

MUSIC THERAPY AND BIOMARKERS OF DEPRESSION TREATMENT

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ABSTRACT ► How can we document change as a function of doing music in a therapeutic setting and how does it work? Biomarkers representing the effectiveness and those representing the music therapy process are related to an accumulation of and a focus on important moments in therapy time. Analysing resting state EEG may inform about group effects, while moments of interest in the improvisational process may reveal synchronization of brain processes. In music therapy it may be an important key to understand where and why change in therapy occurs. We will discuss the promises of biomarkers and neurometrics for music therapy, will draw on results of depression research, on recent work with wireless EEGs and improvisation, music performance, neurofeedback and game applications in psychiatric and neurorehabilitation.

ANTIDEPRESSANT REDUCTION OR INTERACTION?

Activating brain circuits inducing pleasure gives rise to the hope that the right music therapy intervention stirring up the emotions of the individual client at the right time, may *reduce medication* prescribed for mental health issues, as music can replace the drug's desired effects. For example, in a study with depressed clients comparing treatment with Indian 'relaxation' music or hypnotics, the authors discussed that "*the effects of music could be equivalent to 10 mg of Chlordiazepoxide or 7 mg of Diazepam*"¹.

Reductions of medication have been demonstrated in medicine employing music, for example, as an adjunct to anaesthetic medication^{2, 3}. For instance, sedatives are regularly administered before surgery to reduce a patient's anxiety. However, sedatives often have negative side effects (drowsiness, respiratory depression, etc.), and may interact with anaesthetic agents, prolonging patient recovery and preventing discharge. Therefore, increased attention is being paid to the introduction of music to reduce medication during⁴ and reducing anxiety before⁵ surgery. These

few examples may indicate that there is hope that we can use music as a decrement of medication.

The word 'complementary' means 'in addition to' or 'allied to' and is seen as an addition to standard care. For example, research into treating chronic pain with music therapy indicates that "*music therapy is an effective adjuvant intervention for patients suffering from chronic non-malignant pain, doubling the effects of pharmacological treatment*"⁶.

Our own research into the treatment of depression with music therapy indicates that a complementary interaction between improvisational music therapy and antidepressant medication may facilitate standard care⁷. Clients receiving music therapy and standard care showed significantly decreased depression and anxiety symptoms compared to those receiving only standard care.

PERSONALISED MEDICINE

On one hand we may strive for a reduction of medication but on the other hand the right medication may support psycho- or music therapy. This is desirable from the stance of personalized medicine⁸. Prescriptions are

ideally based on the bio-psycho-social identity of a particular person and not solely on a diagnostic classification. Personalized medicine hopes to address the right medication based on genotypes and biomarkers reflecting the client's biological condition⁹, aiming to administer an individualized combination. While an antidepressant may be adequate for moderate or severe depression, it may not be the right choice for a first episode of mild depression. However, antidepressant prescriptions are on the rise¹⁰ and once the proposed 'chemical imbalances' are treated with antidepressants, they "may reduce sense of self and soul into dopamine, serotonin, neurons, milligrams"¹¹.

A striking example of the dominance of medication in depression treatment is a Finnish study¹² that explored the treatments offered to people who were retired prematurely because of depression. The study revealed that 89% of the retired individuals during 1993 to 2004 never received any form of psychosocial treatment. Without a doubt, a better balance between the treatment choices could be achieved. There is convincing evidence that a combination of psychosocial support (such as psychotherapy) and medication is the best treatment, with psychotherapy acting as the initial treatment¹³.

BIOMARKING MUSIC THERAPY TREATMENT

A distinction among outcome types in clinical trials is between clinical endpoints and surrogate endpoints or *biomarkers*. A clinical endpoint may reflect "how a patient feels or functions, or how long a patient survives"¹⁴. In contrast, a biomarker is an objectively measured indicator of normal or pathological processes. Nevertheless, the process of selecting a measure remains subjective. A biomarker is objective only in the sense that it is not easily influenced by social expectancy bias and similar biases that may be encountered in clinical assessments. That is, "a measure can only be objective once it is decided which measure to use"¹⁵. How well this indicator reflects a clinical endpoint may vary. One of the biomarkers aiming to be a surrogate for predicting and estimating the effectiveness of a pharmacological intervention in depression treatment^{16,17} are EEG measures, as for example Frontal Alpha Asymmetries¹⁸. This article reflects on its use in an RCT on music therapy and depression.

In a randomised controlled trial (RCT), an outcome research method of proving treatment effectiveness, researchers were interested in whether music therapy

added to standard care of depression treatment produced different outcomes from standard care only¹⁹. Here it was important to develop a balance between a flexible and spontaneous practice of responding to the client and a standardisation of a treatment practice. Standardisation meant, for example, using the same musical instruments and a shared reference system created by all therapists taking part in the study, in terms of understanding depression, research and treatment practice and its philosophy²⁰. By constructing treatment fidelity, i.e. a consensus of understanding limitations of aims and common techniques employed, for example to be clear that this is a model of a normal treatment and not a normal treatment as such, a baseline to start from was developed and supervised on the way²¹. The results indicated a significant effect of music therapy added to standard care compared to standard care only. Three of the outcome measures indicated a substantial improvement, i.e. a reduction of depression and anxiety scores and an increase of overall global function - and most clients were not happy that the treatment ended after 20 sessions⁷.

EMOTION, DEPRESSION AND FRONTAL BRAIN ACTIVITY

Clients with depression have difficulties in expressing and processing emotion²², and, given the frequent comorbidity with anxiety²³, are more likely to act in a withdrawn and anxious manner in social interaction²⁴. A heuristic concept explaining affective disorders links the withdrawal behaviour of depressed clients to increased right frontal activity, i.e., pathological asymmetric frontal processing of emotion²⁵. Depressed clients tend to use rumination and expressive suppression as strategies to regulate their emotions instead of actively approaching them²⁶.

A few studies have demonstrated an immediate effect of pleasurable music listening on frontal processing in depression, i.e., during and after music listening a relatively right-sided frontal activity of depressed adolescents^{27,28} and depressed mothers²⁹ shifted towards relatively left-sided activity. These results indicate an immediate influence of music listening on frontal processing in depression. Fachner et al's aim was to find out whether these effects are lasting, and can be observed in an additional resting EEG recording, i.e., one not taken during or directly after listening, as in the study with depressed mothers from Field et al (1998), but after a course of active music therapy³⁰. Correlations between anterior EEG, Montgomery-Åsberg Depression Rating Scale

(MADRS) and the Hospital Anxiety and Depression Scale - Anxiety Subscale (HADS-A), power spectral analysis (topography, means, and asymmetry) and normative EEG database comparisons were explored.

NEUROMETRICS

Normative EEG comparisons allow to distinct excessive or abnormal EEG patterns against a database of age, gender, and condition-matched controls³¹ in order to estimate z-scored deviation from normality on measures at baseline and after treatment. The z-transformation is a nonlinear transformation in which each measured value is translated to a deviation from the typical value of a healthy person of the same age.

In Case study designs normative EEG databases may help to provide an objectivist measure to estimate a client's brain process before and after a therapy session or sequence³² or guide neuro-feedback goal setting in music therapy³³. Ideally a client returns to normal processing. Neurologists have used EEG tools for decades, but research asks for generalizability of these biomarkers in the music therapy realm^{15,30}.

BRAIN PLASTICITY, MUSIC AND LANGUAGE PROCESSING IN MUSIC THERAPY

The results of the EEG study were quite interesting and may shed another light on Felicity's work on vocalisations. Many functions of the brain are bilaterally processed. For example, the left frontal operculum (Broca's area) organizes motor processes of speech production, while the contralateral site may influence the tone of the voice³⁴, a function reduced in aprosodic clients after cerebral damage³⁵. F. North's three examples show how vocalisation changed and became a tool for musical communication in therapy. In the depression study outlined above, the EEG resting state measures employed, a simple and easy to apply indicator of neuroplasticity, as utilised in Pharmac-EEG studies³⁶, pointed to fronto-temporal changes as a signature of difference between both groups and between the pre and post music therapy treatment [30].

Fronto-temporal areas have broadly been investigated in research on common areas of music and language processing³⁷. Emotional modulation of limbic structures, activation of the perception-action mediation in premotor areas, and intentional processes of social cognition in frontal and temporal areas are discussed as possible neuroscientific concomitants of music-therapeutic action³⁸. A study on fronto-

temporal lobar degeneration in 26 patients indicated the importance of fronto-temporal areas for the recognition and processing of emotion in music³⁹. Further, increases in the density of grey matter of Broca's area have been found in orchestral musicians [40], indicating the relevance of musical training for fronto-temporal brain plasticity.

At intake the depressed clients perceived emotions in film music excerpts representing sadness and anger differently from normal controls. That is, they detected anger and fear more often than normal controls²². Non-verbal expression of emotional content through music creation, and subsequent verbal reflection of its personal meaning, is part of the therapeutic relationship established during music therapy²⁰. Considering that about 70% of the therapy sessions were used for verbal reflection and 30% for improvising, fronto-temporal changes may prove that doing music therapy initialised neural reorganisation in areas which were busy with processing music and language in manifold ways, while offering the client a context to experience and embody a playful means of emotional expression supporting reduction of anxiety among and depressive withdrawal from others. Felicity's work shares this offer to the clients: 'an invitation to change'.

Prosody and emotion in music therapy treatment

Previous music therapy research has encouraged a closer enquiry into music therapy and the enhancement of pre-verbal skills in expressing and communicating emotions⁴¹. In her three musical excerpts F. North exemplifies how vocalisation and communication link to music and language processing, and how the emotional colour of the voice can change in a musical dialogue. In the depression study, right-hemispheric activity increased after music therapy³⁰. Panksepp and Trevarthen⁴² discussed the importance of right hemispheric prosody in its connection to emotion processing and communicative musicality and already Patel et al⁴³ X-Ray Computed</keyword><keyword>Wechsler Scales</keyword></keywords><dates><year>1998</year><pub-dates><date>Jan</date></pub-dates></dates><isbn>0093-934X (Print had suggested a shared neural resource for prosody and music. In psychotherapy research speech prosody measures indicated emotional involvement during an interview on childhood memories⁴⁴. Koelsch et al⁴⁵ has stressed the close connection of semantic and syntactic functions in music and speech processing. Processing of melody is connected to pre-motor speech process activation at a laryngeal level, initiating pre-motoric level movement

processes, especially when meaningful and rewarding emotional processes trigger perception-action mediation³⁸. Examining patients with lesions in Broca's area, Sammler et al⁴⁶ discussed the left Inferior Frontal Gyrus as a functional prerequisite for processing musical syntax. Results with aphasic patients undergoing melodic intonation therapy showed plasticity changes in the fibre tract connecting the superior temporal and inferior frontal lobes and the motor cortex in the right anterior hemisphere^{47,48}. Right hemispheric activity at fronto-lateral sites is also linked to prosodic processing³⁵. Williamsen et al. correlated reduced alpha, theta and delta power at F8 demonstrating that aprosodic expressive deficits of a client were "caused by cerebral damage to the right hemisphere region homologous to Broca's area"³⁵. Taking the fronto-lateral asymmetry changes in Fachner et al's study and the findings on prosodic processing in these regions together, we may look at traces of emotional processing that occurred in music therapy with depressed clients.

OUTLOOK

Music therapy is increasingly recognized as an area full of applied potential in the field of neuroscientific research⁴⁹. Music therapists are attracted by brain research as some principles applied in therapy, such as the social aspects of music making⁵⁰, seem to be confirmed in neuroscientific research. However, music therapists and neuroscientists recognize the limitations of the tools and

paradigms of neuroscientific heuristics, but also their potential to visualize components of a music therapy action mechanism⁵¹⁻⁵³. Furthermore, outcome research aims to detect biomarkers and predictors of treatment response^{15,30}. Biomarkers like neurotransmitters (see below), hormones, cytokines, lymphocytes, vital signs, and immunoglobulins indicating music-related changes of psychoneuroimmunological status are seen as promising tools to study stress reduction and wellbeing from a music psychology perspective, that is to say, to use music more systematically,⁵⁴. Brain imaging methods are becoming more sophisticated and provide insights into formerly *hidden* cerebral processes related to human functioning and pathologies. Studies of the brain aim to show how music plasticizes fibers⁴⁸, sparks neurotransmitter cascades⁵⁵, and synchronizes body movement⁵⁶ and biological rhythms⁵⁷.

Interest is growing in the area of flow states, for instance, training musicians to enter a relaxed but highly concentrated state in preparation for an artistic performance in the orchestra. In jazz and rock bands neurofeedback (NFB) methods have been successfully applied in this area^{58,59} and aim to train the participant to control brainwaves that represent certain brain states, moods and emotions. However, engaging in NFB and bio-guided music therapy means that people learn to perform according to rules that put the music and the body into a harmonic relationship³³.

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