Music therapy in Huntington's disease

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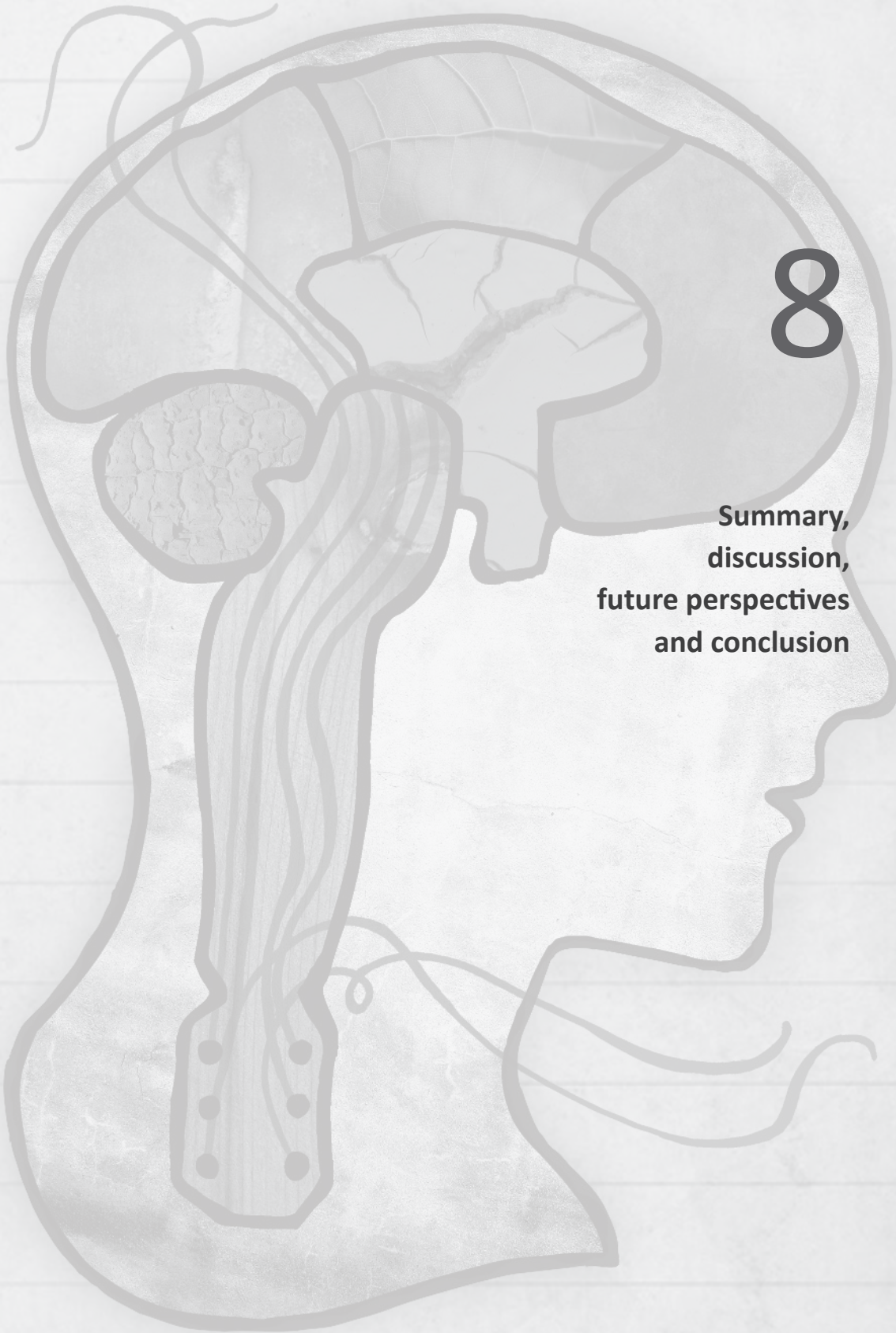

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Summary, discussion, future perspectives and conclusion

“Musik ist die schönste und zugleich die einzige Sprache,
die überall auf dieser Welt verstanden wird”

Johann Wolfgang von Goethe (1749 – 1832)

Summary

Huntington's disease (HD) is an inherited, progressive, neurodegenerative disease that is characterized by a triad of motor, cognitive, and psychiatric problems. The motor disturbance mainly consists of characteristic unwanted movements. The cognitive changes affect concentration, memory, executive functions, and acquisition of new information. Emotional disturbance often appears before the onset of motor or cognitive problems, and depression, irritability, impulsiveness and anxiety are common symptoms [1,2,3].

Due to the physical and cognitive skills, communication skills are gradually deteriorating, which contributes to a sometimes rapidly increasing inability to participate in different life situations [4]. This has a huge impact on the autonomy of the patient, often leading to an increase of behavioral problems. As a result, the quality of life (QoL) deteriorates along the progression of the disease. While there is no cure for the disease, the emphasis should be on the care of the patients, and more specifically on improvement or consolidation of their quality of life [4].

Music therapy is a non-pharmacological intervention that may have beneficial effects on improving communication and expressive skills in patients with HD. It is hypothesized that by improving these skills, the behavioral problems will improve, leading to an overall improvement of the QoL of patients with HD [5]. The general aim of this thesis was to determine whether this hypothesis could be confirmed through an experimental, quantitative study.

The first goal was to review the literature to define the state of knowledge on music therapy (MT) for patients with Huntington's disease **(Chapter 2).** This review revealed a paucity of literature on this topic. Precise aims and methods in relation to the stage of the disease, mostly derived from small scaled observational studies, are not well determined. This confirmed our assumption that there was a need to study the effectiveness of MT in this population.

Subsequently, we conducted a focus group study to investigate whether six experienced clinicians from different disciplines recognized a possible beneficial role for the music therapist at improving the QoL in patients with HD. The outcome of this study, described in **chapter 3**, revealed that the QoL-issues that were most mentioned, were psychosocial aspects, with sense of security, confidence and structure being the qualifications most outstanding. According to the focus group participants, as the ability to communicate and express oneself deteriorates over time, MT could play an important role in the treatment of patients with HD in all stages of the disease.

The insights of the focus group participants along with the literature review described in chapter 2 were used to design an empirical trial looking at the effects of MT on improving the quality of life of patients with HD by improving their communication skills. We designed a quantitative randomized controlled trial (RCT). This study was the first RCT with music therapy in patients with Huntington's disease with a large number of participating patients in the late stage of their disease. The design of this study is described in **chapter 4.**

The results of this single-blinded, multi-center randomized controlled trial are described in **Chapter 5.** Sixty-three HD-patients, admitted to four long-term care facilities in The Netherlands, were randomized to receive either group music therapy or group recreational therapy in 16 weekly sessions. The primary outcome measure was the communicative and expressive skills. The secondary outcome measure was problem behavior. Assessments took place at baseline, after 8, 16 and 28 weeks using (subscales of) the Behaviour Observation Scale for Huntington (BOSH) [6] and the Problem Behaviours Assessment-short version (PBA-s) [7]. A linear mixed model with repeated measures was used to compare the scores between the two groups.

The results of this study revealed that the beneficial effects of music therapy, recorded in many, mainly qualitative case reports and studies, could not be confirmed with the design and outcome measures we used in our study.

Before starting the trial we planned to perform a comprehensive process-evaluation alongside the effect study to investigate how the study was performed and to elucidate the results of the effect study. This evaluation, described in **chapter 6**, revealed several barriers and limitations of the study concerning (1) the characteristics of the source population, (2) the research methods and the outcome measures that were used, and (3) the set treatment goals. In the discussion below we will elaborate on these barriers and limitations, resulting in recommendations for future studies in regard to design and measurement tools.

Due to the vulnerability of the study population, in none of the aforementioned qualitative studies (i.e. the focus group study and the process-evaluation) the patient himself was directly involved. For this reason, giving the patient a face and a voice, and to show insight in the real-world context in which music therapy is practiced, two case-reports of patients with a successful response were described in **chapter 7**.

Discussion

The beneficial effects of music therapy could not be proven with the design and outcome measures that have been used in the present effect study [8]. This outcome could imply that either music therapy is not effective in HD, or that the chosen study design or the primary endpoints (communication and expressive skills and behavior) were not appropriate to show the effectiveness of music therapy.

Study design

When the efficacy of healthcare interventions has to be evaluated, the randomized controlled trial (RCT) is commonly accepted as the gold standard. Being the first study to assess the effect of group music therapy in advanced stage HD patients, the major strength of the present study is that an active control group receiving recreational therapy was involved. In most studies, the control group receives treatment as usual or no treatment.

The process-evaluation revealed the following limitations:

1. Randomization: the diversity of the clinical expression of HD and the characteristics of the source population mean that randomization is likely to be ineffective in distributing confounders evenly between groups [9].
2. As the study took place in four different facilities, we decided to do a center-stratified, block-permuted randomization to generate the random allocation sequence and to minimize the impact of any between-center differences on the trial results [10]. Taking the patients' feasibility and willingness to participate in the study into consideration, due to their cognitive deterioration, their highly fluctuating physical and emotional responses to treatment, and their diverse demographical, psychosocial and musical backgrounds, we anticipated a small group-size with a maximum of 5 participants.
3. Outcome measures: the set treatment goals (improving communicative and expressive skills) was the same for all participating patients.
4. Assessment tools: there are indications that the assessment tools that were used might not have been sensitive enough to capture changes in the intervention's primary and secondary endpoints (communication and expressive skills and behavior).
5. Below we will elaborate on these limitations, which are all conflicting with the definition of music therapy [4,5] in which it is specifically stated that treatment goals are to be individualized, addressing the patient's functional goals and adapted to their functional level.

The outcome measures in our study were chosen, based upon the premise that improving the communicative and expressive skills of the patients would lead to improvement of behavior, eventually leading to improvement of the patient's quality of life [5].

The choice for the BOSH and the PBA-s as assessment tools was based on the expectation that the items of these tools would detect changes in the chosen outcome measures [8]. However, according to the assessors who participated in the process evaluation [11] and in line with the literature [6,12], due to the cognitive state of the participants these tools might not have been sensitive enough to capture what we intended to measure. Besides that, a large floor effect could have been expected due to the nature of the study population for the PBA-s [13]. A paucity of efficacy studies of non-pharmacological interventions in HD may be a reflection of the lack of disease-specific standardized assessment tools for collecting consistent and reliable information relating to the clinical effects of interventions across the disease progression [12].

The existing standard tool that is used for clinical assessments (UHDRS) is considered to lack sensitivity to marginal clinical effects, particularly with regard to cognitive and psychiatric symptoms in the late stages of the disease [14]. A new scale, the UHDRS-FAP (For Advanced Patients) was developed in 2013 and appears to be more sensitive to change than the original UHDRS for cognitive and motor domains. The UHDRS-FAP is the only scale that detects decline in patients with a TFC-score ≤ 1, indicating a very low cognitive functionality. The tool was not validated yet when the present study was designed and executed.

Recently, a disease specific assessment tool for music therapy was developed for patients with advanced HD: The Music therapy Assessment tool for Advanced HD (MATA-HD) [12]. Since there is no evidence yet to support whether musical behaviors and responses in advanced HD bear any relationship to physical, psychological or social domains [12] a valid assessment tool capturing both musical and non-musical behaviors may reveal whether such relationships exist. The tool includes a total of 15 items across six subscales: arousal/attention, physical presentation, communication, musical, cognition and psychological/behavioral. 11 of the 15 items have a shared focus of engagement in therapy, while the good construct validity demonstrated by the communication items highlights the robustness of the tool in this important area. This is the first tool to guide clinical practice and assess responses to music therapy intervention. A pilot validation study of this newly developed tool has just finished in the UK [12]: preliminary data indicate that the MATA-HD is a promising tool for measuring patient responses to music therapy interventions across psychological, physical, social and communication domains of functioning in patients with advanced HD. The MATA-HD was not available yet when designing and executing the present study.

Adjusting the outcome measures to anticipated individualized goals, as stated in the aforementioned definition of music therapy, is desirable. Besides that, in advanced HD-patients the floor effects of the assessment tools mentioned above hamper the evaluation of these tools, thus calling for an adjusted scale. The Goal Attainment Scale (GAS) [15] is an eligible assessment tool: goal attainment scaling is a mathematical technique for quantifying the achievement of personalized goals that are set for each individual that is included in the study [16]. It must be noted that setting individual goals is challenging, specifically for patients with HD who are known to have poor insight in their condition [5], due to the cognitive decline.

Improvement of study design

Although the dialogue of clinical effectiveness in music therapy should not be dominated by the biomedical hierarchical model of evidence-based practice, Bradt [16] states that it is possible to design rigorous music therapy RCTs that accurately estimate music therapy treatment benefits if certain conditions are met and adjustments made. No matter how complex the intervention and the study population, with an unambiguous written protocol, the carefully and accurately chosen outcome measures and assessment tools, and a continuous evaluation and monitoring throughout the whole study, barriers can be by-passed or avoided, and facilitators can be empowered [16].

Different research questions demand different types of research methods and evidence [16]. Experimental studies with quantitative outcome measures stay important for clinicians and policy makers. Quantitative data alone however give insufficient information to come to a good judgement concerning the effects of a complex intervention and the impact these effects have on the patients.

When developing a complex intervention, it is important to consider the context and circumstances in which the intervention will be executed. Often, observational or qualitative research is necessary preceding the RCT to clarify which aspects of the problems are appropriate to reach the set goals. When designing such interventions, knowledge of the context is essential and using qualitative or observational studies alongside the quantitative experiment may support meeting the set goals [17].

In the present study, the above-mentioned recommendations were met for the most part: preceding the RCT a comprehensive literature study was executed [4], followed by a qualitative study using focus group discussions [5]. Alongside the present RCT we performed a process evaluation using a mixed method of qualitative and quantitative data [11].

Recommendations for improvements or adjustments for the clinical practice and future studies are made below.

Future perspectives

For future study designs, the following possibilities can be taken into consideration to avoid the barriers and limitations that were encountered:

- Executing a pilot or feasibility study [16]: during the pilot study, issues related to study recruitment, attrition, and treatment adherence can be explored, and preliminary data on treatment efficacy can be obtained. During this phase, the research team develops the treatment manual, the protocol for training study personnel, and treatment fidelity procedures.

- Individual therapy sessions: the care for vulnerable patients as the ones with HD demands an individual approach in order to meet the complex needs of these patients. Taking the differences in cognitive state of the group-members into consideration, individual therapy to deliver the planned intervention components is recommended.

- The power of music therapy lies in the fact that the sessions can be tailor-made, meeting the individual set goals of each patient [4,5]. The use of the aforementioned GAS assessment tool [15] is recommended to set these goals.

- Other good alternatives for future studies might be the use of the aforementioned UHDRS-FAP (Unified Huntington's Disease Rating Scale- For Advanced Patients) [14] or the MATA HD (Music therapy Assessment Tool for Advanced HD) [12] after being validated.

- Designing a multiple single subject design study: this is a research design often used in applied fields of psychology and human behavior in which the subject serves as his/her own control, rather than using another individual or group. These designs are highly flexible and highlight individual differences in response to intervention effects on different domains [18]. With single-case course studies we comprehend the process of change of clients or patients with regard to the complexity of music therapy [19].

- Involving family members: in future research designs, the involvement of caregivers in the experiment should be taken in consideration, as this will help improve communication skills between the patient and his caregiver outside of the music therapy [5]. This will be the most beneficial outcome and will undoubtedly lead to improvement of the QoL for both patient and caregiver [5]. Also, the voice of the HD patient and caregiver can be an invaluable resource in helping to determine directions for clinical trials [20].

In order to prove the effectiveness of music therapy, the randomized controlled trial (RCT) as a "stand-alone" study is not the appropriate research design unless it is preceded by, executed alongside or supplemented with other observational or qualitative studies and unless the most eligible and feasible endpoints are being chosen and assessment tools are being used (see the aforementioned recommendations).

Conclusion

When evaluating interventions that have the potential to improve quality of life, finding the best study design and the best outcome measures for patients in the advanced stage of HD remains the major challenge. The challenge for the music therapy researcher is to find alternative study-designs and to learn from the experiences of other complex intervention studies. This asks for all multidisciplinary team members surrounding the patient with Huntington's disease and academic scholars to be willing to learn, to cooperate and to be creative [17].

In an effort to contribute to the evidence base of music therapy through RCT-research (based on the aforementioned assumption of the RCT being the gold standard research design to prove the efficacy of healthcare interventions), this design was chosen for the present study. Performing a multi-center RCT studying the efficacy of music therapy with vulnerable patients in a long-term care facility turned out to be feasible but challenging.

However, in the practice of music therapy, the rules that apply for conducting a RCT, where the intervention to be studied must be standardized in order to compare the intervention and the control group, are considered impediments or difficulties to be overcome [9,21]. The definition of music therapy, stating that goals are to be adapted to the clients' functional level to accomplish individualized goals are in conflicting with the RCT-rules.

The added value of music therapy is that the intervention can be adjusted to the individual needs and possibilities of the patient. The individualized way of engaging with music in therapy is what makes the therapy effective. Therefore, it is not the content of the intervention that should be standardized, but the function of the intervention. In so doing, the therapists are free to integrate any techniques or method to reach specific goals while following a standardized process [9,21].

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