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MUSIC-BASED INTERVENTIONS FOR NEUROPSYCHIATRIC SYMPTOMS OF DEMENTIA

ABSTRACT

Background: *Progressive ageing-related processes of deteriorating cognition, such as Alzheimer´s disease, present as both cognitive and neuropsychiatric symptoms. Insufficient effects and severe adverse effects of medications have led to increasing interest in non-pharmacological treatments. Music-based therapies have been accepted in guidelines as supplementary treatment of dementia. Yet, optimal implementation has not been defined and evidence for symptom-specific effectiveness of music is still contradictory.* ***Material and Methods:*** *We analysed all (n=55) randomized controlled trials registered in PubMed database investigating the effects of music on neuropsychiatric symptoms of dementia. Positive outcome was defined as superiority of music over standard care or non-musical intervention. Negative outcome was defined as lack of effect compared to standard care.* ***Results:*** *The trials applied both active and passive interventions, i.e. various types of physical participation in music making or mere music listening. The outcomes included behavioural and psychological symptoms of dementia (BPSD) en bloc, or specifically depression, agitation, anxiety or apathy. Music-based interventions resulted in positive outcome in 70%, 45%, 42% or 35% of interventions measuring BPSD, anxiety, depression or agitation, respectively. Negative outcome was obtained in good fourth of the interventions measuring BPSD, depression or agitation.* ***Conclusions:*** *The evidence for beneficial effects of music is firmest for unspecified BPSD or depression, moderate for agitation and anxiety, weak for aggressiveness and very weak for apathy. Mixed results may be due to heterogeneity in study design, clinical scales or make-up of patient cohorts.*

KEYWORDS: MUSIC-BASED THERAPY, DEMENTIA, NEUROPSYCHIATRIC SYMPTOM,DEPRESSION, AGITATION, ANXIETY

INTRODUCTION

Ageing of populations has resulted in increased prevalence of progressive memory symptoms, foremost Alzheimer´s disease (AD), manifesting gradually as deteriorating cognitive capacity and proceeding eventually to dementia (1). Other aetiologies of ageing-related processes of deteriorating cognition include cerebrovascular insults, Parkinson´s disease (PD), Lewy body disease (LBD) and frontotemporal degeneration (FTD). Progression of these conditions can be slowed down to some degree in AD, PD and LBD by acetylcholinesterase inhibitors or memantine. Anti-amyloid drugs lecanemab and donanemab offer a new pharmacological strategy to tackle the pathogenesis of AD and have been accepted for clinical use (2). The inevitable course of the progressive memory symptoms gradually leads to dementia, loss of cognitive skills needed to cope with activities of daily living or work and waning of social network.

Neuropsychiatric symptoms, most often depression, may be the initial symptom of incipient memory disease and precede cognitive problems (3). More commonly, deteriorating cognition is accompanied by behavioural and psychological symptoms of dementia (BPSD) at the advanced stage. These include anxiety, agitation, aggression, apathy, disturbances of sleep and diurnal rhythm or other unspecified behavioural symptoms. In a meta-analysis by Zhao et al. (4), the prevalence of symptoms suggesting psychotic disorder was 31% for delusions and 16% for hallucinations. Appearance of BPSD and its treatment with psychotropic medication may endanger the patient´s safety due to wandering and increased fall risk, particularly for those living alone. Manifestation of BPSD also commonly leads to exhaustion of the spouse or other caregivers and is often a

decisive factor leading to transition of the patient from home care to long-term care facility. Neuropsychiatric symptoms often significantly increase the workload of institutional staff and may erode their wellbeing at work.

Medication specifically targeting the deteriorating cognition, even if applied at an early stage, may temporarily curb the neuropsychiatric manifestations to some degree, but eventually the treatment must be supplemented by psychotropic medication, the potency of which, in managing the symptoms and yet maintaining reasonable capability and autonomy of the dementia patient, is limited (1). Psychotropic medication often brings about serious adverse effects, such as increased risk of injurious falls (5) and negative impact on the patient´s quality of life. For these reasons increasing interest has arisen in various non-pharmacological therapies, such as music, other forms of art, and interventions including cognitive, social or multisensory stimulation, or physical exercise (6). A growing body of evidence has accumulated showing the potential of music interventions in producing beneficial therapeutic effects in persons living with dementia (7). Although music-based therapies are now accepted as supplementary therapy of dementia in several national and international guidelines as supplementary rehabilitation method of dementia (8, 9), their effectiveness in managing specific neuropsychiatric symptoms is still contradictory.

Here we review the current literature concerning the efficacy of music-based interventions in relieving neuropsychiatric symptoms of dementia. Neuropsychiatric outcomes used in the studies include unspecified BPSD, depression, agitation, anxiety and apathy.

MATERIAL AND METHODS

The data analysed here were collected by literature search in the database PubMed using the search strategy "music AND dementia" and covering all published studies registered by March 31, 2025 (Figure 1). Search strategies "music AND (major) neurocognitive disorder" yielded one and 53 RCT´s, respectively, none of which dealt with dementia-level disorder. The initial search results were scrutinized independently by two investigators (PZ, SS). We included randomized controlled trials (RCT) applying both active and passive music interventions, i.e. the subjects physically participating in music making by singing or instrument playing or merely listening to music. We included interventions combining music with any form of simultaneous motor activity, varying from guided exercise or free movement in time with the music, to informal or formal dancing or casual movements, such as hand clapping. For cross-over studies, the period containing music intervention defined the length of intervention. Studies using repeated measures design (consecutive interventions with musical and non-musical periods offered for the same subjects) were included only if they involved a control group specifically for the music period. We excluded reviews, letters, commentaries and case reports.

Our objective was to analyse the factors behind mixed results of music-based therapies reported for BPSD. For this purpose, we categorized the responses of each intervention in superiority over standard care or superiority over non-musical control intervention: positive effects, significant difference at $p<0.05$ on the outcome measure used, indicating improvement of the patients´ condition, null effects (lack of positive effect compared to non-musical intervention or standard care) or negative effect (worsening compared to standard care, significant difference at $p<0.05$ on the outcome measures used, indicating worsening of the patients´ condition).

Statistical analysis was performed using Fisher´s Exact Test.

RESULTS

The search strategy is shown in *Figure 1* and the yield is summarized in *Table 1* and described in detail in *Table 2* (supplementary material). The total number of trials analysed was 55, comprising 65 interventions and 5430 subjects. The subject number is based on the primary recruitment, not taking into account reductions due to drop-out during the intervention or follow-up. The average number of patients per trial was 99 ± 181 (SD), range 14-976.

Intervention format was defined either as individual vs. group-based setting, or active (including physical participation) vs. passive (comprising mere listening) setting. Five trials lacked information on the first type of setting, while information on active vs. passive nature of the intervention was reported in all trials (65 interventions). 29 interventions (48%) used individual setting, and 31 interventions (52%) were group-based. 34 interventions (52%) included active participation, e.g. playing, dancing, hand clapping or other physical activities, while 31 interventions (48%) were passive, including mere music listening.

In the following analysis, we report the number of trials showing or failing to show beneficial effect of music for each class of symptom, and then specify the favourable or lacking effect of music intervention in comparison with non-musical control intervention or standard care (*Figure 2*).

22 trials, including 34 interventions, evaluated behavioural and psychological symptoms of dementia (BPSD) en bloc without further classification according to the Neuropsychiatric Inventory (NPI) (10). 15 trials showed in 21 interventions (62% of all interventions) an overall positive effect, i.e. alleviation of BPSD in response to music. Music rose above non-musical intervention in seven trials (10 interventions, 48% of positive responses) and above standard care in nine trials (11 interventions, 52% of positive responses). Eight trials showed in 13 interventions null effect, i.e. lack of positive effect by music as compared to non-musical intervention (five trials/interventions, 38%) or to standard care (six trials, eight interventions, 62%). No trials reported negative effect, i.e. increased BPSD due to music.

Depression was measured in 22 trials (28 interventions). Several validated clinical scales were used: Beck´s Depression Inventory (BDI) (11), Cornell Scale for Depression in Dementia (CSDD) (12), Geriatric Depression Scale (GDS) (13), Hospital Anxiety and Depression Scale (HAD-D) (14), Montgomery-Åsberg Depression Rating Scale (15) or Minimum Data Set (MDS) of the Resident Assessment Instrument (RAI) (16). 11 trials/interventions (39% of all interventions) reported positive effect, i.e. relief of depression. Response to music exceeded that of non-musical intervention in five trials/interventions (45%) and that of standard care in six trials/interventions (55%). Null effect was observed in 11 trials (15 interventions, 54% of all interventions). In five trials (eight interventions,53 %), music and non-musical interventions were equally effective. Six trials (seven interventions (47%) reported no response to music compared to standard care. Two trials/interventions (7% of all interventions), not shown in Fig. 1, reported a negative response, i.e. significant increase in depression score in the music group, while a decrease occurred in the non-musical control intervention group (17,18).

27 trials consisting of 32 interventions measured unspecified agitation using either long or short version of Cohen-Mansfield Agitation Inventory (CMAI) (19). No trial showed superiority of music over non-musical intervention. In seven trials (nine interventions, 28% of all interventions), music had a positive (soothing) effect compared to standard care. Null effect was reported in 19 trials (23 interventions, 72% of all interventions). Music and non-musical control showed an equal effect in 16 interventions (70%). Music had no effect over standard care in seven trials/interventions (30%).

Agitation was further classified as non-aggressive and verbally or physically aggressive subtypes in nine trials (12 interventions). Music produced a positive effect on non-aggressive agitation in four trials (six interventions, 50% of all interventions). It did not exceed non-musical intervention in any trial, yet it decreased non-aggressive agitation compared to standard care in four trials (six interventions). Music produced null effect on non-aggressive agitation in seven trials (10 interventions) including effects equal to non-musical control in six trials (9 interventions, 90%), and equal to standard care in one trial (10%). No intervention produced a negative effect, i.e. increase in non-aggressive agitation.

The effect of music on aggressive agitation failed to exceed that of non-musical interventions. As compared to standard care, music produced a positive effect in one intervention (8% of all interventions). Null effect on aggressiveness was observed in seven trials (10 interventions, 83% of all interventions). The effect of music was equal to non-musical control in five trials (six interventions, 60%) and equal to standard care in four trials (four interventions, 40%). In one trial/intervention (8% of all interventions), verbal aggression was increased after both music intervention and non-musical control intervention (20).

Anxiety was measured in 10 trials (13 interventions) using three scales, namely Rating of Anxiety in dementia (RAID) (21), Hospital Anxiety and Depression Scale (HAD-A) (14) or Hamilton Anxiety Rating Scale (22). Five trials/interventions (38%) reported a positive effect, i.e. decreased anxiety. In two trials/interventions (40%) music was superior to non-musical intervention and in three trials/interventions (60%) it was superior to standard care. Null effect was reported in six trials (eight interventions, 62% of all interventions), all of which were based on lack of difference between responses to music or non-musical interventions. No intervention increased anxiety.

Apathy was measured in only one small study using Dementia Care Mapping (23). The subjects listened to their preferred music (24). Live music resulted in relief of apathy, while recorded music had no effect compared to standard care.

In order to investigate whether the intervention format (individual vs. group; mere listening vs. active participation) is related to positive effect, we performed 2x2 analysis using Fisher´s Exact Test. No significant differences were observed.

Other neuropsychiatric manifestations included in NPI, such as disturbances of sleep, diurnal rhythm or nutrition, were not specifically reported in the present collection of studies.

Figure 1. Flow chart of the search strategy realized in PubMed using search terms "music AND dementia" and processed according the PRISMA 2020 Guideline (Page MJ et al., BMJ 2021;372:n71. doi: 10.1136/bmj.n71).

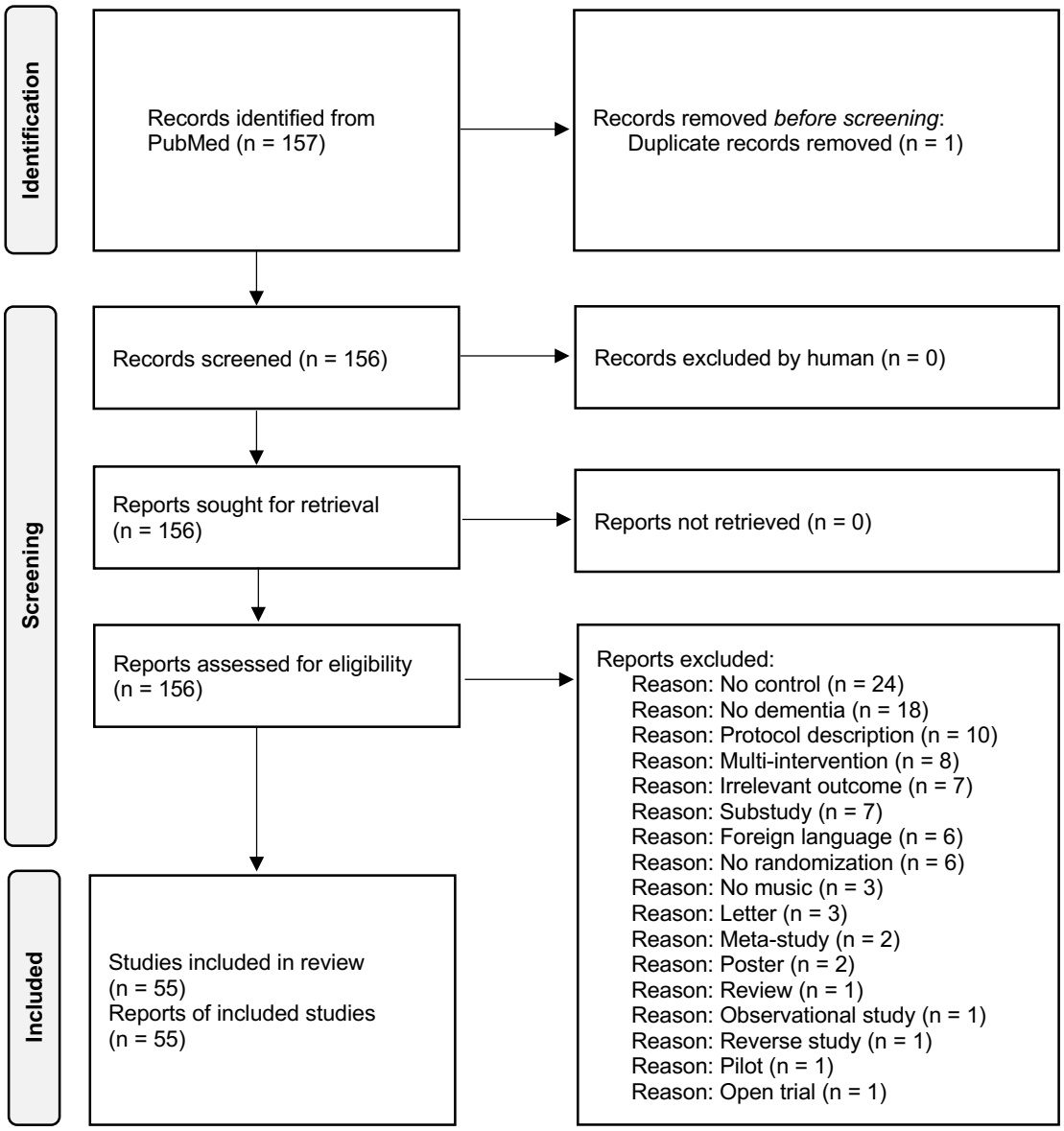
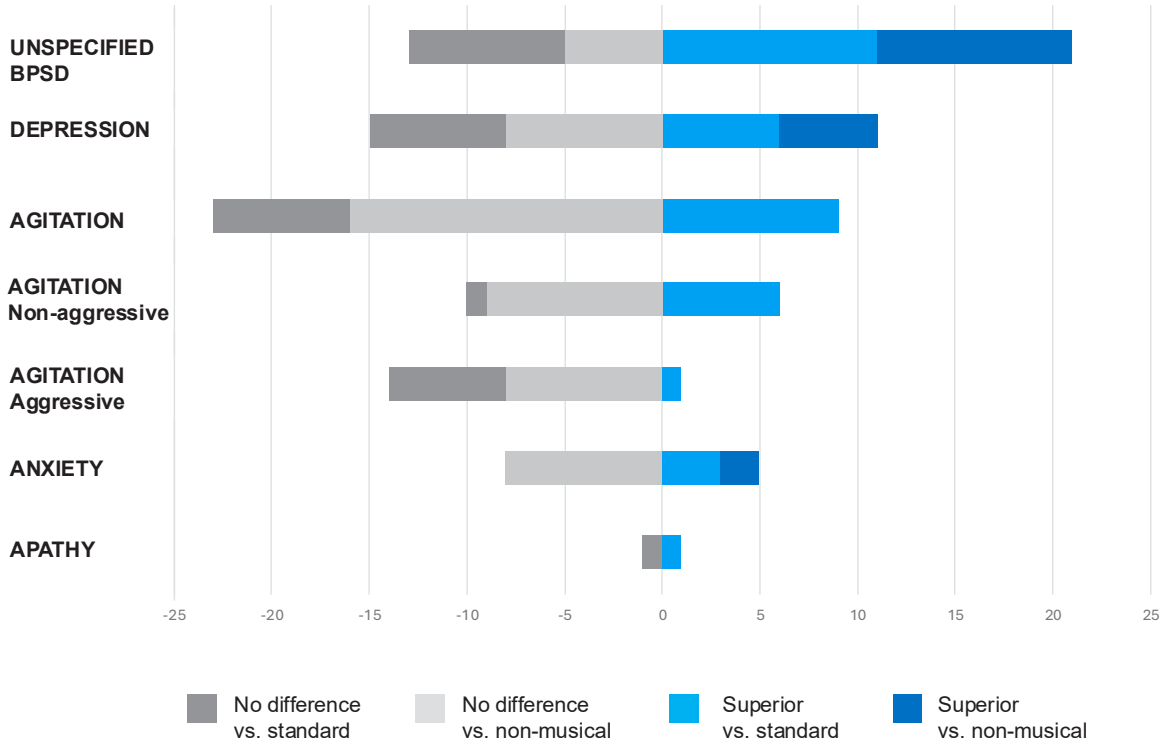


Table 1. Summary of randomized controlled studies analysed for neuropsychiatric symptoms.

		Neuropsychiatric symptom assessed	Number of studies	Number of subjects*
Total number of studies	55	Unspecified (BPSD)	22	1 466
Total number of subjects	5430	Depression	22	1 458
Studies applying preferred music	34	Agitation, unspecified	23	3 049
Studies including non- musical control intervention	28	Agitation, aggressive	9	653
Median duration of intervention (d)	56	Agitation, non-aggressive	9	653
Range 10 min - 224 d		Anxiety 10	10	551
Mean number of subjects	99	Apathy	1	32
Range 14 - 976				

BPSD=behavioural and psychological symptoms of deme
*Total number of subjects measured for each variable including musical and non-musical intervention groups and standard care group

Figure 2. Responses of persons with dementia to music interventions. Horizontal axis shows the number of interventions reporting the response indicated by the colour code. BPSD = behavioural and psychological symptoms of dementia. Please note that the number of interventions producing positive or null effect on non-aggressive agitation is greater than the total number of interventions, since in four interventions the effect was null or positive, depending on comparison with non-musical intervention or standard care, respectively. The bars representing null effects on aggressive agitation include two trials (four interventions) in which the response of music failed to differ from both non-musical intervention and standard care, making the total number of comparisons 14, although the true number of interventions producing null effect was 10.



DISCUSSION

Since 1997, over 100 systematic reviews and/or meta-analyses on music-based therapies for persons living with dementia have been published. The largest coverage so far is in the review by Lam et al., in 2020 [25], analysing 43 RCTs, some assessing outcomes other than neuropsychiatric symptoms. Of the most recent publications, the Cochrane Systematic Review (7) included 30 studies, 14 of which analysed neuropsychiatric symptoms. To the best of our knowledge, the present review of 55 RCTs, focusing exclusively on neuropsychiatric symptoms of dementia is the most comprehensive report published so far in this field.

In the present material, beneficial effects of music were reported for all outcomes studied. Yet, the percentage of interventions resulting in positive or negative outcome varied greatly. Music seems to be most beneficial in studies measuring unspecified BPSD (70% of interventions), followed by anxiety (45%), depression (42%) and agitation (35%). Apathy was measured only in one study applying two interventions, which resulted in contradictory responses. In estimation of overall effectiveness of music-based therapies, significance of positive outcomes is diluted by negative outcomes reported for all entities except for anxiety: BPSD (22% of interventions), depression (27%) and agitation (27%). In previous meta-analyses, negative outcomes have been reported for BPSD (26-28), depression (26,29-31), agitation and aggression (26,28,29,32-35). Considering this, our results are in line with the previous studies (7,25) in showing beneficial effects of music on neuropsychiatric symptoms of dementia, the firmest evidence obtained for general BPSD and depression, moderate level of evidence for agitation and anxiety, weak evidence for aggressiveness and very weak for apathy.

POSSIBLE EXPLANATIONS OF CONTRADICTORY RESPONSES

Our major goal was to appraise the divergence of responses to music interventions observed in the present material. The studies reviewed were published over a period of almost 30 years, during which time the diagnostic accuracy of dementia has substantially improved and led to earlier treatment onset. For around the same time, general awareness of the impact of music in rehabilitation has grown, and standard care has increasingly adopted musical elements. For these reasons old and recent patient cohorts may differ in clinical characteristics.

Heterogeneity of study design, measuring and reporting is a striking feature of the reviewed material. Recommended checklist for systematic reporting of data in studies of music-based interventions was first published in 2011 (36), and an attempt to reach a consensus on standardization of trials came out in 2022 (37). Yet, the analysis by Lepping et al. (38) revealed that standardization has been poorly applied. The checklist was updated in 2025 (39,40) to provide an efficient guideline for future studies.

Comparison of interventions resulting in positive or null effect does not support the hypothesis that the divergence is explained by the type (group vs. individual) or duration of intervention or by selection of music by patient vs. researcher. Estimation of the effect of disease severity is challenging, since only one study carried out severity-based subgroup analysis and only four studies exclusively included patients with defined severity of dementia (advanced stage of AD). In most studies the degree of dementia was not defined and varied from mild to severe. The possibility that the lack of effect of music may be due to natural disease progression warrants further investigation on subgroups of different severities. This issue would be clinically significant for optimal targeting of music-based therapies.

Failure of music in relieving depression in a third of the interventions is surprising, especially the observation that two studies reported worsened depression although patient-preferred music was selected for the intervention. Negative outcome did not correlate with the mode or length of intervention or the type of music, nor is it explained by difference in baseline depression. The possibility remains that depressive mood or clinical depression, which are both multifactorial and prevalent among elderly adults, are independent variables and may be caused by factors not addressed in baseline analyses.

In some studies, the data were provided by caregivers or institutional staff, in others they were collected by research personnel. Thus, the data may be subject to reporter bias due to over- or underestimation. Institutional staff and caregivers likely have a longer experience with the patient assessed and therefore may be more sensitive to observe minute changes in behaviour. Also, differences in care culture and leadership between facilities and exhaustion of personnel may have affected the accuracy of collected data.

RELEVANCE OF CONTROL GROUP

Music intervention was compared with standard care for all outcomes. This has been criticized for lack of specificity in meriting music for positive outcomes. Depending on context, musical intervention may include factors significantly influencing the outcome, such as positive social interactions, exchange of memories and inherent tendency to motor

activation. Therefore, lack of non-musical control intervention may lead to overestimation of music´s potency. On the other hand, increasing use of music in standard care may diminish apparent responses observed in trials. Therefore, in future studies it is necessary to describe the content of standard care in sufficient detail and preferably include both non-musical intervention and standard care as controls.

Some interventions included physical activity accompanied by music. Estimation of the specific effect of music would require a control group performing identical activities without music. Yet, both traditional music therapy, other music-based interventions and even music listening include various forms of motor activity, which cannot be controlled. Therefore, interventions combining music and motor activities were allowed to be included in the present analysis. We also included the study by Moreira et al. (30), in which the content of intervention changed over time, yet music was an essential factor in all interventions. Since processing of music in the brain involves extensive sensory, cognitive, emotional and motor activation and arouses individual associations (41), the question of music per se being therapeutic is highly elusive.

For all outcomes, except for apathy, music intervention was also compared with a large variety of non-musical interventions, including massage, reading, audiobook, simulated presence of relatives, cooking, art, aromatherapy, yoga, and educational, social or physical activities. Use of non-musical control emanates from the assumption that some of music´s effects may be due to other factors inducing positive responses. Generalizing conclusions of the results are difficult to draw, since some of the non-musical activities used are part of standard care in some, but not in all care units. Most studies applying non-musical control fail to present speculation of common effectors, let alone common brain mechanisms, of musical and non-musical stimuli

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STRENGTHS AND LIMITATIONS OF THE PRESENT REVIEW

We believe this is the largest collection of RCTs published so far on the effects of music-based interventions on neuropsychiatric symptoms among persons living with dementia. Notably, the temporal scope of the studies extends over almost 30 years, in which period the standards of research have changed, and therefore old and recent studies may not be fully comparable.

The competence of the persons giving the therapy varied. Some studies involved a trained music therapist, others used personnel instructed by a music therapist and some studies did not specify the competency of person providing the therapy.

Our analysis is semi-quantitative in nature, and comparisons between standard care, music and non-musical interventions are based merely on the number of trials or interventions without regard to the number of subjects in these studies.

Previous meta-analyses have aimed at revealing true positive outcomes, while the reasons for negative outcomes have not been systematically discussed. We have attempted to cover this gap.

CHALLENGES FOR FUTURE RESEARCH

We still have insufficient understanding of how the aetiology of dementia, patient´s age, gender, previous musical activity, cultural background or local resources of the healthcare system might affect the responses.

Most studies included in the present review are based on patients in institutional care, although, in fact, most persons living with dementia reside at home (42). Newly available diagnostic strategies will bring forward the time of diagnosis and increase the proportion of home-dwelling patients. A major goal for music-based rehabilitation is to postpone patient´s transfer to institutional care, which often is triggered by caregiver´s exhaustion. Future studies should focus on defining ways to optimize the caregivers´ compliance with music rehabilitation.

Implementation of music rehabilitation in persons living with dementia inevitably raises the question of added costs. In most studies professional music therapists have carried out the research protocols. Yet, in clinical reality implementation is left to regular staff. More research is needed to understand the personnel´s viewpoints, needs of training, demands for realization and rewards of music-based therapies (43). Newly developed technical devices, such as smartphone apps, online singing groups or virtual reality glasses, may offer novel and feasible opportunities with modest cost. On the other hand, most economical ways to realize effective music rehabilitation may be based on traditional set-ups, such as singing in group or group music reminiscence therapy, both shown to be effective for treatment of BPSD (44,45).

The studies reviewed here assess BPSD varying from mild to severe degree, yet remaining non-psychotic. Actually, many study protocols have excluded psychotic patients. Although psychotic symptoms are relatively common in dementia (4), the effects of psychotropic medication on music therapy´s effectiveness have not been addressed in the current material. Dopamine antagonists, such as risperidone, which is commonly used to manage BPSD, diminished healthy volunteers' reward experiences induced by music listening (46). Systematic study on these issues in clinical material is clearly needed. Interestingly,

incipient evidence is available to suggest that music therapy may be effective in treating dementia-related psychosis (47).

In conclusion, the present review demonstrates solid evidence for the efficacy of music-based interventions in managing neuropsychiatric symptoms in people with dementia. As for clinical implementation, the current data suggest that beneficial effects may be obtained regardless of format, i.e. both in individual and group setting, applying either mere music listening or formats involving active participation. Equally positive effects elicited by music and non-musical intervention in several studies raises the possibility that combination of various pleasant experiences may provide an optimal non-pharmacological treatment battery to manage PBSDs.

Supplementary Material

Supplementary data are available at Psychiatria Fennica online.

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