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Receptive Music Therapy for the Treatment of Depression: A Proof-of-Concept Study and Prospective Controlled Clinical Trial of Efficacy

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Current psychosocial and antidepressant treatments [1] result in similar response rates [2, 3] with mostly reduction, but not complete remission, of depressive symptoms [4]. Poor adherence to recommended treatment is a further issue complicating the management of depression and prevention of recurrent episodes [5, 6]. Therefore, new therapies, which alone or combined with present treatments can significantly improve outcomes, urgently need to be developed. Evidence suggests that music therapy should be further explored as a possible treatment [7]. Music therapy is generally not associated with negative side effects and can be easily implemented. These factors contribute to high adherence and favorable treatment outcomes. Previous efficacy studies of music therapy for depression treatment suffered from a lack of specific stimuli, methodological shortcomings, or utilization of small samples [8]. We conducted the largest trial to date investigating 2 forms of receptive music therapy among adults with depression.

Recruited through media and by contacting doctors, potential subjects were screened online using the Goldberg Depression Questionnaire (GDQ) [9]. All subjects provided written informed consent before participation in the study. The study was reviewed and approved by the Ethics Commission of Vienna and registered with the National Institute of Health's clinical trial registry (www.clinicaltrials.gov, NCT00644527). The first 204 respondents who completed the GDQ and met the inclusion criteria (aged $\geq$18 years with a GDQ score between 15 and 65) underwent more comprehensive baseline assessments. Respondents were not accepted if they had changed therapists, therapeutic session frequency, antidepressants, or antidepressant dosage in the 6 months prior to study initiation. Further, individuals were only included if they agreed not to make any such changes during the course of the study period. Subjects with alcohol abuse or an associated disease, and those under psychiatric treatment for psychoses, were excluded. One subject was excluded due to cognitive disability. The remaining 203 subjects entered the study protocol. The study design included 4 arms: music therapy 1 (MT1), music therapy 2 (MT2), placebo (nature sounds), and waiting-list control. Assignment to study arms was based on subjects' preferences for the date of their initial study appointment (only on working days).

The subjects were followed over 4 consecutive 5-week study periods (T1, T2, T3 and T4). The T1 period represents the central trial element of this study, while the additional study periods (T2, T3 and T4) were employed to explore wash-out effects, subject adherence, and treatment preferences. This report only draws on data from T1. During T1, the subjects were asked to strictly follow their assigned study protocol with the aim of determining the effects of MT1 and MT2. Subjects who received audio programs (i.e. MT1, MT2, or placebo) were blinded to the program they had received and could not switch from their assigned program to alternative music programs during T1.

MT1 and MT2 were individualized music-focused audio therapies developed by the study investigators as receptive music therapies for depression treatment. Both programs were developed and refined through a series of case studies and included 2 specific programs for different times of the day. MT1 incorporated newly composed polyphonic modern music and MT2 consisted of specifically arranged classical music. Subjects listened twice daily for 30 min.

Depression status was assessed at the beginning of T1 and T2 using the Hamilton Rating Scale for Depression (HAM-D) [10], the Beck Depression Inventory (BDI) [11], and the Hospital Anxiety and Depression Scale (HADS-D) [12]. HAM-D was administered by trained psychologists blinded to each subject's arm assignment. A composite (COMP) depression scale was constructed based on the HAM-D (double weighted), BDI, and HADS-D z-scores. Change in scores on each individual scale and on the COMP between the beginning of T1 and T2 were calculated. At the beginning of T1, each subject also completed an extensive questionnaire covering various potential confounders. Separate multivariate linear regression models were constructed for each of the depression change variables with stepwise backward elimination of possible confounders. Analyses were carried out based on an intention-to-treat approach with significance assessed both at the $p \leq 0.05$ and $p \leq 0.0125$ levels [13].

The overall drop-out rate at the beginning of T2 equaled 17.2% (35/203). Compared to the control arm, a significant positive effect in COMP was observed for MT1 in T1 ($\beta = 1.44$, $p = 0.030$), but not for MT2 (table 1). Both MT1 and MT2 were associated with a sig-

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Table 1. Final models, relationship between study arm and change in depression scales in T1

	β	p value	95% CI
Change in HAM-D[1]			
MT1	3.12	0.013*	0.68 to 5.56
MT2	2.58	0.031*	0.24 to 4.91
Placebo	2.05	0.115	–0.51 to 4.61
Change in BDI[2]			
MT1	1.23	0.361	–1.43 to 3.90
MT2	2.99	0.030*	0.30 to 5.67
Placebo	–1.13	0.430	–3.95 to 1.69
Change in HADS-D[3]			
MT1	1.68	0.014*	0.35 to 3.02
MT2	1.56	0.024*	0.21 to 2.34
Placebo	0.80	0.303	–0.73 to –0.07
Change in COMP[4]			
MT1	1.44	0.030*	0.14 to 2.73
MT2	1.14	0.059	–0.04 to 2.33
Placebo	0.57	0.397	–0.76 to 1.90

Depressive symptoms, based on the HAM-D, BDI, HADS-D and COMP, were assessed at the beginning of T1 and at the beginning of T2, 5 weeks later. The comparator group for all analyses was the control arm. * $p \leq 0.05$.

[1] Adjusted for age, gender, family status, education, worries, self-rated health, and sleep quality.

[2] Adjusted for age, gender, family status, psychosocial stress at work, exhaustion, and stressful life events.

[3] Adjusted for age, gender, psychosocial stress at work, disruptions in social relationships, and sleep quality.

[4] Adjusted for age, gender, family status, education, source of income, and worries.

nificant positive effect on HAM-D and HADS-D scores. MT2 subjects experienced a positive effect on BDI scores, but not MT1 listeners. No significant change in any depression score was detected in the placebo arm. HAM-D, BDI, and HADS-D score changes correlated only moderately, with the highest correlation observed between BDI and HADS-D ($\rho = 0.59$). In bivariate analysis, a 'worries' scale was the only possible confounder significantly associated with all 4 depression scores, suggesting that the HAM-D, BDI, and HADS-D scales may focus on different aspects of the construct of depression (e.g. cognitive and emotional factors).

A recent Cochrane review identified 16 potentially relevant studies on music therapy for the treatment of depression, but only 5 studies met the methodological criteria for inclusion [8]. Of these studies, 4 involved subjects listening to music [14–17], but only 1 study [17] asked subjects to listen to music individually (in contrast to group sessions [14–16]). Our study represents the largest study to date and is the only controlled trial to investigate the effect of audio programs without additional guided imagery or relaxation techniques.

Our study included both subjects who used music therapy or used music therapy combined with existing treatment approaches. Due to our study's sample size, we were unable to investigate interactions between music therapy and concurrent treatments. To limit potential bias, however, we excluded subjects who had changed their therapeutic approach in the 6 months prior to study initiation.

Based on possible neurophysiologic and neurochemical effects [7], receptive music therapy, as explored in this pilot controlled trial, appears to be associated with reduced depressive symptoms and high treatment compliance, and may therefore potentially represent an effective depression treatment alternative, alone or in combination with psychosocial and pharmacological approaches.

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