow delta activity and fast beta activity reflects functional synchronisation between limbic and cortical brain systems (Putman, 2011). Anxiety states are positively correlated to alpha power but negatively correlated to delta power (Knyazev, Savostyanov, & Levin, 2004; Knyazev, Schutter, & van Honk, 2006), indicating that delta–beta and delta–alpha anti-correlation reflects high anxiety states (Knyazev et al., 2004, 2006; Putman, 2011). Thus, stimulation of these frequencies by the adapted music might have impacted the disturbed synchronisation between limbic and cortical brain systems that marks anxiety.

Some limitations have to be considered when interpreting our data. First, we employed a per-protocol analysis, meaning that only data from participants who completed the study were included. This runs the risk of undermining the randomisation and introducing bias. However, in a pilot study, this analytic approach enables assessment of the efficacy potential of an intervention under optimal conditions. Second, the generalizability of our results is limited by the small sample size as well as by the preponderance of female patients (64%). The small sample size also causes a power problem. Given the exploratory nature of the study, we abstained from applying a Bonferroni correction for the multiple chi-square tests of the subcategories of the BSI, which would have rendered most of the findings non-significant.

Conclusion

Despite the limitations, this pilot study provides some evidence that a long-term intervention using rhythmically adapted music is effective in ameliorating symptoms of psychosis, anxiety and phobic anxiety, and the findings may hold relevance to clinical practice. The symptom complexes of psychoticism and anxiety, which have neuroanatomical and neurophysiological commonalities, were both found to be ameliorated by music specifically adapted for the abnormal brain oscillations associated with psychotic symptoms, whereas symptoms without these commonalities, such as depression and obsession-compulsion, were largely unaffected. On the basis of fundamental research of neuroplasticity and brain rhythms in animal models, we assume that the adapted music is able to influence pathologically disturbed oscillation patterns and potentially induce neuroplastic processes. Future studies should explore the structural mechanisms and neuroplastic processes induced by the specific frequencies more specifically in an attempt to develop a music intervention that can function as an effective treatment for psychiatric disorders.

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Supplementary material

Supplemental Material is available via the "Supplementary" tab on the article's online page (http://dx.doi.org/10.1080/13546805.2013.879054).

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