Music therapy in Huntington's disease
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Music Therapy in Huntington's Disease

Monique van Bruggen- Rufi

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Music therapy in Huntington's disease

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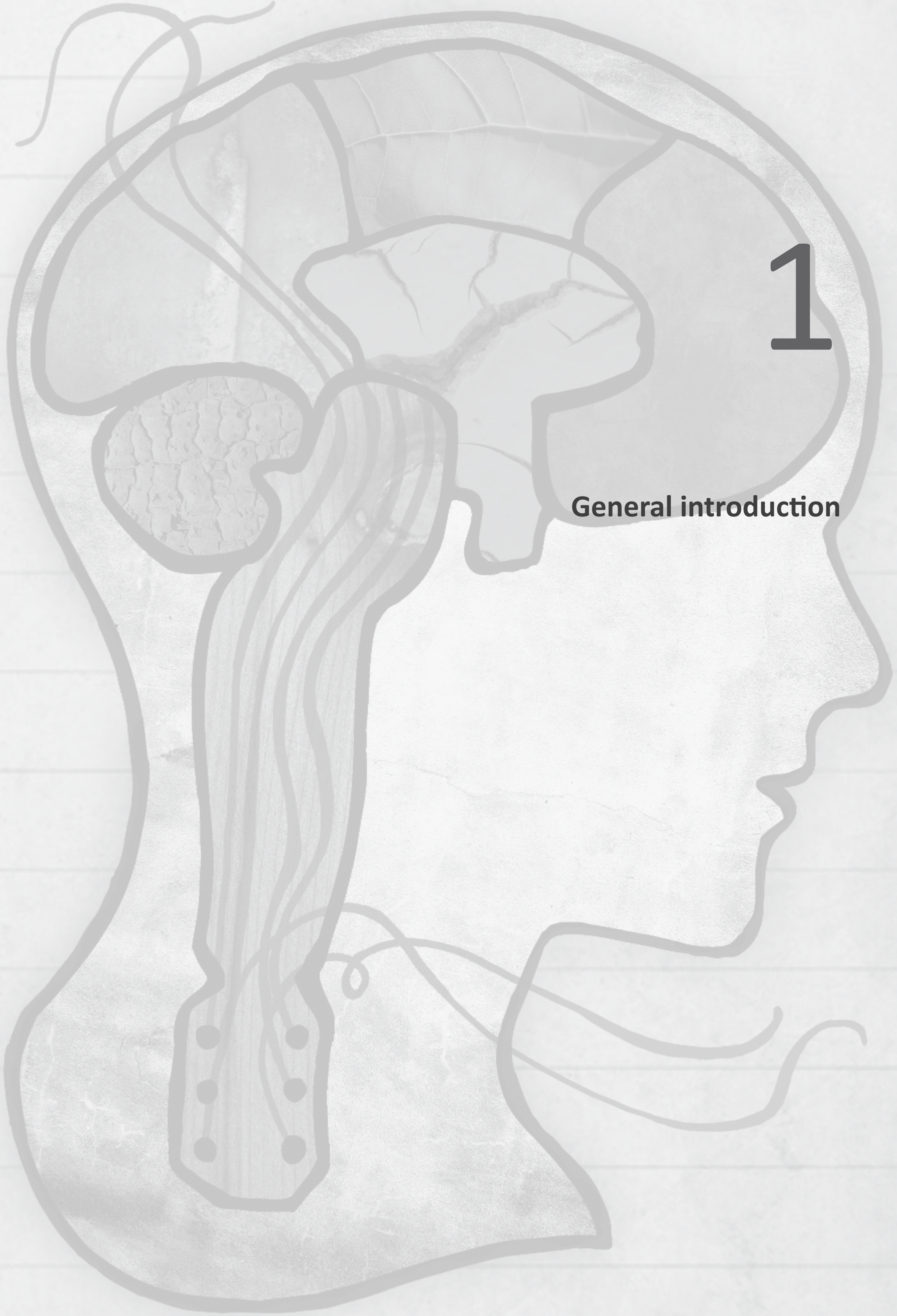
Prof. dr. G. Kwakkel, Vrije Universiteit van Amsterdam

Contents

*Die Tanzenden wurden für verrückt gehalten von denjenigen,
die die Musik nicht hören konnten.*

Friedrich Wilhelm Nietzsche (1844 – 1900)



1

General introduction

Huntington's disease

Huntington's disease (HD) is an inherited rare autosomal dominant disorder, caused by a mutation in the HTT-gen, causing progressive neural degeneration of the basal ganglia and gradual atrophy of frontal and temporal cortex [1]. The disease is characterized by movement disturbances, neuropsychiatric disturbances and cognitive deterioration leading to a complete dependency for daily life activities [2]. Clinically, a great variation in age at onset, duration of illness, and course of the disease is seen. The mean age of onset is between the age of 30 and 50 years, and once manifest, the patient's life expectancy is about 15-20 years [3]. Three clinical stages can be described: Stage I, in which patients develop initial symptoms but are still independent. Stage II, patients become more dependent as the disease progresses. Stage III is the end-of-life stage: patients become completely dependent for all daily life activities [2,3]. The prevalence of HD in Europe, North America and Australia is about 10 per 100.000 [4]. In the Netherlands there are approximately 1,700 persons with HD.

Communication problems in HD

The characteristics mentioned above often result in loss of expressive and communicative skills, especially in the advanced stage of the disease. Verbal communication is often affected, due to motor impairment of speech. In addition, as a result of the cognitive decline, word retrieval is often impaired, although the knowledge of vocabulary is retained. As the disease progresses, the language content can no longer be processed properly and adequate communication becomes challenging [1].

The gradual deterioration of the communication skills contributes to a sometimes rapidly increasing inability to participate in different life situations [5]. The communication problems may have a great impact on the quality of life of the patients and formal and informal carers.

Behavioral problems in HD

Behavioral problems are common among patients with HD. They are an important feature of HD and contribute to impairment of quality of life [6]. The most common symptoms are loss of energy and initiative, poor perseverance and quality of work, impaired judgment, poor self-care and emotional blunting. Affective symptoms such as depression, anxiety, apathy and irritability also occur frequently [7].

While there is no cure for HD, the emphasis is on the care of patients with HD, especially those in the advanced stage of the disease [2]. The aim of all treatment is on improving the quality of life of patients with HD. Music therapy could be a complimentary, non-pharmacological intervention to reach this goal.

Music therapy

Among the many definitions of music therapy, the most used one is the one from the American Music Therapy Association (AMTA) which describes music therapy as follows:

> " Music therapy is the clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program" [8].

Music therapists assess emotional well-being, physical health, social functioning, communication abilities, and cognitive skills through musical responses. Music therapists design sessions for individuals and groups based on client needs using music improvisation, receptive music listening, song writing, lyric discussion, music and imagery, music performance, and learning through music. Finally, they are part of the multidisciplinary team and thus participate in interdisciplinary treatment planning, ongoing evaluation, and follow-up [8].

Music Therapy and Huntington's Disease

As the ability to communicate and express oneself deteriorates over time, music therapy could play an important role in the treatment of patients with HD in all stages of the disease. Through music therapy an additional means of communication can be provided, enabling the patient to express his or her needs and emotions, and to recall life experiences which in patients with HD is also affected.

Specific literature about MT in HD is scarce. Research into the effect that music therapy has on HD began to develop in the late 1970's and early 1980's. Studies include: speech facilitation through singing [9], music and movement programs [10], emotional expression by use of song-writing [11], participation and communication [12]. The results of a music therapy referral audit by Daveson (2007) revealed that patients with HD were most likely to be referred to a music therapist due to a need for emotional expression, and the maintenance of communication skills and social relationships. [13]. In a comprehensive systematic literature review (see chapter 2 of this thesis), Bruggen-Rufi Van and Roos [14] conclude that music therapy interventions vary throughout the different stages of the disease and are not yet applied optimally. Not the stage of the disease, but the individual treatment goals (see table below) seem to be more determinative for the music therapy indications.

In conclusion, precise aims and methods in relation to the stage of the disease, as well as the effectiveness of music therapy, are not well determined (see table "Music Therapy and HD: Referrals and Goals" in chapter 2). There is a need for a systematic study to determine the indications to use music therapy and to study the effectiveness of music therapy in HD [14].

Despite positive findings in the field, studies linking music therapy and HD together are limited. Therefore, review of the broader field of neurodegenerative diseases that have similar symptoms to HD is essential to develop the theory building about MT and HD further.

Over the past decades, music therapy (MT) has been developed for patients with other neurodegenerative diseases, such as dementia [15,16]. There is evidence that music therapy influences emotional well-being positively and that participation in music therapy increases social response in persons with dementia, thus providing additional means of communication and enabling the patient to express his or her needs and emotions [17,18]. Through music, contact can be established, especially as language functions deteriorates during the later stages of the dementia process [19]. Furthermore, enhancing the ability for self-expression, contributing to improvement of the quality of life, has been reported by Lee and McFerran who describe five females in a multiple case study with profound and multiple disabilities using patient preferred song-choices in music therapy [20]. The patient can be stimulated to recall life experiences through music. In the music therapy session this can be used as a catharsis to experience emotions. In a recently update Cochrane review on music-based therapeutic interventions for people with dementia [21] the authors conclude that music therapy may reduce depressive symptoms.

Based on the above-mentioned benefits, the assumption can be made that MT is beneficial to patients with HD on communicative and expressive skills. Improvement of these skills might lead to improvement of behavior, eventually leading to improvement of the quality of life of patients with Huntington's disease [14].

Aims and outline of this thesis

The specific aim of this thesis was to explore the effectiveness of music therapy in patients with HD. To achieve this goal, the first step was to study the available literature on music therapy in HD. The result of this literature search is described in **chapter 2**.

Subsequently, we conducted a focus group study to investigate whether six professionals from different disciplines, who all have a considerable amount of years of clinical experience with patients with HD, recognized a possible beneficial role for the music therapist in relation to improvement of the quality of life for people with HD. The outcome of this study is described in **chapter 3**.

Both the literature and the focus group study helped us to design a randomized controlled trial to study the effect of music therapy in HD. The protocol of this RCT is described in **chapter 4**. The study and the results of the RCT are described in **chapter 5**.

Performing a multi-center RCT studying the efficacy of music therapy with vulnerable patients in four different long-term care facilities is considered to be a complex intervention. In order to elucidate the results and to investigate how the study was performed, we conducted a process-evaluation. This process-evaluation, described in **chapter 6**, highlighted the many barriers and facilitators to perform such a complex intervention, and the outcome helped us to elucidate the results of this quantitative effectiveness study, resulting in recommendations for future studies in regard to design and measurement tools.

In **chapter 7**, two case reports with two patients who benefit from music therapy are described for illustration. At the same time, these case examples give the reader some insight in the real-world context in which music therapy is practiced.

Finally, the main conclusions of this thesis are summarized and discussed in **chapter 8.** In this chapter we will build on the definitions of music therapy to determine whether the methods that we used throughout this thesis were in compliance with these descriptions, followed by future perspectives and closing remarks**.**

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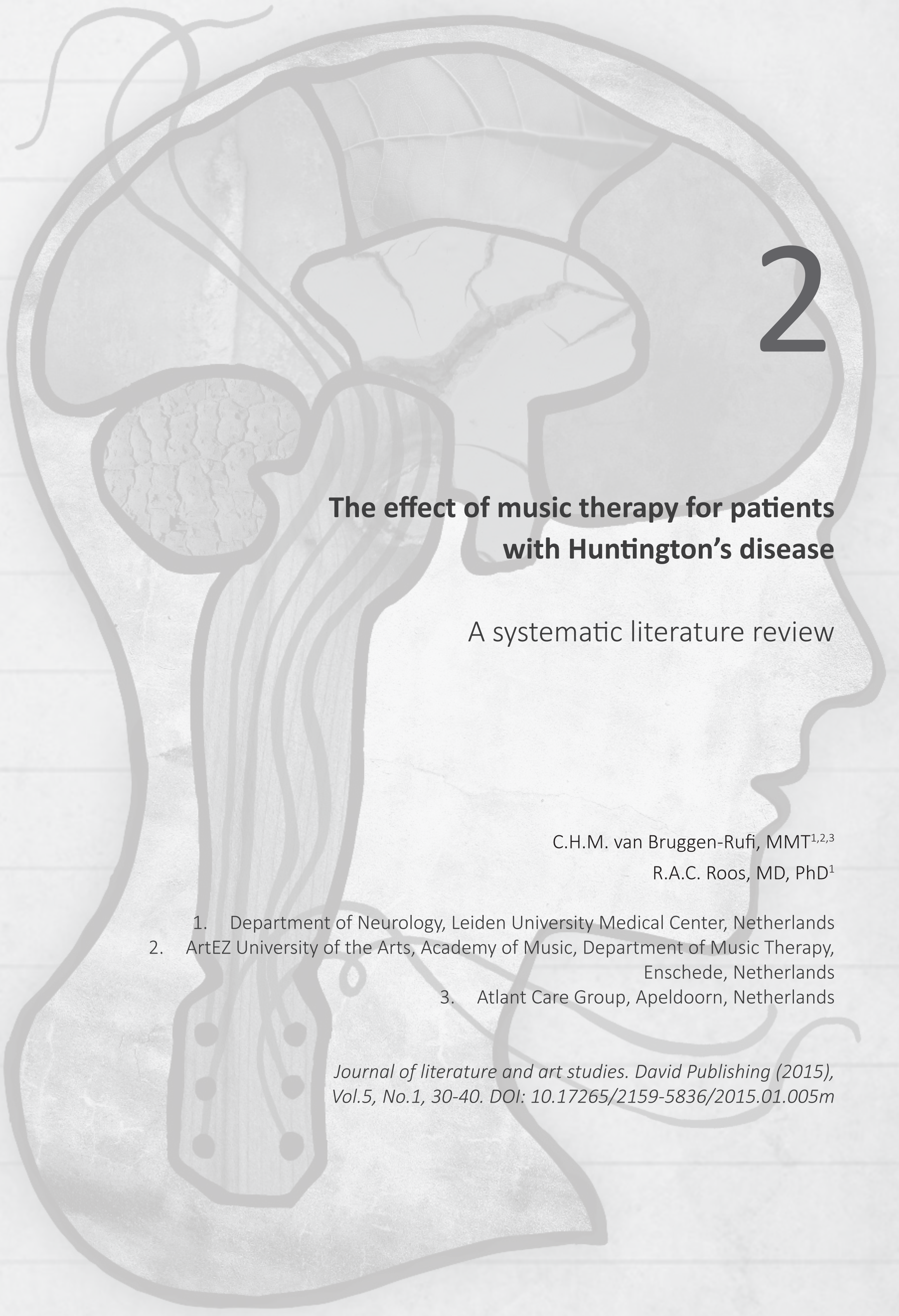
“One good thing about music, when it hits you,
you feel no pain”

Bob Marley (1945 – 1981.) Uit: “Trenchtown rock”



2

The effect of music therapy for patients with Huntington’s disease

A systematic literature review

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Journal of literature and art studies. David Publishing (2015), Vol.5, No.1, 30-40. DOI: 10.17265/2159-5836/2015.01.005m

Abstract

Huntington's disease is a progressive, neurodegenerative, autosomal dominant disease characterized by motor- and psychiatric disturbances, and cognitive decline. Since there is no cure, all treatment is aimed at improving quality of life (QoL). One form of non-drug therapy which is barely recognized, is music therapy. The literature on its use and effect in patients with Huntington's disease is limited. We therefore performed a detailed literature survey in order to delineate the different types of music therapy interventions and their aims. Music therapy studies were included when targeting: (1) motor disturbances; (2) cognitive disturbances; (3) psychiatric disturbances; and (4) emotional/social disturbances. A total of eight studies that met these criteria were analyzed. We found that music therapy interventions vary throughout the different stages of the disease and are not yet applied optimally. Not the stage of the disease but the individual treatment goals seem to be more determinative for the music therapy indications. In conclusion, precise aims and methods in relation to the stage of the disease are not well determined. There is a need for systematic study of this treatment option.

Introduction

Huntington's disease (HD) is a rare neurodegenerative disorder of the central nervous system. It is a progressive, autosomal dominant disease, characterized by a triad of symptoms and signs, consisting of: (1) motor disturbances: chorea and hypokinesia; (2) cognitive decline; and (3) psychiatric disturbances: depression and behavioral changes (Roos, 2010). The prevalence of HD ranges from 1 : 143 in Venezuela to 1 : 10.000.000 in the black population of South Africa. In the Caucasian population the prevalence is estimated to be between 5 and 10 per 100,000 (Al-Jader, Harper, Krawczak, & Palmer, 2001).

The disease can be roughly divided into three stages: the early, the middle, and the late stage. As the disease progresses, the dependability of the patient increases. Admission to a long term care facility (LTCF) is unavoidable in most cases.

To date, there is no drug to cure or delay the onset of the disease. The majority of drugs is prescribed to treat the motor and psychiatric signs. Besides medication, many other non-drug interventions are available such as physiotherapy, occupational therapy, speech therapy, dietician advice, psychological support, social worker help, and music therapy. All treatment must be individually tailored, as the symptoms and signs are different for each person and change over time. The intention of all forms of treatment is to improve quality of life (Roos, 2010).

The term quality of life reflects the overall status of a combination of factors: a person's health, symptoms, and level of physical and social functioning. Functional and cognitive impairment are significantly correlated with the patient' s QoL (EHDN website[1]; Ready, Mathews, Leserman & Paulsen, 2008). Health-related quality of life (HrQoL) is defined as follows: "The optimum levels of physical role and social functioning, including relationships and perceptions of health, fitness, life satisfaction and well-being" (Bowling, 1995).

Ho, Gilbert, Mason, Goodman, and Barker (2009) conclude that depressive mood and functional ability are critically linked to health-related QoL in HD. In a previous study, Helder, Kaptein, Kempen van, Houwelingen van, and Roos (2001) conclude that physical and psychosocial symptoms have a great impact on the patient's well-being.

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In 2011, the European Huntington's Disease Network (EHDN) Quality of Life Working Group initiated a qualitative research study on the impact of HD across the entire disease spectrum (Ho & Hocaoglu, 2011). The outcome provides important implications for the management and development of interventions throughout all stages. The physical/functional theme peaked throughout the different stages, indicating that these issues were raised more frequently over the course of the disease. There were no significant changes between stages for the emotional and social themes. The cognitive impairments only featured in the early and middle stages. In the advanced late stage, the cognitive theme hardly featured any more, probably due to the degree of cognitive impairment which affects insight at this stage (Ho & Hocaoglu, 2011). Also, in the late stages, the physical impairments become more and more evident which makes determination of the cognitive, emotional and social themes extremely difficult.

In the attempt to meet the needs of the individual, the challenge is to find adequate responses and to develop relevant and effective therapeutic strategies (Gilbertson, 2005; Aldridge, 2005). One form of non-drug therapy which is barely recognized, is music therapy. Music therapy recognizes individual needs and can be adapted to meet them. Over the past decades, music therapy is developed for patients with neurodegenerative diseases, recognizing the individual needs of the patients (Cohen-Mansfield, 2000).

What is Music Therapy?

The American Music Therapy Association (AMTA)[2] defines music therapy as follows:

> "Music therapy is the clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program".

Music therapists assess emotional well-being, physical health, social functioning, communication abilities, and cognitive skills through musical responses. Music therapists design music sessions for individuals and groups based on client needs using music improvisation, receptive music listening, song writing, lyric discussion, music and imagery, music performance, and learning through music. Finally, they are part of the multidisciplinary team and thus participate in interdisciplinary treatment planning, ongoing evaluation, and follow-up (AMTA website).

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[2] American Music Therapy Association [homepage on the Internet. Retrieved from: http://www.musictherapy.org. Last accessed December 23rd, 2013].

History of Music Therapy

The first use of music in relation to illness can be traced back to ancient Egypt. More systematic studies on the effects of music on physiological processes such as cardiac output, respiration, pulse rate, and blood pressure were first carried out at end of the 19th century. Nowadays music is provided for relaxation purposes and pain relief (Bradt & Dileo, 2009).

The 20th century discipline began after the First World War when musicians went to Veteran hospitals around the country to play for the thousands of veterans suffering from physical and emotional traumas. It was soon evident that the hospital musicians required some prior training before entering the facility and so the first music therapy degree programme was initiated in 1943 in the United States. In 1998, the American Music Therapy Association (AMTA) united the National Association for Music Therapy (founded in 1950) and the American Association for Music Therapy (founded in 1971) (AMTA website).

During the last decades, new MRI techniques have made it possible to visualize the brain while playing or listening to music (Peretz & Zatorre, 2009). Studies have revealed that each musical parameter (e.g., rhythm, melody, harmony, pitch) seems to engage a broad network of brain regions (Patel, 2008). Processing the musical structure appears to trigger networks in the prefrontal and the interior frontal cortex, superior temporal poles and the cerebellum. When the music is emotionally meaningful to the listener, activity extends to the ventral tegmental area, the accumbens nucleus and the hypothalamus (Levitin, 2009).

It has been revealed that music and motor control share specific neural circuits. This has led to the assumption that music could improve movement problems in patients with Parkinson's disease and Huntington's disease (Thaut & McIntosh, 2010). Also, music has been shown to activate distinct neural pathways in the brain associated with emotion, such as the insula and cingulate cortex, hypothalamus, hippocampus, amygdala, and prefrontal cortex (Juslin & Sloboda, 2010). It has, therefore, been suggested that many more patients with dementia and other age-related conditions, developmental and learning disabilities, substance abuse problems, brain injuries, physical disabilities, and acute and chronic pain, could benefit from this treatment (Magee & Davidson, 2008; Schmid & Aldridge, 2004; Thaut, 2005).

There is evidence that rhythmic auditory stimulation improves gait in patients with Parkinson's Disease (PD) (Thaut et al., 1996). Pacchetti et al. (2000) showed in a randomized controlled, single-blinded study beneficial effects of music therapy on affective and behavioral functions in PD patients.

Based on the insights mentioned above one can assume that music therapy could be a suitable non-drug intervention for HD. We, therefore, reviewed the literature to find out the different techniques, the primary outcome measures, and assessments used in music therapy in HD.

Methodology

A systematic literature search was conducted for any related publication, published between 1950 and 2014, in the following databases: Medline/PubMed; Embase, Cinahl, PsychINFO/PsycIndex, and Web of Science. The following terms were included: music, music therapy, in combination with the terms Huntington and Huntington's disease.

Furthermore, (hand)searches were carried out in specific music(therapy) databases, such as:

- CAIRSS (Computer-Assisted Information Retrieval Service System), a bibliographic database of music research literature, including national and international Music Therapy journals;
- The Center for Biomedical Research in Music (CBRM);
- The digital database of the Music Therapy Neurology Network (MTNN);
- The Nordoff Robins Music Therapy Research Program.

Also, specific music therapy journals were (hand)searched including the Journal of Music Therapy and Music Therapy Perspectives, as well as reviewing reference lists of the relevant publications. Finally, conference proceedings and dissertation abstracts were reviewed.

The following inclusion criteria were used:

- Participants had to be formally diagnosed as having Huntington's disease;
- Music therapy had to be involved, targeting any of the following symptoms and signs that play a role in the quality of life of patients suffering from HD: (1) motor disturbances; (2) cognitive disturbances; (3) psychiatric disturbances; and (4) emotional/social disturbances.

The references used in this article were purposefully limited to publications that focused specifically on music therapy. All music therapy references in relation to Huntington's disease were retrieved and reviewed (see Figure 1).

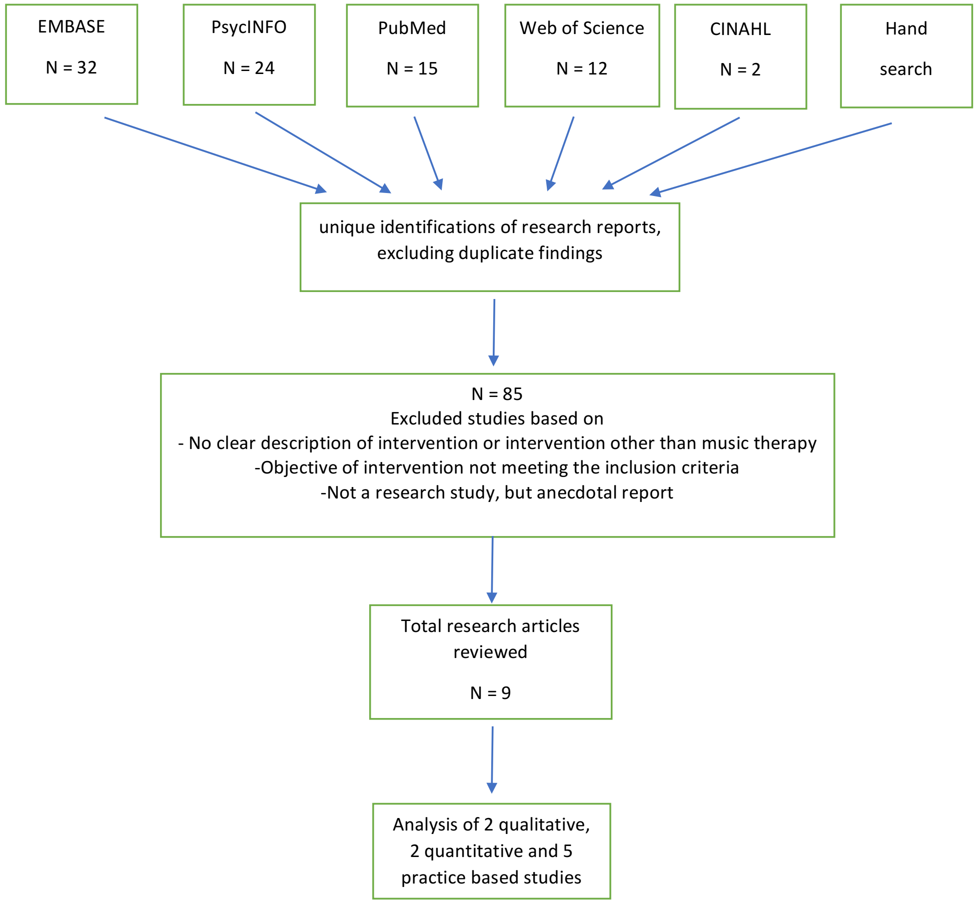

Figure 1. Flow chart search string (last search May 13th, 2014).

Results

The literature contains many case reports suggesting that music therapy may have an effect on the function of people with neurodegenerative diseases. The majority of these articles describe the development of music therapy practice, illustrated by single case studies, clinical reports, and descriptions of methodology. The reported benefits of music therapy for neurodegenerative diseases in general are summarized in Table 1 (Aldridge, 2005).

Table 1 Benefits of Music Therapy for the Neurodegenerative Diseases

Meets the needs of individual patients and their characteristics
Promotes dialogue and the maintenance of an identity that has a broad repertoire of possibilities
Reintegrates the person within a communicative ecology and prevents isolation
Offers a flexible temporal structure for processing temporal information where timing can be temporarily recovered and practiced
Utilizes gestural abilities, including utterance, binding events together that are indicative of ability
Gestures seen as attempts to regain cognition, not seen as failed abilities
Encourages rhythmical movement
Regulates emotional arousal in terms of expression and inhibition with implications for sufferers and caregivers
Needs can be expressed
Motivates communication and participation without being speech dependent
Attention, arousal, affect and action embodied in musical form

Note. Source: Aldridge, 2005.

When searching for the (MeSH)terms "Huntington's Disease, Music and Music Therapy" we found a total of 85 references. After omitting the duplicates and the articles not fulfilling the inclusion criteria, nine articles remained: five practice based studies, two quantitative studies and two qualitative studies.

The practice based and quantitative studies were screened on research design (see Table 2). The music therapy goals and interventions described in the reviewed articles were categorized according to the targeted symptoms and signs that play a part in the quality of life op patients suffering from HD, i.e., physical (motor) (*n* = 5), cognitive (*n* = 3), psychiatric goals (*n* = 1), and social/emotional goals (*n* = 5) (see Table 3).

Practice Based Studies

Hoskyns (1982) focused on the effects of music therapy on counteracting anxiety and frustration by encouraging relaxation and group participation, and on reducing choreic movement by use of singing, playing, and listening. The most significant findings were that group singing seemed to be very beneficial and that playing musical instruments increased the choreic movement. Observation indicated a positive change in behavior of the participants, but little long term effect. Observation also suggested that listening to music aids in relaxation.

Rainey Perry (1983) conducted another relevant study in 1983. Over a period of eight month she offered music therapy sessions to small groups (six to eight participants). She developed three types of sessions: (1) music and movement; (2) music and communication/relaxation; and (3) sing along. She found that small music therapy groups helped maintain and improve functioning in the following areas: participation, communication (both verbal and nonverbal), concentration, memory, relaxation, movement, self-esteem, self-expression, and social interaction.

Magee (1995a, 1995b) focused on different stages of HD and how different music therapy interventions could be shaped to meet the changing needs throughout disease progression. She states that in the early stage the need for active participation in music therapy is desirable, preferably individual sessions. In the mid-stage group, participation is recommended, firstly because participating in a group gives the patient more time to react (and thus less confrontation with his decline), secondly because the other patients in the group can be used as a model for other group members. Finally, in the late stage the use of receptive methods is recommended in group-settings. Active playing of an instrument for as long as possible is encouraged.

Brandt (2000) investigated the effect of performing a favorite song on the involuntary movements of six HD patients in the mid- and late stage. She concluded that there was no significant difference in effect between singing the favorite song and reduction of involuntary movements. Davis and Magee (2001) explored the use of a particular music therapy intervention. They describe a study about the use of structure within musical (active) improvisations with an HD-client. The main goal was to improve the expressive responses and to support interaction by increasing communicative contact through musical parameters.

Quantitative Studies

Grocke-Erdonmez (1976) conducted the first study into HD and music therapy in 7 HD patients. She focused on the stimulation of expressive speech through melodic speech therapy. She did find that several patients were able to sing out words that they had previously had trouble articulation through speech.

Thaut, Miltner, Lange, Hurt, and Hoemberg (1999) investigated the rhythmic synchronization ability of 27 HD patients under different conditions and circumstances using the Rhythmic Auditory Stimulation (RAS) techniques. The gait speed of most of the patients could be changed in the direction of the RAS cue. Synchronization of the steps was more difficult for patients in the early stage of the disease. Thaut et al. (1999) concludes that the ability to process auditive stimuli decreases as the disease progresses, due to deterioration of the cognitive abilities.

Table 2 Practice Based and Quantitative Studies, Screened on Design

Author and year of publication	Design	Setting	Participants and HD-stage	Goals	Outcome measure	Outcome results
Erdonmez-Grocke, 1976	Clinical observational trial with control group	Clinical setting, individual treatment	*N* = 2 mid-stage *N* = 5 late stage	Stimulation of expressive speech	Rating of 3 tests (pre-mid-post) through discussion tapes	No statistical evidence for improvement of expressive speech
Hoskyns, 1982	Observational trial	Holiday Care facility, group treatment	*N* varied per session, stage of participant varied per session	Counteract anxiety and frustration, group participation, encouraging relaxation, reducing choreic movement		Playing instruments increases choreic movement. Listening to music aids relaxation. Short term positive change in behavior
Rainey Perry, 1983	Observational trial	Clinical setting, group treatment	*N* = 6-8, middle to late stage	Increase/maintain participation, attention,awaress, interaction, providing opportunities for self-expression Increase relaxation, communication Encourage participation		Improvement of participation, communication, concentration, memory, relaxation, movement, self-esteem, self-expression and social interaction
Magee, 1995	Single case study, needs based perspective	Day care facility, individual treatment	*N* = 1 early stage	Providing emotional outlet and means of expression		Active participation in individual music therapy is recommended
		Clinical setting, group treatment	*N* = 1 mid-stage	Choice making, improving attention, concentration, encouraging verbalization, stimulate participation, improving social skills, avoiding isolation		Group treatment is recommended, both active and receptive music therapy
		Clinical setting, group treatment	*N* = 1 late stage	Maintaining attention, making decisions, expression, identity		Receptive music therapy in group setting is recommended
Thaut et al., 1999	Clinical trial	Individual sessions	*N* = 27 all stages	Velocity modulation and rhythmic synchronization of gait	Baseline setting, pre- and post-test of gait. Statistical analysis (ANOVA)	Gait speed changed using RAS, however synchronization negatively impacted in early stage
Brandt, 2000	Practice based clinical observational trial	Clinical setting, individual treatment	HD mid- and advanced stage, *N* = 6	Reducing unwanted movements/ stimulating voluntary (wanted) movements	Rating videotapes of 1 session by 2 raters	No significant evidence for reducing while listening to favorite song
Davis & Magee, 2001	Practice based single case study		HD *N* = 1	Stimulating interaction and communication, organizing responses		Music can offer opportunities for interaction and communication

Table 3 Music Therapy and HD: Referrals and Goals

Physical (motor)	Cognitive (dementia)	Psychiatric (behavior) And psychosocial (emotional)
Encourage relaxation and reduction in choreic movement (Hoskyns, 1982)	Encourage group participation (Hoskyns, 1982)	Counteract anxiety and frustration (Hoskyns, 1982)
Increase/maintain movement, increase relaxation, (Rainey Perry, 1983)	Providing opportunities for self-expression, encouraging participation (Rainey Perry, 1983)	Stimulating communication (Rainey Perry, 1983)
Preservation of vocal abilities, demonstrate and maintaining physical strength (Magee, 1995a, 1995b)	Improvement of memory function, organizing information, musical interaction, initiation (Magee, 1995a, 1995b)	Stimulating active participation, avoiding isolation (Magee, 1995a, 1995b)
Gait improvement (Thaut et al., 1999)	ecall of information espite memory function terioration (Magee, 1995a, 1995b)	Developing relationship, increasing communicative contact (Davis & Magee, 2001)
Modulating velocity (Thaut et al., 1999)	Choice making (Magee, 1995a, 1995b)	Stimulating expressive speech (Grocke-Erdonmez, 1976)
Reducing involuntary movements/stimulating voluntary movements (Brandt, 2000)	Increasing/organizing responses (Magee, 1995a, 1995b)	Preserving expressive and communication skills (Daveson, 2007)
Improvement of physical presentation (Daveson, 2007)	Improving cognitive skills (Davis & Magee, 2007)	Enabling emotional expression (Daveson, 2007)
		Improving behavior problems (Daveson, 2007)

Qualitative Studies

In two qualitative studies the indication for music therapy is discussed and categorized according to the targeted symptoms and signs that play a part in the quality of life of patients suffering from Huntington's disease. The first study conducted by Daveson (2007) details the findings of an audit of music therapy referrals in a specialist in-patient setting for 16 patients with advanced Huntington's disease. These findings indicated that patients were most likely to be referred due to a need for emotional expression (*n* = 10; 29%), maintenance of communication skills and social relationships (*n* = 9; 26%). Furthermore, 14% of the referrals were due to occupation (*n* = 5), 11% to physical presentation (*n* = 4), 11% to behavior (*n* = 4). Cognitive factors were seldom a reason for referral (*n* = 3; 9%).

The second study (Bruggen van-Rufi, 2010) details the findings of a qualitative study, conducted among different members of the multidisciplinary team (*n* = 14) in a nursing home specialized in HD in The Netherlands. As in the study by Daveson (2007), the aim of the study was to investigate the music therapy indications in this setting and to compare the findings with the referrals in four other specialized care HD units in The Netherlands.

In this study, emotion, communication, and self-expression are most often mentioned as treatment goals for music therapists. Goals in cognitive and physical areas are less recognized. Multidisciplinary collaboration is well established in most of the clinics.

Discussion

In this study we reviewed the literature describing the effect of music therapy on improvement of the quality of life of Huntington's disease patients. In doing so we specifically aimed at the effect of music therapy to influence (1) motor disturbances; (2) cognitive disturbances; (3) psychiatric disturbances; and (4) emotional/social disturbances. Furthermore we studied the different music therapy techniques used, the primary outcome measures and assessments used in music therapy with people suffering from Huntington's disease. Subsequently we tried to discover a relation between these issues and the indication for music therapy, the stage of the disease, and the quality of life.

There seems to be a discrepancy between the indication for music therapy and the quality of life issues mentioned by the clients themselves (Ho & Hocaoglu, 2011). On the one hand, conclusions are drawn stating that psychosocial and emotional issues are most often mentioned as being indications for music therapy (Daveson, 2007), while on the other hand, physical and functional problems seem to peak throughout the different stages (Ho & Hocaoglu, 2011). In a later study, the focus was on the role of music in assisting patients to organize their responses. This indication is recognized and supported by the rationale of Davis and Magee (2001). Improvement of motor features during the musical intervention was, however, beyond the scope of their study.

There seems to be no significant change in treatment goals between the different stages as far as the emotional and social themes are concerned, whereas Magee (1995a, 1995b) emphasizes that different goals should be met throughout the different stages. However, Magee bases her conclusions on observational studies in only one patient. Not the stage of the disease but the individual treatment goals seem to be more determinative for the music therapy indications. However, a relation between these two issues is plausible.

Thaut et al. (1999) state that certain goals can no longer be met, most probably because of the decline of cognitive abilities throughout the different stages. This is more obvious when patients are given different instructions. Delval et al. (2009) confirm the difficulties with multi-tasking in people with HD, due to attention deficit.

The sample size of Brandt (2000) was too small (*n* = 6) and the study consisted of only one music therapy session, so no useful conclusions could be drawn. Furthermore, the type of music as well as the manner in which it is offered in the different interventions raises questions (Magee, 1995b; Brandt, 2000): would different music styles, different instruments, different approaches have made the difference? Unfortunately there are no comparative studies of how these factors influence meeting the treatment goals.

The outcome of the two aforementioned qualitative studies confirms the lack of referrals to music therapy due to a cognitive need. Obviously, in contrast with Alzheimer's disease where cognitive decline is the primary outcome measure, this is not an indication for music therapy in Huntington's disease. These findings can be supported by Leng et al. (2003) who identified that therapeutic interventions cannot assist with regaining cognitive abilities throughout HD progression.

The findings of the two qualitative studies (Daveson, 2007; Bruggen van-Rufi, 2010) are in line with the role that has been highlighted within the practice literature: Music therapy can be used to provide a means of self-expression, social interaction, and communication.

Conclusion and recommendation

Music therapy interventions used to improve quality of life for people with HD vary and are not applied optimally. In none of the studies that we reviewed quality of life was the primary outcome. In our opinion, this also has to do with the fact that there is no consensus about which items of quality of life matter most for HD-patients, or at which stage of the disease (Ho et al., 2009; Helder et al., 2001; Ho & Hocaoglu, 2011). Due to the changing needs of the patient, the treatment itself has to be adjusted to the individual needs that are important at that specific moment. Being alert to the patient's signals demands flexibility from all members of the therapeutic team. The aim of the therapy might not be to restore or regain function, but rather to maintain function and provide opportunities for compensatory behavior to be supported, developed, and rehearsed (Thaut et al., 1999). Functional training can be combined with cognitive, emotional, and communicative/relational approaches. In so doing, the music therapist makes a link between medical and psychological treatment. Within music therapy, the medium of intervention (the music itself) does not have to be changed. In our opinion, therefore, music therapy could be a suitable non-drug intervention for improving the quality of life of those living with HD in every stage.

The majority of articles that examined different music therapy interventions to improve quality of life of people living with HD were derived from observational studies. However, it must be noticed that the studies were often small scaled and the number of music therapy sessions were limited. Therefore we plan a systematic study of the effect of music therapy in HD.

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“La musique exprime ce qui ne peut être dit
et sur quoi il est impossible de rester silencieux”

Victor Hugo (1802 – 1885)

3

Improving quality of life in patients with Huntington’s disease through music therapy

A qualitative explorative study using focus group discussions

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Abstract

Huntington's disease (HD) is a progressive, neurodegenerative, autosomal dominant disease, characterized by motor disturbances, behavioral and psychological symptoms and cognitive decline. These characteristics often result in loss of expressive and communicative skills, especially in the advanced stage of the disease, frequently giving rise to behavioral problems such as anxiety, irritability and apathy. Music therapy is potentially a good non-pharmacological intervention to improve communication skills and thus possibly reduce behavioral problems, leading to a better quality of life (QoL) overall.

As there is little knowledge on how music therapy may contribute to improve the QoL in HD, a qualitative research was conducted to gain insight: a focus group study was performed, following the guidelines of naturalistic inquiry and grounded theory. In three open-structured group discussions, participants (six HD professionals with different experience with and knowledge about music therapy) were asked to reflect on what defines QoL in HD and on the potential role of music therapy for clients with HD.

The results show that, according to the focus group participants, psychosocial aspects seem to be the most important aspects which contribute to improve QoL in HD-patients, with sense of security, confidence and structure being the qualifications most mentioned. Autonomy and self-esteem are other important QoL factors. The participants stated that the stage of the disease and the living conditions of the patient are crucial. Poor insight, unawareness and denial, all due to cognitive decline, mean that it is extremely difficult for patients to reflect on their own QoL. As the ability to communicate and express oneself deteriorates over time, music therapy could play an important role in the treatment of patients with HD in all phases of the disease. By providing an additional means of communication, thus enabling the patient to express emotions, music could be used as a mood-indicator to determine in which state of mind the patient is.

This article describes six HD-clinicians' perception of quality of life for patients with HD and the potential role music therapy can play in improving the QoL of patients with HD using focus group discussions. These insights were used to inform an empirical trial looking at the effects of music therapy on improving the quality of life of patients with HD.

Introduction

Huntington's disease

Huntington's disease (HD) is a rare autosomal dominant neurodegenerative disorder, caused by a mutation in the HTT-gene. This progressive disease is characterized by movement disturbances, neuropsychiatric disturbances and cognitive deterioration leading eventually to a complete dependency for daily life activities (Roos, 2010). Once manifest, the patient's life expectancy is about 15-20 years (Bates, Tabrizi, &Jones, 2014). Three clinical stages can be described: Stage I, in which patients develop initial symptoms but are still independent. Stage II, patients become more dependent as the disease progresses. Stage III is the end-of-life stage: patients become completely dependent for all daily life activities (Bates et al. 2014; Roos, 2010).

Many patients first present with neuropsychiatric or cognitive disturbances. Affective (mood) disorders (e.g. depression, anxiety, apathy, irritability) and behavioral problems (e.g. obsessive compulsive behavior and aggression) are often observed (Duijn van, Kingma, & Mast van der, 2007) and are recognized as being most distressing for both patients and their caregivers; they are often the main reason for institutionalization (Hamilton, Salmon, Corey-Bloom, Gamst, Paulsen, Jerkins, Jacobson, & Peavy,(2003) . Psychosocial stressors may include feelings of sadness and anxiety about the cognitive and physical decline and about changes in social role. They cause a great burden on the emotional well-being of patients with HD and their quality of life (A'Campo, 2012).

Verbal communication is often affected because of motor impairment of speech rather than a reduced desire for verbal communication (Ho, Robbins, Walters, Kaptoge, Sahakian, & Barker, 2004). A qualitative study on communication in HD, using interviews and focus groups with patients, family members and professional caregivers, found that all participants acknowledged the need for increased involvement in social life in order to enhance communication (Hartelius, Jonsson, Rickeberg, & Laakso, 2010). However, the gradual deterioration of communicative skills contributes to a decrease in functional health and an increasing inability to participate in various life situations. This may have a great impact on the quality of life of the patients, often leading to behavioral problems (Nance, Paulsen, Rosenblatt, &Wheelock, 2011).

Due to the progressive nature of the disease, cognitive losses accumulate throughout the different stages. The cognitive decline often results in behavioral problems and dysexecutive behavior (Ho & Hocaoglu, 2011). However, the patient's self-image doesn't seem to change throughout the stages. According to Ho, Robbins, & Barker (2006), patients with HD tend to underestimate consistently and persistently the degree of their dysexecutive behavior. There are three underlying components: cognition, self-regulation and insight. McCusker & Loy (2014) use the term “unawareness” when a patient’s perception of obvious disease manifestations and impact differ from that of observers, such as clinicians or family members. Unawareness (or anosognosia), also described as denial and coping mechanism, correlates with disease progression, disease severity contributing to it to a more significant extent than disease duration (Sitek, Thompson, Craufurd, & Snowden, 2014).

To date, there is no cure for HD, nor can its progress be reversed or slowed down. All treatment must be individually tailored, as the symptoms and signs are different for each patient and change over time. The goal of all forms of treatment is to reduce any discomfort and pain, eventually leading to improvement of quality of life (Roos, 2010).

Quality of Life

One of many definitions of Quality of Life (QoL) is “…an individual’s perception of his position in life in the context of the culture and value systems in which he lives and in relation to his goals, expectations, standards and concerns” (World Health Organization (WHO), 2002). QoL is multidimensional and includes domains that are related to physical, mental, emotional and social functioning and the social context in which people live (Ferrans, 2005). How these domains are related to patients with HD is illustrated in figure 1.

A distinction has to be made between the term QoL and Health-related Quality of life (HrQoL). The first term reflects the overall status of a combination of factors: a person’s health, symptoms and level of physical and social functioning (Ready, Mathews, Leserman, &Paulsen, 2008). The latter is defined as “an individual’s perception of his or her health and health-related domains of well-being” (WHO). In the present study we will use the term QoL indicating the health-related domains.

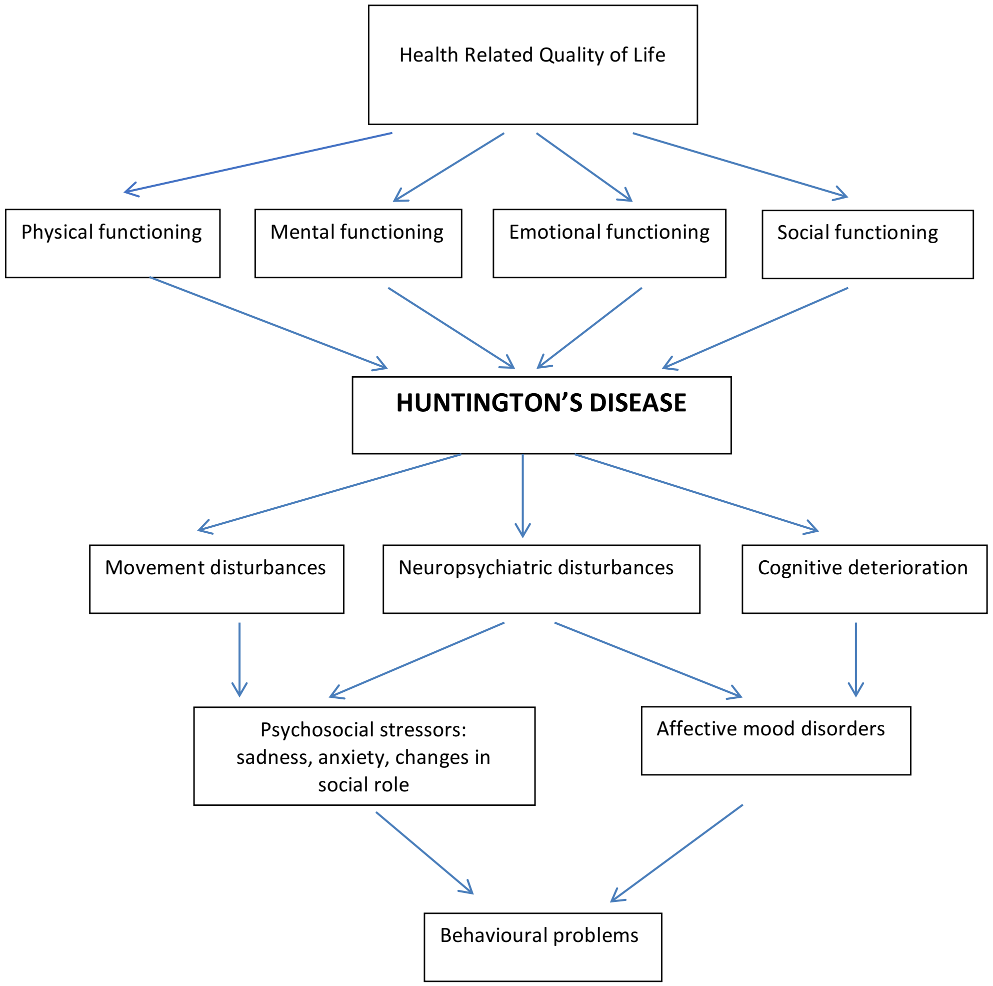

Figure 1: The four domains of health related quality of life in relation to Hungtington’s disease

Quality of life and Huntington’s disease

During the last few decades, several studies have been performed with the aim of determining which factors matter most with regard to the QoL of patients with HD. Helder, Kaptein, Kempen van, Houwelingen van, & Roos, (2001) concluded that physical and psychosocial symptoms have a great impact on the well-being of HD-patients, the latter being more severely affected. The accompanying motor, cognitive and personality changes can be held responsible for this outcome. It should be noted that in this trial the researchers restricted themselves to assessing motor and cognitive disabilities of HD-patients; no depression measure was included. Ho, Gilbert, Mason, Goodman, & Barker, (2009) conclude that depressive mood and functional ability are critically linked to QoL in HD. This outcome is underlined by Ready et al. (2008) who state that depression is a strong predictor of QoL in HD and that motor impairment, independent functioning and cognitive impairment had lesser yet significant associations with QoL. When focusing on the QoL and HD, there is reason to suspect that neuropsychiatric symptoms are particularly harmful. These symptoms are common in HD and include high rates of depression, suicide, obsessive compulsive disorder and personality change. Also, psychopathology tends to be more severe in HD (Ready et al., 2008).

In 2011, the European Huntington's Disease Network (EHDN) Quality of Life Working Group initiated a qualitative research on the impact of HD across the entire disease spectrum (Ho &Hocaoglu, 2011). Semi-structured face-to-face interviews were individually conducted with 31 persons living with different stages of HD, from pre-clinical gene carriers to advanced stage. Physical and functional decline peaked throughout the different stages, indicating that these issues were raised more frequently by the patients over the course of the disease. There were no significant changes between stages for the emotional and social domains. Cognitive impairments were only raised in the early and middle stages. In the advanced late stage, the cognitive impairments hardly featured any more. As mentioned previously, the patient's self-image is most probably the cause of this contradiction; it is the degree of cognitive impairment which affects insight at this stage. Also, in the late stages, the physical impairments became increasingly evident which makes determination of the cognitive, emotional and social domains extremely difficult (Ho &Hocaoglu, 2011).

Until a decade ago the QoL of patients with HD could only be assessed using generic QoL-measurement scales (Helder et al., 2001), (Hocaoglu, Gaffan and Ho, 2012). These generic tools are unlikely to capture the total and true impact of the more specific and unique consequences of HD, particularly the many non-physical aspects of the disease.

There has been little consistency in QoL models within the literature in the past 10 years. Providing an overview of the many concepts is beyond the scope of the present study. However, in the process of finding the concepts that best describe QoL in HD, the World Health Organization International Classification of Functioning, Disability and Health-model (WHO-ICF) is worth mentioning (WHO). This model is not specific to measuring HrQoL, it is more a mapping and classification framework than a guide for hypothesis generation in the area of HrQoL (Bakas, McLennon, Carpenter, Buelow, Otte, Hanna, Ellett, Hadler, & Welch, 2012). This model focuses on functioning (body-functioning and structures) and disability (activities and participation), but also addresses contextual factors (both environmental and personal). There are several disease-specific tools that measure QoL-related domains for patients with HD, such as the Behavioral Observation Scale Huntington (BOSH) (Timman, Claus, Slingerland, Schalk van der, Demeulenaere, Roos, & Tibben, 2005), the Problem Behaviour Assessment (PBA) (Kingma, Duijn van, Timman, Mast van der, & Roos, 2008), or the Unified Huntington's Disease Rating Scale (UHDRS) (Huntington Study Group, 1996). However, these tools all have limitations or lack sensitivity to marginal clinical effects in the later stages of the disease (Timman, 2005). The UHDRS-FAP (For Advanced Patients), developed in 2013 (Youssov, Dolbeau, Maison, Boissé, Cleret de Langavant, Roos, & Bachoud-Lévi) is more sensitive to change in the advanced stages of the disease.

A disease-specific patient-reported QoL outcome measure was developed in 2012 by Hocaoglu et al., 2012: the Huntington's Disease health-related Quality of Life questionnaire (HDQoL). The HDQoL consists of three sets of scales: (1) the primary scale representing the core factors underlying health-related quality of life in HD, (2) the specific scales representing clinically meaningful HD-specific profiles of pertinent aspects of health-related quality of life, and (3) the summary scale. The different scales that can be derived from the HDQoL can suit different clinical or research purposes. The HDQoL aims to fully capture the impact of HD on the everyday life of the sufferers. The HDQoL is valuable in promoting more fully informed decision-making in the management of HD, eventually leading to more effective treatments (Hocaoglu et al., 2012).

Music therapy, Huntington's disease and other neurodegenerative diseases

The literature on the use of music therapy and its efficacy in patients with Huntington's disease is limited. In a detailed literature review, Bruggen van-Rufi & Roos (2015) describe that music therapy interventions used to improve QoL for people with HD vary greatly. Most articles that were analyzed were derived from observational studies, were often small-scaled and the number of music therapy sessions was limited.

In none of the reviewed studies, was QoL the primary outcome. Music therapy interventions vary throughout the different stages of the disease. It is not the stage of the disease but the individual treatment goal which seems to determine the indication for music therapy. Precise aims and methods in relation to the stage of the disease have not been well established.

Since there is a paucity of literature about the effects of music therapy in HD-patients,
it is justified to search for such effects in other, similar neurodegenerative diseases, especially

dementia in general, dementia of the Alzheimer's disease (DAT) and Parkinson's disease (PD). Since the prevalence of these diseases in today's society is much larger than HD, there has been more extensive music therapy research into DAT and PD. However, comparison with these disorders needs to be done with some caution as these conditions have different impacts on the brain and central nervous system.

HD has some similarities with dementia and PD in that these disorders cause the brain, as in HD, to deteriorate progressively, affecting mental, cognitive and motor functions. Dementia (loss of mental abilities) is common in neurodegenerative disorders (Liou, 2010). Dementias are often classified by the region of the brain that is affected. PD and HD are sub-cortical based and AD is cortical based. Although this classification is rather controversial among researchers and physicians, some differences do exist, but there is disagreement on the degree of differences. Cortical dementia (AD) has more impact on semantic and episodic memory while patients with sub-cortical dementia (HD and PD) do not experience degradation of semantic memory per se; they find it challenging to accomplish cognitive tasks that require retrieval, but this will improve under the right conditions (i.e. being "cued") . Furthermore, sub-cortical dementias almost always result in motor disorders. In terms of cognitive effects, differences between dementias are still being studied (Liou, 2010).

The literature provides us with useful conclusions from scientific research investigating the benefits of music therapy with dementia and PD that may also apply for HD.

Music therapy provides stimulation and may help to prevent social isolation for elderly individuals suffering from more advanced dementia. If words are no longer recognized, familiar music may provide a sense of safety and well-being, which in turn may decrease anxiety (Brotons, 2000). Listening to music is significantly more effective in increasing levels of engagement and well-being than not being exposed to music, regardless of the level of cognitive impairment in people with slight to severe dementia (Sheratt & Thornton, 2004). In an in 2011 published updated Cochrane-review, an overall beneficial effect of music therapy with dementia could not be supported, but positive effects were found specifically in decreasing problem behavior (Vink, Bruinsma, & Scholten, 2011). In the recently update Cochrane review on music-based therapeutic interventions for people with dementia the authors conclude that music therapy may reduce depressive symptoms (Steen van der, Soest van-Poortervliet, Wouden van der, JBruinsma, Scholten, & Vink, 2017). Music therapy can decrease agitation and has a positive effect on enhancing communication and emotional well-being (Vink, Zuidersma, Boersma, Jonge de, Zuidema, & Slaets, 2012). Music therapy enables the recall of life experiences and the experience of pleasant emotions. Through music, contact can be established, especially as language deteriorates during the later stage of the dementing process (Vink, 2013).

In a "state-of-the-art"-article on music therapy and Parkinson's Disease, Raglio (2015) concludes that interventions that involve music can offer important starting points in PD rehabilitation, effectively acting on motor, as well as non-motor symptoms. Although only a limited number of studies take the psychological outcome into account, an earlier research by Pacchetti, Mancini, Agilieri, Fundaro, Martignoni & Nappi (2000) showed a significant overall effect on motor improvement and beneficial effects on emotional functions, activities in daily living and quality of life. They concluded that MT is effective on motor, affective and behavioral functions.

In general, throughout the literature on music therapy and neurological disorders it is suggested that researchers need to focus on the remaining abilities of patients rather than focusing on the abilities that are diminishing (Van Beek, 2012). In a trial where the cognitive burden in HD is explored throughout the different stages, Papoutsi, Labuschagne, Tabrizi, & Stout (2014) support this idea by stating that "...enhancing cognitive reserve through cognitive interventions is very promising, because these interventions are noninvasive and readily available to be used (...) together with other more invasive therapeutic approaches for later disease stages. Such research has been limited thus far in HD (...) HD would be an ideal model to test such methods..." (Papoutsi, Labuschagne, Tabrizi, & Stout, 2014), p. 680).

Elaborating on this assumption, we decided to develop a focus group study to explore if music therapy could be such an intervention. The main purpose of the present study was to describe the perceptions of different HD-clinicians on music therapy. Understanding these perceptions will help us gain insight in the potential role the music therapist can play in the multidisciplinary team surrounding patients with HD.

Method

The focus group method is a qualitative research method to collect data using guided group discussions in order to generate a rich understanding of participants' experiences and beliefs. The discussions create a process of sharing and comparing among the participants, investigating issues of context and depth, and generate their own interpretations of the topics (Morgan, 1998). Powell & Single (1996) state that the focus group method is appropriate if

- a certain topic is very complex (as is QoL) and needs to be explored from different points of view.
- a large number of variables needs to be reduced to the most essential ones; since QoL is such a wide concept, the question what matters most in QoL was discussed extensively.
- little is known about a certain topic (music therapy to improve QoL); the focus group method has an explorative character and generates hypothesis.

Guidelines of two methods were followed: the naturalistic inquiry (Lincoln & Guba, 1985) and the grounded theory (Glaser & Strauss, 1967). The first is a method in which a series of techniques is used to conduct qualitative research. Using these techniques, the method emphasizes the trustworthiness of the trial, which is important in evaluating its value.

The second is a systematic methodology that is used to construct a theory through the analysis of data. On reviewing the collected data, recurring ideas and concepts become apparent. As more data are collected and reviewed, concepts become categories which form the basis for new theory.

The three main research questions were:
Based on your own clinical experience

- what is QoL in general for patients with HD?
- what are the most important aspects of QoL in patients with HD?
- Could music therapy play a role in order to improve QoL in patients with HD?

These questions were continuously repeated during all three meetings.

Participants

Six HD-professionals specialized in five different treatment areas participated in the study. They were recruited by way of homogeneous purposive sampling: they were chosen because of their rich clinical experience with HD. The sample consisted of one neurologist, one elderly care physician, one psychologist, one physical therapist and two music therapists. They were all working in The Netherlands but each in a different care facility specialized in HD-care, so none of them were direct colleagues. One participant had a working relationship with the principal researcher (the first author). The average age of the participants was 46 years and the average number of years of expertise with HD-patients was 15 years. Apart from the two music therapists, one participant had much clinical experience with music therapy, one had little experience and two had no experience at all. All six respondents had experience in scientific research: two of them had a PhD-Degree, two had a Master's Degree and two had a Bachelor's Degree.

Prior to the first meeting, the first author of this article visited all the participants separately and gave them extensive verbal and written information about the aim of the research, the methodology and the protocol. She handed out a topic guide in which she revealed the main topics of the discussions. The topic guide consisted of several articles about QoL (Helder et al., 2001, Ho et al., 2009 and Ho et al., 2011) and about music therapy (Bruggen van- Rufi, 2009 and 2010). She instructed all participants to read these articles before the first meeting, giving each participant the same level of knowledge to use as a starting point for the discussions.

Moderator and assistant moderator

The discussions were guided by a moderator. The moderator did not participate in the discussion itself but raised issues and encouraged participants to reflect on topics openly. She summarized what had been said during the discussion. The moderator was completely familiar with the questioning route and knew the rationale for each question (Krueger, 1997). An assistant moderator was also present to make sure all the equipment worked correctly and to make notes. After each meeting the moderator and the assistant evaluated the notes taken.

Procedure Data collection

We conducted a total of three focus group meetings lasting two hours, followed by a telephone call made by the moderator to each participant to enable them to reflect on the last (third) group meeting. The three research questions (see above) were the guideline throughout all three meetings and all topics were open to discussion.

The group-discussions were audio-recorded once all the participants had given informed consent. The recordings were transcribed verbatim by either the assistant moderator or the first author. Prior to each meeting, the participants were asked to write down their thoughts about the topics to be discussed. These papers were handed to the moderator and were accounted for in the analysis. Furthermore, notes were taken during each session by both the assistant moderator and the moderator. After the third meeting, no new themes seemed to emerge, leading to the conclusion that data saturation had been reached.

Trustworthiness

To ensure credibility and trustworthiness (two evaluation standards that are characteristic for the naturalistic inquiry approach), we used the following procedures:

Triangulation, member check, peer debriefing

We used different methods of data collection: focus group discussions and notes taken during the discussions (methodological triangulation). Also, as a form of data triangulation, prior to each meeting the participants were asked to write down their thoughts about the topics to be discussed, thus producing a written record of each participant's thoughts. Should time restrictions prevent them from expressing their thoughts during the meeting, these could still be accounted for in the analysis (authenticity). From the second meeting onwards, the moderator started by confirming that everybody had received the summary of the previous meeting and had been afforded the opportunity to give their comments, thus ensuring that no important information was missing and that they recognized themselves in the conclusions so far (confirmability, member check). During the analysis, the moderator examined the analysis process and records for accuracy (confirmability). All three audit reports were shared with all participants. These reports can be provided upon request. Furthermore, the preliminary results were presented and discussed with music therapists and neuroscientific researchers at an international music therapy congress (poster and oral presentation) (peer debriefing). Here, they challenged the interpretations of the data and the preliminary conclusions of the focus group study. Their objective feedback was used to finalize the conclusions of the study.

Analysis

The verbatim transcripts were analysed by the first author. The themes and concepts were derived from the data by using the open coding system: the descriptions used by the participants during the discussion were identified and codes that described the same themes were clustered or deducted. A content analysis was performed according to the constant comparison method, based on the grounded theory of Glaser & Strauss (1967). Data were extensively collected, coded and organized. In this approach the process of induction (determining what premises can logically be derived from the emerging themes) leads to deduction (what else would have to be true if these premises are true). The whole process of constant comparison leads to general conclusion(s) which can logically be derived from the data (Boeije, 2005), (Copi, Cohen & McMahon, 2015).

Throughout the whole analysis process the codes and (sub)categories were checked with the moderator. The participants received a summary of every meeting, describing the (preliminary) analyses and highlighting the key findings. They were asked to check the content (member check/member validation), in certain instances resulting in modifications (negotiate outcomes).

Results

The results presented below first describe the participants' perceptions of

- QoL in general for patients with HD the most important aspects of QoL in patients with HD
- Subsequently, elaborating on the results of the first two research questions, the participants' perceptions on the third research question will be presented:
- the potential role of music therapy in improving QoL in patients with HD.

In the discussion we will expand on these interpretations in more depth, reflecting the participants' perceptions, tying together their ideas with the rationale for music therapy with patients with HD from the literature.

Q: What is QoL, based on your own clinical experience?

Analysis of the verbatim transcripts revealed several themes and subcategories (see fig. 2) which are presented below, illustrated with the most distinct quotes, accompanied by a short interpretive summary.

In each of the three sessions, the participants cited a number of items. The one theme being mentioned most often was the subjectivity of QoL:

> *"…One patient can have a very low self-esteem because his involuntary movements are so conspicuous. Another patient doesn't mind that his motor functions are poor, as long as his cognitive skills are still good. No matter how badly a person moves, he can still feel good about himself… "*

> *"…the only person who can say something about it is the patient himself. We, the professionals, can only ask, or guess…"*

A typical comment where all participants agreed upon was that patients have difficulties reflecting about their own QoL due to the cognitive decline. Besides that, one of the participants felt that patients do not express themselves in QoL-terminology, because in his opinion, QoL is a term used by the professionals, who must listen beyond what has actually been said and "translate" it into QoL-issues. All participants agreed that this "translation" might not fully reflect the patient's perception of his own QoL, as it is the interpretation of the professional. Elaborating on this, another comment was that the professionals tend to be too protective towards the patients:

> *"…Life consists of ups and downs, that is part of life. We cannot and must not protect our patients from that…"*

All participants agreed that recognition of the individual needs of the patient is most important when thinking about his QoL. They all emphasized that functionality and autonomy of the patient himself must be maintained and supported as long as possible. Involving family members in achieving this was also recognized by all participants as being very desirable.

One of the participants who is involved with patients at the earlier stage of the disease, before admission to a nursing home, or even before onset of the symptoms, stated:

> **"***…Quality of life is not an issue that is raised frequently in the doctor's office because the doctors have only little to offer in that aspect. The emphasis should be on care, and not on cure…"*

Following this statement, the discussion continued more specifically in the direction of QoL and the disease itself.

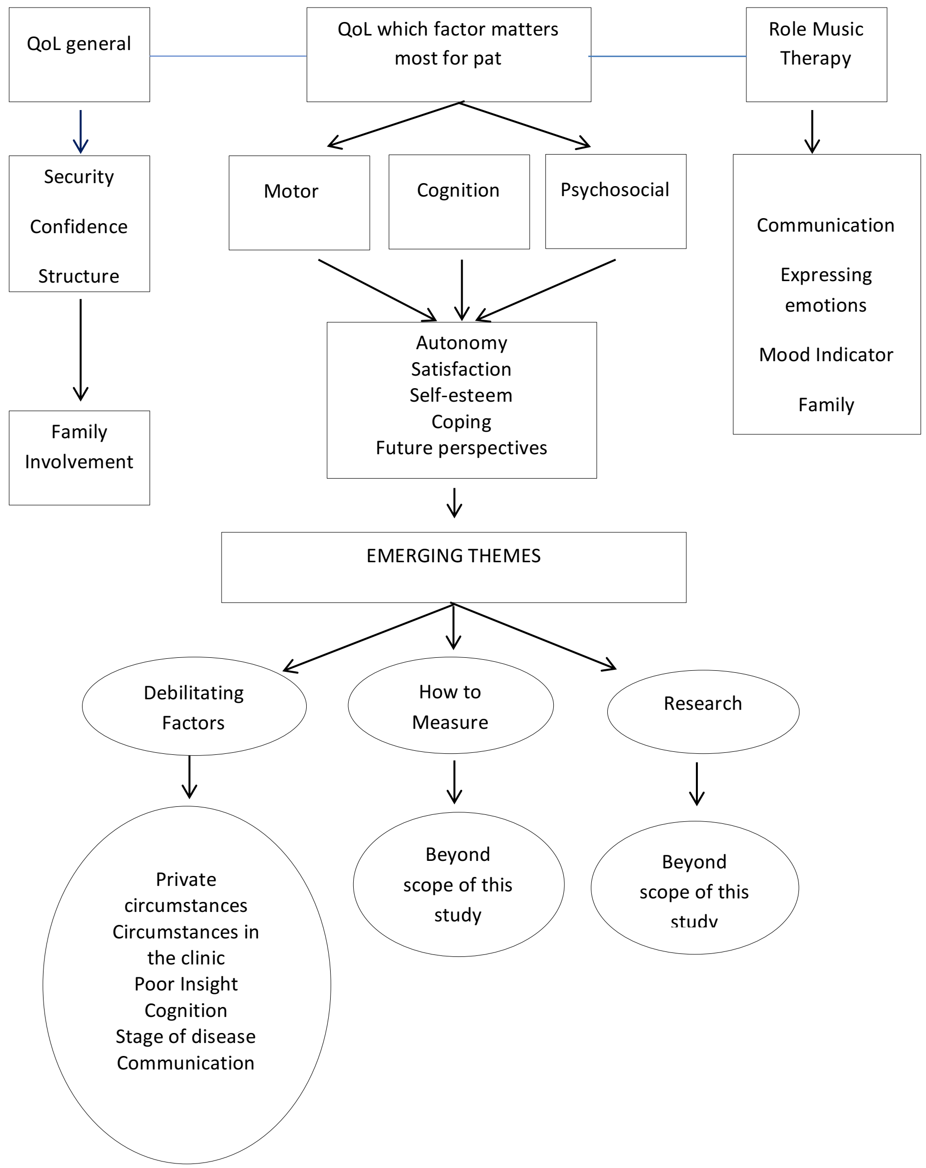

Figure 2: (sub)categories and emerging themes

Q: What are the most important aspects of QoL in patients with HD?
The content analysis of the transcripts revealed that, according to all participants, psychosocial and cognitive symptoms influence QoL most. Three major themes were identified: stage of the disease (1), cognitive decline (2) and circumstances/living conditions (3). While discussing these major themes, three subcategories emerged: (sense of) security (a), confidence (b) and structure (c).

In fig. 2 the findings are summarized in subcategories under each theme. How the subcategories relate to the three major themes is illustrated in fig. 3. In fig. 4, the consequences of the cognitive decline in relation to self-reflection about QoL is highlighted. Together they form an overall view of the participants' ideas of (health-related) quality of life and HD.

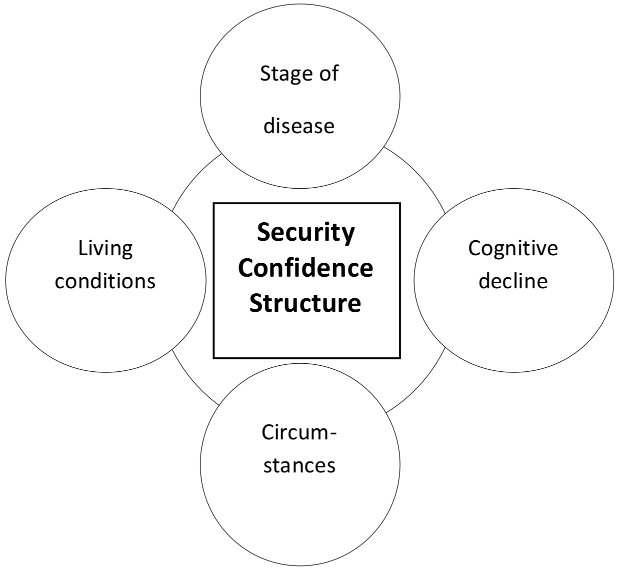

Figure 3: Relation subcategories and major themes

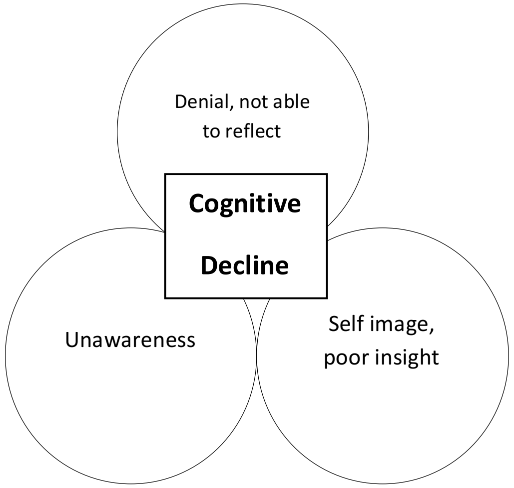

Figure 4: Consequences of cognitive decline i.r.t. self-reflection

Stage of the disease and cognitive decline
All participants agreed that the stage of the disease and the cognitive decline are inextricably related. The cognitive deterioration becomes more distinct as the disease progresses. All participants recognized the patient's inability to reflect about his own QoL. Denial, poor insight and poor coping skills were mentioned as the most debilitating factors in being able to do so adequately:

> *"...in the earlier stage of the disease, the patient tends to deny the symptoms and signs while in the later stage the patient can no longer reflect about it..."*

> *"...Denial comes from the patient himself, while poor insight is a result of cognitive decline in the later stage of the disease. Self-image does not grow with the progression of the disease, often resulting in behavioral problems..."*

One participant shared her experience with the group: when asking the patient about how he feels, he will often score himself "average" on a rating scale, adjusting to new circumstances.

> *"...Everybody has his own highs and lows, no different in patients with HD. The average will always be in the middle..."*

The discussion that followed, as one of the participants raised the question how HD-patients react differently from (healthy) persons in certain circumstances, focused specifically on the cognitive decline of patients with HD.

One of the participants commented that the cognitive decline can be beneficial for the patient:

> *"…it can be a relief for the patient as he is no longer aware of his decline. He is coping with and adjusting to his new situation…"*

Following this comment, the participants agreed that the cognitive decline results in yet another paradox: the impact of the disease seems to be less of a burden for the patient than for the people around him. This can cause much stress, especially when patients still live at home. All participants agreed that family support is very important. More specifically, they agreed that all people surrounding the HD-patients must have a comprehensive knowledge of the disease in order for the patient to feel confident and secure.

The discussion continued with these emerging themes on security, confidence and structure. One of the participants stated that

> *"…sense of security and confidence come from within the patient himself; structure must be provided by the people around the patient. The conditions and circumstances he lives in must be created by the people surrounding him…"*

This statement resulted in the unanimous recognition that another important distinction has to be made: Is the patient still living at home, does he receive daily care from family members, does he visit a day care facility or is he living in a long-term care facility.

Circumstances/living conditions
As the cognitive decline affects the patient's ability to structure his own life as the disease progresses, he becomes more and more dependent on his surroundings. One of the participants shared his perception with the group by commenting that

> *"…structure is the basis of feeling safe. We have to make sure that patterns, rituals, everything that the patient is used to, continue every day…"*

Following this comment, the discussion continued with reflecting about structure.
Participants agreed that structure seems to be best secured by living in a long-term care facility that is specialized in HD care because of the specific expertise these facilities have.

> *"…it takes very much time for a patient with HD to build trust. The more knowledge and affinity you have, the sooner this trust is a fact. This is an absolute necessity to treat the patient effectively…"*

However, once admitted to a LTCF, autonomy, self-esteem and future perspectives for the patient are QoL issues which are raised more often. The discussion continued while reflecting on these emerging themes:

> *"…each new situation results in severe tension and stress. Processing new information is extremely difficult, due to cognitive decline of the disease in the later stages..."*

> *"…the patient sitting in front of us is someone who still wants to be heard. A person with needs and wishes like all other human beings..."*

When autonomy is jeopardized, the participants agreed that living in a LTCF specialized in care for HD-patients is most desirable. They will find themselves surrounded by specialists, resulting in an improved feeling of security and confidence.

> *"...Even though the patient might not want to be here, he feels at ease, safe. All the people around him, fellow patients and nursing staff, know what he is going through…"*

When no more new emerging themes seemed to be raised by the participants, the monitor summarized the results so far of the group discussion. While all participants recognized that the subjective nature of the QoL-concept requires self-report by the patient for as long as possible, it was agreed that this becomes more and more challenged due to disease progression. When the HD-patient loses his ability to express himself in the later stage of the disease, other means of communication should be provided. The monitor used this conclusion to introduce the last and foremost important question, encouraging the participants once again to reflect open minded and freely:

Q: Can music therapy play a role in improving QoL in patients with HD?
Before going into the different themes, it is worth mentioning that some general yet distinctive "opening"-thoughts were shared by some of the participants on which the rest of the discussion elaborated:

> *"...as long as there is still no medication to cure the disease we should try every possible (non-pharmacological) intervention and treatment. Music therapy could very well be one of them (...), well worth giving it [MT] a try..."*

Elaborating on the aforementioned themes that emerged from the first two QoL-questions, three major themes were found: new ways of communication and expression, mood-indicator and family-participation *(*see fig. 5). Below, the participants' perceptions on these themes will be presented and quotes will be used to illustrate each theme.

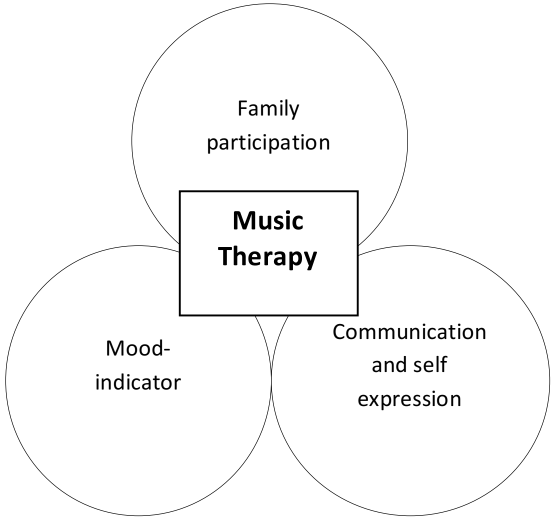

Figure 5: Potential roles of music therapy

Communication and expression

One of the participants felt that if a person loses the ability to communicate with others, music could take over:

> *"...music could be a new way to communicate again and to come to the inner self of the patient, to his emotions. The non-verbal character of music allows the patient to express himself in a different way (...) when a person can no longer give words to his feelings, music can give him new ways of expressing himself..."*

Another participant added:

> *"...Within music therapy the patient can express himself both non-verbally (playing musical instruments) and verbally (writing song lyrics, listening to existing songs and reflecting about the lyrics, "translating" them to his own life). In doing so, he gives meaning to his own emotions..."*

Mood indicator

Following these thoughts, the discussion continued when a new theme emerged: the use of music as a mood indicator. Some of the participants shared their own personal experience with music. Another participant who has no affinity with music whatsoever shared her thoughts as well, directing the discussion about the benefits of music in both positive and negative ways. However, putting their own personal thoughts about music aside, all participants agreed that for some patients music could be helpful.

One of the participants recognized the potential role of music, stating that

> *"...music could be used as an indicator to determine in which state of mind a patient is..."*

> *"...in music therapy the patient can create his own song, record it and give this to his family members. In this way the family could not only recognize the mood the patient is in, but also the person behind the patient, the partner or the father he once was, and still is or wants to be..."*

The participants agreed that even though the patient might no longer be able to reflect on the state of mind he is in, his choice of music or his reaction to the music played for him might help him express his feelings and help the people around him understand the patient better.

This last thought led the discussion to yet another emerging theme:

Involving family members

In relation to improving the QoL, all participants agreed that involving the direct family members or other caregivers is desirable.

"...the family relation between the patient and his partner and/or his children can be reinforced through music therapy..."

"...within music therapy partners could relive good experiences from before the disease kicked in hard (...) but also they can experience what is still there..."

"...music therapy could be a resource to give a positive change to an often problematic relationship. The healthy partner can recognize the "old" partner again..."

Discussion

This study is a first attempt to highlight the different opinions of a heterogeneous group of experienced professionals about quality of life in (advanced) Huntington´s disease, and the possible role music therapy could play. The main purpose of the research was to describe different clinicians' perceptions of music therapy in improving the quality of life in patients with Huntington's disease. Six professional clinicians from varying disciplines, all specialized in HD, discussed three major themes: QoL in general, QoL in HD and music therapy for HD-patients. In the discussion below we will first expand on the participants' perceptions about QoL, tying together their ideas with the literature. Subsequently we will do the same for the perceptions of the participants about music therapy.

In general, it was stated that reflecting about a patient's QoL, when he is incapable of doing so himself (as is the case in most HD-patients, especially in the later stages), is extremely difficult, given the subjective nature of the topic. Participants agreed that functionality and autonomy of the patient are the most distinct QoL-factors. When focusing on QoL of HD-patients, psychosocial and cognitive symptoms seem to influence QoL most. Stage of the disease, cognitive decline and the circumstances/living conditions of the patient are being recognized as the most important determinants of QoL.

Furthermore, HD-patients face many psychological issues such as anxiety, stress and hopelessness. Once their symptoms have become manifest, the patients realize their future perspectives, which has an immense impact on their QoL. As a result of the inability to express oneself due to the lack of (verbal) communication skills, it is highly likely that psychosocial problems will occur (Vervoort & Zuuren van, 2009).

The patient should feel secure, safe and confident. Sense of security and confidence are intrinsic factors and come from within the patient himself. However, structure in his daily life and the conditions and circumstances in which he lives seem to be decisive and are extrinsic factors which must be provided by the people surrounding the patient. In short, interaction between patient and caregiver is crucial, inevitably causing yet another area of stress (Vervoort & Zuuren van, 2009).

Determining which aspects are most important with regard to the (health-related) quality of life of patients with Huntington's disease is hindered by the many debilitating factors surrounding the patient, both physically and psychologically.

Because of this, it is justified and common to rely on the report of the caregivers and other proxies of the HD-patient, even though "...the subjective nature of the concept of QoL requires its assessment to be carried out by self-report where possible..." (Hocaoglu et al, 2012, p. 1793).

There is, however, the risk of being too paternalistic and overprotective. McCusker & Loy (2014) state that "...the primary ethical dilemma for all care providers is the balance between a patient's family's concern regarding care and safety and maintenance of the patient's autonomy, privacy and engagement..."(p. 6).

Relying on proxies presents another dilemma to be taken into account: many people with serious and persistent disabilities experience a good or excellent quality of life, while to external observers it seems these individuals live an undesirable daily existence. The impact of the disease appears to be less of a burden for the patient than for the people around him. This so-called disability paradox can also be recognized by people with HD (Albrecht & Devlieger, 1999).

In short, the different perceptions about QoL of the focus group participants are consistent with the literature. While there are many debilitating factors that influence the QoL in HD, it is important to find a concept that best describes all these disease-specific issues.

As detailed previously, the discussion about the potential role of music therapy in improving QoL for HD-patients resulted in three major themes: new ways of communication and expression, mood-indicator and family-participation (see fig. 5). These findings are consistent and can be confirmed with the music-therapy literature.

Communication and expression

Improving communication skills of individuals have been frequently reported in music therapy (McFerran, Lee, Steel, & Bialocerkoswki, 2009, Bruggen van – Rufi, 2009). As the ability to communicate and express oneself deteriorates over time, music therapy could play an important role in the treatment, in that it could provide an additional means of communication. The results from a music therapy referral audit conducted by Daveson (2007) show that patients with HD were most likely to be referred to music therapy due to a need for emotional expression, and the maintenance of communication skills and social relationships. This outcome can be confirmed by Bruggen van – Rufi (2010) who interviewed 14 members of the multidisciplinary team in a nursing home specialized in HD in The Netherlands. In this research, too, communication and self-expression were mentioned most often as treatment goals for referral to music therapy.

Mood indicator

Due to the affective (mood) disorder that is often manifested in the later stages of the disease, people suffering from HD have a diminished ability to recognize and express emotions, both in themselves and in others. Music and emotion seem to be inextricably connected (Juslin & Sloboda, 2010). Musical experiences can empower people to feel that they are alive and also promote shared experiences with others (McFerran et al., 2009).

Family participation

Music therapy can be offered both individually and in group sessions, with fellow-patients and with family members (Bruggen van-Rufi & Roos, 2015). As the focus group stated that involving family is of prime importance, the beneficial role of music therapy can be confirmed by McFerran et al, 2009; they conclude that using music therapy interventions to help improve communication skills with their carers outside of the music therapy sessions will be the most beneficial outcome.

In conclusion, because of the changing needs of the HD-patient, inherent to the stage of the disease, the treatment itself has to be adjusted to the individual needs important at that specific moment (Davis & Magee, 2001, Daveson, 2007). In HD the stage of the disease is crucial; while in the early stage denial might be an issue, in the middle and late stages poor insight into the disease itself might be the reason why QoL issues are raised less frequently by the patient. In the later stage of the disease, the patient might no longer be able to reflect about his own QoL.

Although the literature shows that precise aims and methods in relation to the stage of the disease are not well established yet (Bruggen van-Rufi & Roos, 2015), the focus group results suggest that music therapy may be beneficial throughout the various stages. Music therapy can combine functional training with cognitive, emotional and communicative/relational approaches. In so doing, the music therapist can forge a link between medical and psychological treatment. Methods and techniques can be constantly adapted, guided by the individual treatment goals of the patient, bearing in mind all of his or her limitations and skills. In short, the sessions can be "tailor-made" to the patient and his needs (Bruggen van-Rufi & Roos, 2015).

Strength and limitations

The strength of our study lies in the richness of experience of our participants. Collaboration with other professionals is imperative in order to meet the patient's needs. Except for the two music therapists, all participants came from different disciplines, and each was working in a different health care institution. Also, all of them had many years of experience with Huntington patients and had experience with or knowledge about scientific research. They represented the well-being of the patient with HD in every aspect. Furthermore, the number of participants was small enough to allow us to examine their responses in depth. They needed little encouragement to describe their experiences in detail.

At the same time however, having only six professionals participating in the study is a major limitation. Although the participants contributed a variety of different opinions, different issues might have been raised if more clinicians would have participated. Also, all participants were from The Netherlands. It is possible that clinicians from other countries may have different opinions, especially because long term care facilities (LTCF) where only HD-patients reside are not so common outside The Netherlands.

Another weakness of the research might have been the involvement of two music therapists with the four other clinicians who may have felt inhibited by their presence to provide negative views about music therapy. The reason for this was to make sure that at least one music therapist would be present at every session, anticipating possible absence of one of them. We cannot rule out the possibility that both music therapists were, unintentionally, advocating the use of music therapy during the group discussions, or stimulated socially desirable answers. We tried to minimize this by instructing them beforehand not to *advocate* but to *inform about* music therapy. This was a pragmatic choice**,** however we are well aware that instructing participants is contradictive for the naturalistic method. This is another weakness in the study.

The results obtained in this research must be regarded in the light of some more limitations. First of all, the participants were all acquainted with the main researcher and were aware of her ideas about setting up a music therapy research for HD-patients. For this reason, the researcher herself was never present at the meetings, nor talked about the trial while meeting the participants on different occasions.

Also there could be concern that the "must-read-articles" about music therapy, written by the main researcher, could have influenced the participants and led them to be more positive about music therapy and to conceal their criticism about music therapy.

Another weakness of the study was that in the first two meetings not all participants were present. However, the absent members were all given sufficient opportunity to participate in the group discussions by inviting their comments on the preliminary reports of each meeting, sent to them prior to the next session. At the start of the next meeting, those who had been absent from the previous meeting were given the opportunity to ventilate their thoughts. All participants were present at at least two of the three meetings.

Finally, in the attempt to find a representative and homogeneous sample where participants had a certain comparable level/degree of (scientific) experience, expertise and knowledge, we decided not to involve patients, caregivers or nurses. The results of this research reflect the opinions of professionals, not of the patients or caregivers themselves. Taken the aforementioned pitfalls into account (unawareness, disability-paradox, etc.), an additional focus group study in which patients and caregivers are the participants is recommended.

Although over the last few decades there has been an increasing number of clinical trials focused on the search for new therapeutic (pharmaceutical) strategies to manage HD, unfortunately few advances have been made. While there is still no cure, the emphasis should be on the care of patients with HD, especially in the advanced stage of the disease (Roos, 2010). Contributing to this need, a multi-center randomized controlled trial studying the effect of music therapy in Huntington's disease to improve the quality of life of patients with HD, by way of improving communication skills, was conducted from October 2014 until June 2016 in four different long term care facilities in The Netherlands (Bruggen van – Rufi, Vink, Achterberg, & Roos, 2016). The results of the present focus group study helped informing this RCT. Final results of this study are expected in the winter of 2017.

Future prospects

Until recently, there was a lack of a disease specific measurement tool to assess music therapy with HD. Such a tool, the Music therapy Assessment Tool for Advanced Huntington's Disease (MATA-HD), has now been developed. The results of a pilot study to validate this tool were recently published (O'Kelly & Bodak, 2016). 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.

Conclusion

The results of the present focus group study suggest that music therapy can target many facets that are important to the QoL of patients with HD. As the ability to communicate and express oneself deteriorates over time, music therapy could play an important role in the treatment of patients with HD in all phases of the disease. Through music therapy an additional means of communication can be provided, enabling the patient to express his or her needs and emotions. Also, music can be used as a mood-indicator. Finally, involving family members in the treatment is desirable and should be encouraged. In music therapy this can be easily accomplished .

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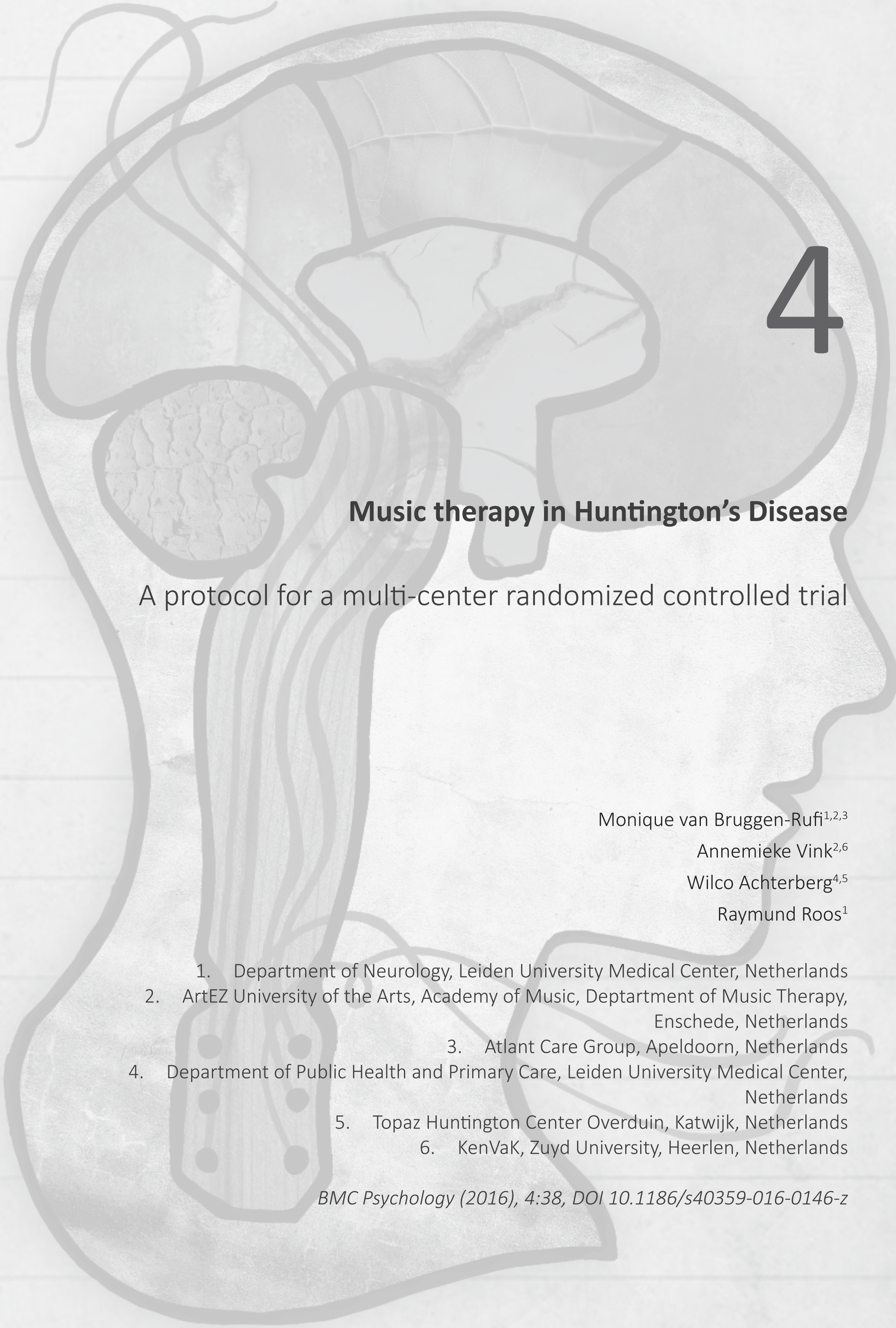
“After silence,
that which comes nearest to expressing
the inexpressible is music”

Aldous Huxley (1894 – 1963)



4

Music therapy in Huntington’s Disease

A protocol for a multi-center randomized controlled trial

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Abstract

Background: Huntington's disease is a progressive, neurodegenerative disease with autosomal dominant inheritance, characterized by motor disturbances, cognitive decline and behavioral and psychological symptoms. Since there is no cure, all treatment is aimed at improving quality of life. Music therapy is a non-pharmacological intervention, aiming to improve the quality of life, but its use and efficacy in patients with Huntington's disease has hardly been studied. In this article, a protocol is described to study the effects of music therapy in comparison with a control intervention to improve quality of life through stimulating expressive and communicative skills. By targeting these skills we assume that the social-cognitive functioning will improve, leading to a reduction in behavioral problems, resulting in an overall improvement of the quality of life in patients with Huntington's disease.

Methods/Design: The study is designed as a multi-center single-blind randomised controlled intervention trial. Sixty patients will be randomised using center-stratified block-permuted randomisation. Patients will be recruited from four long-term care facilities specialized in Huntington's disease-care in The Netherlands.

The outcome measure to assess changes in expressive and communication skills is the Behaviour Observation Scale Huntington and changes in behavior will be assessed by both the Problem Behaviour Assesment-short version and the BOSH. Measurements take place at baseline, then 8, 16 (end of intervention) and 12 weeks after the last intervention (follow-up).

Discussion: This randomized controlled study will provide greater insight into the effectiveness of music therapy on activities of daily living, social-cognitive functioning and behavior problems by improving expressive and communication skills, thus leading to a better quality of life for patients with Huntington's disease.

Background

Huntington's Disease (HD) is a progressive, neurodegenerative disease with autosomal dominant inheritance, caused by an elongated CAG repeat on chromosome 4 [1]. HD is characterized by motor disturbances, cognitive decline and behavioral and psychosocial symptoms. The cognitive disorder in HD effects a broad variety of skills, including learning and memory, perceptual skills, executive efficiency and language [2]. Cognitive and behavioral changes are the most debilitating aspects of the disease and place the greatest burden on the patient as well as on their families and caregivers, and are often the main reason for institutionalization [3, 4]. Affective (mood) disorders (e.g. depression, anxiety, apathy, irritability) and behavioral problems (e.g. obsessive compulsive behavior and aggression) are frequent symptoms [5].

Verbal communication is often affected, due to motor impairment of speech. In addition, as a result of the cognitive decline, word retrieval is often impaired, although the knowledge of vocabulary is retained. As the disease progresses, the language content can no longer be processed properly and in the later stages of the disease, a patient with HD might not be able to communicate adequately [1].

As a result of the communication problems, patients are no longer able to express themselves. Revealing the patients' unmet needs is, therefore, hindered and this might lead to irritability, impulsive and unwanted behavior (frequently signs in HD), causing much distress for patients and caregivers. Because of the behavioral symptoms, cognitive decline and the inability to express oneself, psychosocial problems develop [6]. Psychosocial stressors may include feelings of sadness and anxiety about the cognitive and physical decline, and about changes in social roles [7]. The gradual deterioration in communication skills, in combination with the behavioral problems in patients with HD, contributes to a decrease of functional health and a progressive inability to participate in various life situations, leading to loss of quality of life [8].

Since there is no cure for HD, the aim of all therapy, both pharmacological and non-pharmacological, is to improve quality of life [3]. One form of non-pharmacological intervention is music therapy.

Music therapy uses music experiences and patient-therapist relationships in order to effect therapeutic change [10]. Over the past decades, music therapy has been developed for patients with neurodegenerative diseases [11,12]; its efficacy is shown in table 1.

Table 1 Benefits of music therapy for the neurodegenerative diseases

Benefits	Reference	Population
Improving and regulating emotional wellbeing	13, 31	Dementia, Huntington
Increasing social response	13, 31	Dementia, Huntington
Decreasing agitation	13	Dementia
Recalling life experiences	14,15, 31	Dementia, Huntington
(re)establishing contact	14,15, 31	Dementia, Huntington
Improving communication skills	11, 12, 16, 31	Dementia, Parkinson, Huntington, multiple disabilities
Reducing behavior and psychological symptoms	17, 18, 19, 20, 31	Dementia
Improving gait	9	Parkinson

There is evidence that music therapy influences emotional well-being positively and that participation in music therapy increases social response in people with dementia [13]. It can decrease agitation and has a positive effect on enhancing communication and emotional well-being. Music therapy enables the recall of life experiences and the experience of pleasant emotions. Through music, contact can be established, especially as language deteriorates during the later stage of the dementing process [14,15].

In a comprehensive literature search, Lee and McFerran [16] conclude that the non-verbal communication skills in individuals with profound and multiple disabilities improve as a result of song-choice during music therapy sessions. The results of their study support the belief that, through music therapy, the ability to express oneself will improve, contributing to improvement in the quality of life.

Furthermore, in a literature review, Patel et al [17] demonstrate the effectiveness of MT in reducing behavioral and psychological symptoms of dementia. Several other meta-analyses and literature reviews have concluded that music therapy decreases symptoms related to behavioral problems in dementia [18-20].

On the basis of the above-mentioned literature, the assumption can be made that music therapy might be beneficial to patients with HD. Although knowledge on the use and efficacy of music therapy in HD is limited, it has been suggested that it can improve the communication skills of people with HD [21]. By improving the expressive and communication skills through music therapy (which will be assessed by the BOSH) we hypothesize that behavioral problems (assessed by the BOSH and the PBA-s) will decrease, leading to an overall improvement of quality of life.

To test this hypothesis, we wrote a study protocol to answer the following questions:

1. Does music therapy improve expressive and communicative skills in people with HD?
2. Does music therapy reduce behavioral problems in patients with HD?
3. Does music therapy improve the quality of life of patients with HD?

METHODS

Study design

The study is a multi-center, single-blind, randomised controlled intervention trial with two parallel arms. An overview of the study design is shown in a flow chart (see figure 1). It is single-blinded; the researcher who analyses all the scores is unaware of the allocation of the patients throughout the study. Also, the persons performing the baseline-assessments will be kept unaware of the allocation of the participants they are testing. Sixty patients (see sample size calculation below) will be randomised using center-stratified, block-permuted randomisation following the procedure as described below. Two random groups will be created. The experimental group will be offered a music therapy program according to a structured protocol (see below), and the control group will participate in recreational day activities, following the same protocol as the experimental group. In addition, both groups will receive regular treatment (standard care, treatment as usual). Participants from both the experimental and the control group will not be allowed to receive music therapy outside the study.

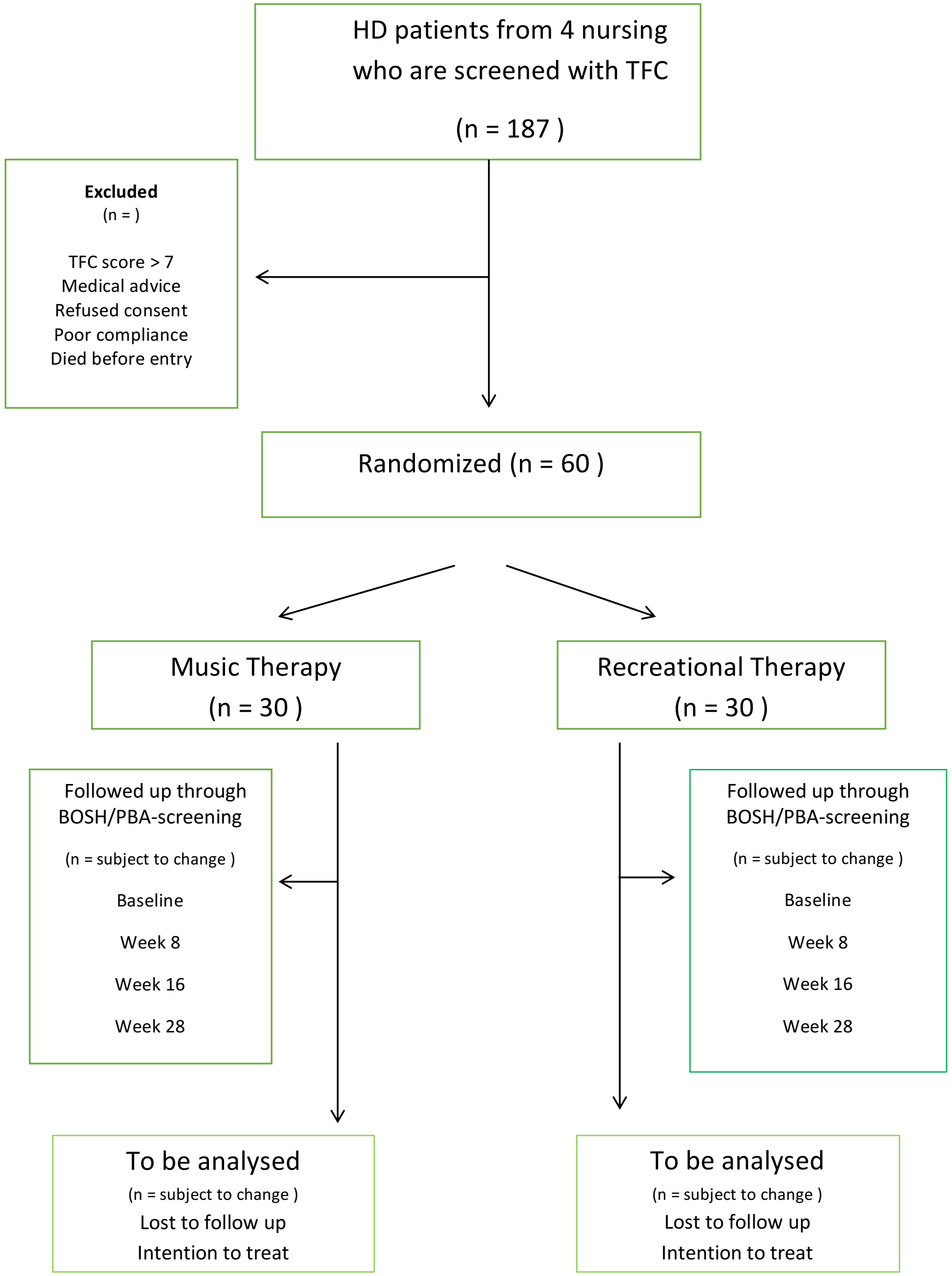

Fig. 1 Flowchart

Procedure

Recruitment

Patients will be recruited from four long-term care facilities (nursing homes) in The Netherlands, all specialized in HD, with one or more units exclusively for HD-patients. Recruitment will be primarily done by the nursing staff and the responsible physician.

Inclusion and exclusion criteria

Eligible patients must meet the following inclusion criteria:

- Age older than 18 years
- Clinically and genetically confirmed Huntington's Disease (CAG ≥ 36 repeats)
- Total Functional Capacity (TFC) ≤ 7

Exclusion criteria:

- patients who suffer from other neurological disorders
- patients with poor comprehension of the Dutch language
- patients who have received music therapy in the past 3 months
- patients with a hearing impairment

Patients will be included irrespective of medication status and will be allowed to continue medication during the study. However, any change in medication should be avoided and carefully registered.

Informed consent

Informed consent will be obtained by the nursing staff from patients who are cognitively able to understand the possible risks and benefits of the study. Proxy consent will be obtained from next of kin, or a legal guardian, if the patient is not able to give an informed consent.

Baseline assessments

Clinical and demographic variables such as gender, age, (changes in) medication, number of CAG-repeats and (estimated) age at onset will be gathered for each participant. The stage of Huntington's Disease will be assessed using the Total Functional Capacity (TFC) [22]. The TFC, part of the Unified Huntington Disease Rating Scale, consists of 13 points and contains 5 domains: work, finances, domestic chores, activities of daily living and care requirements [22]. As the disease progresses, the TFC-score will drop, giving clinicians a good indication about the functional stage of the disease. A score of 7 or lower indicates that the patient is in the mid/advanced stage, and so impaired in his functional capacities that assistance with self-care is needed [22]. Most of the patients that reside in the four long term care facilities that participate in the study have a TFC-score of 7 or lower. To ensure a homogeneous group, patients with a TFC score of > 7 will be excluded from participating in the research The TFC will be administered by the elderly care physician who is responsible for the patient.

The Mini Mental State Examination (MMSE) will be used to assess the cognitive function of the patients at baseline. A score of 23 or lower out of 30 indicates cognitive impairment [23]. The MMSE will be administered by the psychologist or the psychology assistant.

Randomisation

In order to minimize the impact of any between-center differences on the trial results, the participating centers will be stratified in the randomization process. Participants will be randomly assigned to either control or experimental group with a 1:1 allocation . To generate the random allocation sequence we use the method of center-stratified, block-permuted randomization [24]. The block size will vary. To diminish the chance of predictability, the date of signing the informed consent will determine the sequence in which the patients will be randomized. Not until all baseline measurements have been completed, the randomization code will be released to ensure allocation concealment.

Randomization will be conducted without any influence of the principal investigators, raters or therapists.

Intervention

All participants (in both the experimental (intervention) group and the control group) will continue to receive treatment as usual. The intervention group will receive music therapy (MT-group). The control group will receive recreational therapy. The number of sessions (16) is equal in both groups, as are the day of the week and the time of the day at which the sessions will take place. Patients in both groups will participate in group interventions with three to five participants.

It must be noted that each of the four participating facilities have a different music therapist and recreational therapist attached to the research. However, all participating therapist have been instructed thoroughly to follow the same protocol. The reports that each therapist will fill out after each session will be used to monitor if they have followed the instructions.
See also "compliance with treatment".

Intervention group

The music therapists committed to the study are professionally trained and have been specifically informed about the clinical method and its theoretical basis.

The main goal of the music therapy intervention is to enhance communication skills by way of encouraging and stimulating the patients in interaction. The music therapy approach applied in this study is focused on encouraging and engaging patients in expressive musical interaction. The role of the therapist is to use musical parameters and interventions to stimulate expressive and communicative skills. The degree of verbal reflection may vary; the therapist will, however, encourage the participants to express themselves. The therapeutic process is based on the mutual construction of meaning of emerging thoughts, images, emotional content and expressive qualities that often originate from the musical experience [10].

A treatment guide specifies the procedures. It outlines the setting, goals and basic principles of the intervention; Table 1 (the benefits of music therapy for neurodegenerative diseases) is used as guideline. The available music therapy techniques to target the set goals are derived from the protocol "music therapy for Huntington's patients on improving and stimulating communication and self-expression" [25]. However, the guidelines are to be administered flexibly according to the patient's state of mind and his needs at that very moment. The clinical expertise of the therapist will be the guide, providing the therapist with enough "space" for flexible adaptation within the treatment guide. Also, the patients music preference, especially because most of the treatment involves receptive music therapy, is very important. This is the reason why the protocol allows and encourages the music therapist to adjust their treatment by way of "tailor made" sessions, providing each of the participants with his or her music preference.

The process used in each session is standard while the content is flexible. The intervention will be provided at the same time of the same day of the week by a formally trained, experienced music therapist. The sessions will take place once weekly with a total of 16 sessions, lasting 45 minutes. They will be standardized without limiting the music therapists in their interactions. The intervention itself, however, will be (partly) applied according to a protocol. Each session starts with the same welcome song/musical piece and ends with the same farewell song/musical piece. In doing so, the participants become familiar with the start and the end of each session. In between these two songs/musical pieces, the music therapist adjusts the level of each intervention to individual capacities. After the welcome song, the music therapy sessions may be varied: the music experiences can range from listening to music to playing or singing songs to free improvisation. therapist has the freedom to determine what works best at that very moment for that specific patient. The participants will listen to music selected, sung or played by the therapist. Active participation in music activities by singing or playing a musical instrument will be stimulated as much as possible. The music will be selected by the music therapist to incite expressive and communication skills and to reduce agitation, based on musical parameters, such as rhythm, melody, harmony, dynamics, timbre. After each song/ musical intervention, the therapist will encourage and stimulate the participants to reflect verbally on the music [25].

Besides the music therapy intervention during the whole study, participants are not allowed to receive additional individual music therapy.

All participants are allowed to leave the session at all times.

Control group

All activities will be provided by professionally trained recreational therapists who have been specifically informed about the study.

In the control group, recreational day activities will be offered under exactly the same circumstances as the music therapy sessions: a total of 16 weekly sessions, each lasting 45 minutes, every week at exactly the same time as the music therapy intervention. As in the intervention group, a treatment guide specifies the treatment procedures for the control group. In this guide, the setting and general goals are outlined. The main goal of the recreational activities is to enhance communication skills by way of encouraging and stimulating the patients in interaction..

The activities vary from reading the newspaper, cooking, arts-and-crafts/handwork or puzzles/ games. Musical activities, such as singing along or watching a music-video are not allowed, nor will background-music be played. The recreational therapist is well instructed about and fully aware of these restrictions. Besides that, during the whole study, participants from the control group are not allowed to receive music therapy. Both the physician who is responsible for the referrals and the music therapists are fully aware of this limitation. Participation in regular musical activities however (such as watching a music video or attending a music-performance which takes place on the ward occasionally) is allowed. These activities are not considered to be music therapy and are open to all patients that reside in the institution, regardless of participation in the study. Also, listening to music in the privacy of their own room is allowed for all participants.

All participants are allowed to leave the session at all times.

The music therapy and the recreational therapy will be provided in separate rooms, away from the ward. Participants will be taken to the music therapy room or the activity room by the nursing staff. The music therapist and the recreational therapist make sure that they can start the moment all participants are in the room. After the session, the participants will be taken back to the ward by the nursing staff. The therapists will never leave a participant in the room unattended.

After each session, a short report of the activities will be written by both therapists, including an evaluation of each patient. Since a self-report from the patient himself is not feasible, the reports written by the therapists will be used for evaluation purposes and treatment fidelity.

Compliance with treatment

In each participating center a monitor will be identified, to be responsible for adherence to study protocol (including data collection).

Furthermore, after each session, both therapists will document significant events, notable behaviors, and interventions applied. These reports will enable us to determine whether the treatment has been conducted as intended. These reports will provide insight into the patient's state of mind at the time of the intervention. This information can help us explain why certain measurements might be significantly different compared to others in the same patient. Self-reports (the patients' own perception) might not be feasible, due to the rapid decline of cognitive skills (see rationale). Furthermore, this information will also be used to evaluate the process of the study.

Outcome measures

The primary outcome measure, communication skills, will be assessed by the social-cognitive domain of the Behaviour Observation Scale Huntington (BOSH) [26]. The secondary outcome measure, behavior, will be assessed by both the Problem Behaviours Assessment-short version [27, 28] and the third domain of the BOSH (mental rigidity and aggression).

The BOSH contains 32 items in 3 subscales: 1) activities of daily living (ADL) (5 items), 2) social-cognitive functioning (15 items), and 3) mental rigidity and aggression (12 items). Each item is assessed on a 4-point scale. The scores from the first subscale (ADL) range from 1 (self-supporting) to 4 (nursing required). The sum score from the first scale may range from

5 to 20. The scores from the second subscale (social-cognitive functioning) range from 1 (unaffected) to 4 (contact no longer possible); the sum score may range from 15 to 60. Finally, the scores from the third subscale (mental rigidity and aggression) range from 1 (never) to 4 (always); the sum score may range from 12 to 48. Intra- and interrater reliabilities are respectively 0.83 and 0.95 [26].

Assessment of the BOSH will take place within a week before the first intervention (baseline assessment), and will be repeated within a week after the 8th and again within a week after the 16th intervention. 12 weeks after the last intervention, the BOSH will be repeated.

The BOSH takes 15 minutes and will be administered by nursing staff in charge of the daily care of the patients. Blinding the BOSH-assessors might not be feasible as the nursing staff will have to transport the patients to and from the therapy-rooms. Also in daily life, the chance of the patient divulging his or her allocation towards the nursing staff is big. However, in the process-evaluation following the study all the assessors will be asked whether they were aware of the allocation of the patients.

Since the BOSH is a commonly known assessment scale in the participating HD nursing homes in The Netherlands, no formal training will be carried out prior to the start of the study unless the particular nursing home has no experience with the BOSH.

Behavioral problems will be assessed with the Problem Behaviours Assessment-short (PBA-s) version [27, 28]. This is a 5-point rating scale, using the scores 0 (absent) to 4 (severe). The PBA-s is a 11-item semi-structured interview and assesses behavioural problems in the 4 weeks prior to the interview. The sum score may range from 0 to 40. In addition, there is a subscale for severity and one for frequency. The PBA-s is a validated and reliable measurement-tool: the interrater reliability is 0.74 for severity and 0.76 for frequency scores (mean kappa), and 0.94 for severity and 0.92 for frequency scores (weighted kappa) [29] . The respondents of this face to face semi-structured interview are the patient and a knowledgeable informant (spouse or caregiver) together.

Assessment of the PBA-s will take place following the same time-schedule as the BOSH-assessments. The PBA-s will be scored by independent, formerly trained assessors who will be blinded to group allocation of the patients. After the last assessment, the assessor will be asked whether or not he inadvertently found out about the patient's allocation in order to verify the success of the blinding. Where possible, subjects are interviewed in the presence of a knowledgeable informant (primary caregiver).

After consulting a member of the PBA-workgroup we decided to adjust the 4-week retrospective view of the PBA-s to 1 week, due to the short time-frame in which it is administered (every 8 weeks).

Sample size

The minimal clinically important change or difference (MCIC/MCID) in the scale serves as important input for the sample size calculations. Unfortunately, data about these scale-characteristics are unavailable. We anticipate that the population in the present study will differ little from the population previously used in the study by Timman et al. [26] from which we derived data on means and standard deviations for the subscales of the BOSH. If we assume that the values in the control group will change little over the course of the study, whereas those in the experimental group will improve by 25%, and if we further assume an α of 0.05 and a β of 0.20, then the following sample size would be required:

- ADL: original mean ± SD = 2.25 ± 0.88; improvement of 25% will result in a mean of 1.69 and if we conservatively estimate a reduction in SD to 0.75, we would require an N of 30 per group for the ADL subscale (for an effect size of 0.55 (moderate));
- Social-Cognitive: original mean ± SD = 2.10 ± 0.79; improvement of 25% will result in a mean of 1.58 and if we conservatively estimate a reduction in SD to 0.75, we would also require an N of 30 per group for this subscale (for an effect size of 0.52 (moderate)).

Data management and confidentiality

Participant files will be stored in locked cabinets with limited access. Participating centers will only have access to their own center's data. Data will be entered into SPSS by an independent research assistant. After the trial the principal investigators and the statistician will have access to the data set.

Statistical analysis

The primary outcome measures of this study are the differences in total and subscale-scores of the ADL and Social-Cognitive subscales of the BOSH and the PBA-s between groups (control versus MT) when baseline differences are taken into account.

Results will be analyzed on an intention-to-treat basis.
A mixed model analysis with repeated measures will be used to analyze the differential effects

of music therapy versus recreational activities on the four GOSH and PBA-s scores (week 0, week 8 and week 16, and a follow-up score in week 28). The assessment number, ranging from one to four, will be used as the time variable of the repeated measures.

As stratified randomization often leads to correlation between treatment arms, it is necessary to adjust for the stratification factors in the analysis to obtain correct confidence intervals and p-values. By doing so, we maintain the type I error rate at its nominal level (usually set at 5%), and avoid a reduction in power [30].

Discussion

Music therapy is a promising non-pharmacological intervention. Through stimulation of the expressive and communicative skills, it is hypothesized that this therapy will result in improving activities of daily life and social-cognitive functioning as well as reducing behavioral problems, thus leading to an improvement in the quality of life.

In general, music therapy can be offered either individually or in group sessions, with other patients or with family members. The sessions can be "tailor-made" for the patient and his needs.

In this study, patients in both the intervention- and the control group will participate in group interventions with three to five participants. The decision to choose group-interventions rather than individual interventions is based on the assumption that the interaction between group-members will stimulate communication [31]. In this article, Magee concludes that music therapy in groups is recommended in the middle and the advanced stages of HD. Group sessions allow the patient the time needed for delayed responses, allowing natural "time out" from responses which require attention or concentration. The number of participants in each group has to be determined carefully. In a systematic literature review, Ing-Randolph et al [32] suggest that group size matters with music interventions addressing certain stages of dementia-associated anxiety. Although Yalom [33] states that a group consisting of fewer than five members results in a decrease in member interaction, this is not the case when working with HD-patients where smaller groups are preferable [31].

Based on earlier RCTs and a meta-analysis of the dose-effect relationship of music therapy in different settings and populations, we expect a treatment duration of 16 weekly sessions, each session lasting 60 minutes, to be sufficient for detectable developments [13, 14].

The decision to apply the BOSH as the primary outcome measures instead of a QoL-scale requires some clarification; in our opinion, no validated QoL-scale (generic nor disease-specific) is sufficiently sensitive to be used in the very late stage of the disease.

The BOSH was developed to provide an observational instrument for monitoring the behavioural aspects of the patient in later stages. Expressive and communicative skills are specifically measured within the social-cognitive functioning-subscale. In combination with its 2 other subscales (ADL and mental rigidity), we believe that the scale is so broad that it covers most of the QoL-domains. In the present study, we are planning to analyze the total score of the BOSH.

Conclusion

This article outlines the study protocol of a randomized controlled trial providing insight into the effects of a structured group music therapy intervention for patients with Huntington's disease. More specifically, the effects of music therapy on improving quality of life through specifically targeting the expressive and communicative skills, in comparison with an active control intervention, will be tested.

Conclusions that will emerge from this study are expected to contribute to evidence-based treatment for Huntington's Disease patients who experience deterioration of expressive and communicative skills, leading to a reduction in behaviour problems, and resulting in an overall improvement in quality of life.

List of abbreviations
BOSH: Behavioural Observation Scale for Huntington
HD: Huntington's Disease
LTCF: Long Term Care Facility
PBA-s: Problem Behaviours Assessment-short version
QoL: Quality of Life

Nature and extent of the burden and risks associated with participation, benefit and group relatedness

It is not expected that the intervention will be a serious burden for or risk to the participants, nor are physical or physiological discomforts associated with this study.

Reporting of study results

The study results will be disseminated in the following ways:

- A final report
- Formal publications in peer reviewed high impact international journal
- Presentations in different international conferences
- Dissertation and public defense

Protocol amendments

Any modifications to or administrative changes or clarifications of the protocol that have no effect on the way the study is to be conducted will be reported to the Dutch Trial Register (NTR 4904)

Ethics approval and consent to participate

The study has been approved by the Medical Ethics Review Committee of the Leiden University Medical Center in Leiden, The Netherlands (CCMO #NL 48029.058.14, METC # P14.038). All eligible patients and their family-members were informed (both written and verbal) about the purpose of the study, the expected duration and procedure, the right to decline to participate and to withdraw from the research at any given time once participation has begun without any consequences. Written informed consent was obtained from all participants who were enrolled in the study.

Consent to publish

Not applicable.

Availability of data and materials

The complete datasets that will be collected and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

All authors declare that they have no competing interests.

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Authors' contributions

MB is a clinically trained music therapist. She drafted the manuscript.

AV is a psychologist. She reviewed the manuscript.

WA is professor of institutional and elderly care medicine and reviewed the manuscript.

RR is a neurologist and contributed to the development of the study design and reviewed the manuscript.

All authors have been involved in revising the manuscript, and have read and approved the final text.

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“Das wichtigste in der Musik
steht nicht in den Noten”

Gustav Mahler (1860 – 1911)

5

The effect of music therapy for Huntington’s disease patients

A randomized controlled trial

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Abstract

Introduction

Music therapy may have beneficial effects on improving communication and expressive skills in patients with Huntington's disease (HD). Most studies are, however, small observational studies and methodologically limited. Therefore we conducted a multi-center randomized controlled trial.

Objective

To determine the efficacy of music therapy in comparison with recreational therapy in improving quality of life of patients with advanced Huntington's disease by means of improving communication.

Method

Sixty-three HD-patients with a Total Functional Capacity (TFC) score of ≤ 7, 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. They were assessed at baseline, after 8, 16 and 28 weeks using the Behaviour Observation Scale for Huntington (BOSH) and the Problem Behaviours Assessment-short version (PBA-s). A linear mixed model with repeated measures was used to compare the scores between the two groups.

Results

Group music therapy offered once weekly for 16 weeks to patients with Huntington's disease had no additional beneficial effect on communication or behavior compared to group recreational therapy.

Conclusion

This was the first study to assess the effect of group music therapy on HD patients in the advanced stages of the disease. The beneficial effects of music therapy, recorded in many, mainly qualitative case reports and studies, could not be confirmed with the design (i.e. group therapy vs individual therapy) and outcome measures that have been used in the present study. A comprehensive process-evaluation alongside the present effect evaluation is therefore performed.

Introduction

Huntington's disease (HD) is an autosomal dominant inherited, progressive, neurodegenerative disorder, characterized by a triad of motor, cognitive and psychiatric signs and symptoms. [1,2].

These characteristics often result in loss of expressive and communicative skills, especially in the advanced stage of the disease, frequently giving rise to behavioral problems such as anxiety, irritability and apathy. The gradual deterioration in communication skills, in combination with the behavioral problems in patients with HD, contributes to a decrease of functional health and a progressive inability to participate in various life situations, leading to loss of quality of life [3].

Despite the increase in number of therapeutic trials over the last 20 years, there is as yet no cure for HD, nor can its progress be reversed or slowed down. The emphasis of all forms of treatments is, therefore, to improve quality of life [2]. One of these non-pharmaceutical treatments offered to patients with HD in long-term care facilities is music therapy [4].

The American Music Therapy Association (AMTA) defines music therapy as follows:
"Music therapy is the clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program" [5].

Music therapy uses music experiences and patient-therapist relationships in order to effect therapeutic change [6]. Music therapists are part of the multidisciplinary team and participate in interdisciplinary treatment planning, ongoing evaluation, and follow-up [5].They assess emotional well-being, physical health, social functioning, communication abilities, and cognitive skills through musical responses. Music therapists design music sessions for individuals and groups based on the client's needs, using music improvisation, receptive music listening, song writing, lyric discussion, music and imagery, music performance, and learning through music [6].

Specific literature about MT in HD is scarce. In a comprehensive systematic literature review, Van Bruggen & Roos conclude that precise music therapy aims and methods in relation to the stage of the disease are not well determined, and therefore there is a need for a systematic study to determine the effects of music therapy in HD [7].

Over the past decades, music therapy (MT) has been developed for patients with other neurodegenerative diseases [8,9]. There is evidence that music therapy influences emotional well-being positively and that participation in music therapy increases social responses in persons with dementia, thus providing additional means of communication and enabling the patient to express his or her needs and emotions [10, 11]. Through music, contact can be established, especially as language deteriorates during the later stages of the dementia process [12]. The patient can be stimulated to recall life experiences through music. In the music therapy session this can be used as a catharsis to experience emotions. Furthermore, MT can reduce behavioral and psychological symptoms of dementia [4, 14, 15, 16].

Finally, enhancing the ability for self-expression, contributing to improvement of the quality of life, has been reported by Lee and McFerran who in a multiple case study describe five females with profound and multiple disabilities using song-choices in music therapy [13].

Based on the aforementioned benefits, the assumption can be made that music therapy is potentially a valuable non-pharmacological intervention to improve communication skills and thus possibly reduce behavioral problems, leading to a better quality of life (QoL) overall, in people with HD.

The aim of the present study is to evaluate the effect of group music therapy, compared to group recreational therapy (RT), on communicative and expressive skills in relation to behavior changes.

The research questions are

1. Does MT improve expressive and communicative skills in people with HD?
2. Does MT reduce behavioral problems in patients with HD?

Methods

An extensive description of the protocol has been published elsewhere [17].

Participants

Sixty-three patients with a clinically and genetically confirmed diagnosis of HD, 18 years and older, with a maximum TFC-score of 7 [18] were included. They were recruited from four different long- term care facilities in The Netherlands which specialize in HD-care. Patients with poor comprehension of the Dutch language or with hearing-impairments were excluded. Patients with other neurological disorders and patients who had received music therapy within the three months prior to the study were also excluded. Patients were allowed to continue their regular medication during the study, and any change in use was carefully registered. All patients and/or their legal representatives gave informed consent. The study was approved by the medical ethical committee of the Leiden University Medical Center (LUMC) in The Netherlands (registration # P14.038) and all local committees in the four nursing homes.

Patients were allocated to either the intervention group (music therapy) or the control group (recreational therapy). Recreational therapy was chosen over "no intervention/treatment as usual" because being a complex, multi-faceted intervention as is music therapy, recreational therapy to us seemed to be the most appropriate control intervention to make the two groups as homogeneous in personal attention and thus as comparable as possible.

Patients in both groups participated in group interventions with three to five participants. The decision to use group therapy instead of individual therapy was based on Magee [19, 20] who recommends music therapy group intervention in the mid- and late stage of the disease.

Randomization

Participants were randomized using stratified permuted block randomization with a 1:1 ratio of music therapy to recreational therapy. For details see the flowchart in fig.1.

The participants were stratified per center. Two independent persons per center conducted the randomization. The block-size varied from three to five persons, depending on the total number of participants in the center. The date of signing the informed consent was used to determine the sequence in which the participants were randomized. The decoded allocation was revealed after all baseline measurements had been taken. After randomization, the participants were considered part of the study, regardless of whether they decided to leave the study prematurely (intention-to-treat principle).

Data collection

All measurements were collected in patients' files and stored in locked cabinets. Data were entered into SPSS version 22 by an independent research assistant.

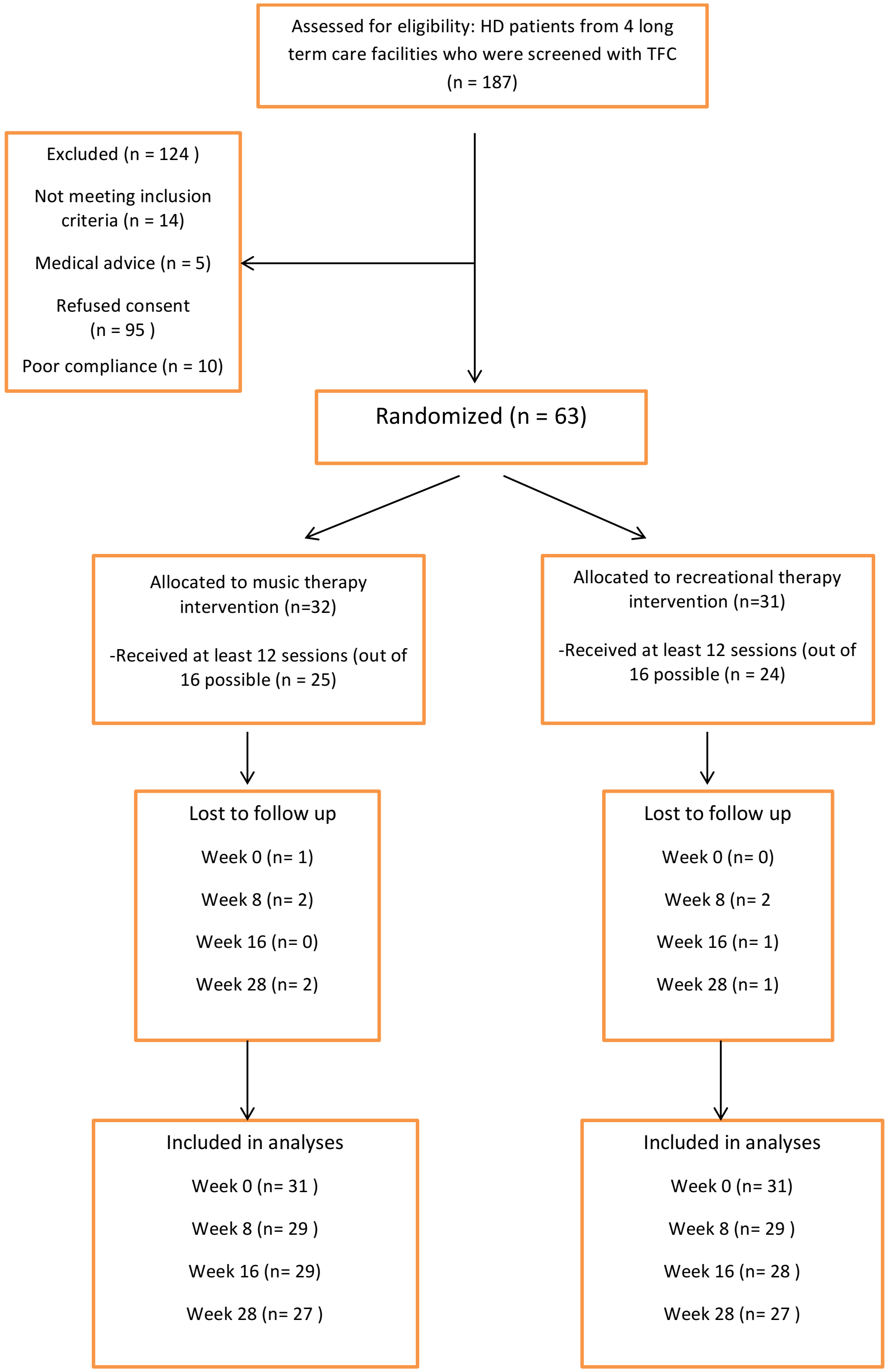

Fig. 1 Flowchart

Blinding

The assessors conducting the measurements were kept unaware of the patient's allocation, as was the principal investigator and the statistician. The allocation was not revealed until all analyses had been completed and conclusions drawn. Blinding the nursing staff, who was responsible for some of the measurements, was not always feasible as some of the nurses were also responsible for transporting the patients to and from the therapy rooms, as the number of available nurses on the ward was limited. Furthermore, blinding of the principal researcher and the statistician, who were responsible for the statistical analysis, was guaranteed: all data were coded, ensuring both were unaware of the allocation, the institute, the gender, the age and the use of medication of each participant. The dataset was not decoded, nor were the allocations revealed until the analysis had been completed.

Baseline assessments

Clinical and demographic variables (gender, age, use of psychotropic medication) were assessed at baseline (see table 1). The Mini Mental State Examination (MMSE) [21] was assessed at baseline to determine whether the cognitive functioning of the patients in the intervention group was different than those of the patients in the control group after randomization. Assessment of the MMSE was carried out by a psychologist or an assistant psychologist at the start and at the end of the study. Due to the severe cognitive state of the participants, the MMSE could not be assessed for 22 participants in the first assessment and for 26 participants in the second assessment. The missing scores were set to zero.

Outcome parameters

For a comprehensive description of the used items of the two measurement tools see appendix 1.

The primary outcome measure of the study was the social-cognitive functioning subscale of the Behaviour Observation Scale Huntington (BOSH) [22]. This scale consists of 15 items which were expected to detect changes in communicative and expressive skills. We choose this subscale as the primary outcome measure because it was hypothesized that through stimulation of these skills, activities of daily life and social-cognitive functioning will improve. As a result, behavioral problems (being the secondary outcome measures, see below) will reduce, overall leading to an improvement in the quality of life [17]. The scores of this subscale range from 1 (unaffected) to 4 (contact no longer possible); the sum score may range from 15 to 60. The BOSH-assessments were administered by previously trained nursing staff in charge of the daily care of the patients. Assessment of the BOSH took place at a random time point, one week before the first intervention (baseline assessment), and was repeated after the 8th and the 16th intervention. Finally, the last BOSH-assessment took place 12 weeks after the last intervention (week 28).

Table 1. Demographic and clinical characteristics of the study population

	Music therapy (n = 32)	Recreational therapy (n = 31)	Total (n = 63)
Total number of sessions			
- Attended/maximum	410/512	383/496	793/1008
- Missed (%)	102 (19,9%)	113 (22,8%)	215/(21,3%)
Mean age (years)	54,5	54,3	54,4
n (%) men	10 (31,2%)	10 (32,3)	20 (31,7)
n (%) women	22 (68,8%)	21 (67,7%)	43 (68,3)
Mean TFC-score at baseline	1,0 (S 1,48)	1,90 (SD 1,72)	1,44 (SD 1,65)
Mean MMSE-score			
- at baseline	14,9 (n=18)	18,7 (n=23)	16,8 (SD 8,09)
- after session 16	13,5 (n=17)	18,0 (n=20)	15,8 (SD 9,25)
Mean MMSE-score after setting missing scores to 0			
- at baseline	8,34 (n=32)	13,87 (n=31)	11,11
- after session 16	7,19 (n=32)	11,58 (n=31)	9,39
No. of patients who received psychotropic medication throughout the trial (week 0 – week 28)	25 (78,1%)	23 (74%)	24 (76%)
- antipsychotics	19	17	18
- antidepressants	18	18	18
- anxiolytics	19	12	16
- hypnotics	8	7	8
- anti-epileptics	2	4	3

The secondary outcome measures, behavioral problems, were assessed by the third subscale of the BOSH [18] and the Problem Behaviours Assessment-short version (PBA-s) [23, 24].

This subscale of the BOSH, the mental rigidity and aggression subscale, consists of 12 behavior-related items; the scores range from 1 (never) to 4 (always); the sum score can range from 12 to 48.

The PBA-s consists of 11 semi-structured interview items and assesses behavioral problems in the 4 weeks prior to the interview. After consulting the PBA-workgroup, however, we adjusted the retrospective 4 weeks to 1 week, due to the short time-frame in which the PBA-s had to be

administered. The PBA-s is a 5-point rating scale with subscales for severity and for frequency. The severity subscales uses the scores 0 (not at all) to 4 (severe/intolerable). The frequency subscale scores from 0 (absent) to 4 (all day, every day). Severity and frequency scores are multiplied to produce an overall PBA-score for each symptom. The PBA-s was scored by independent, trained psychologists who were blinded to group allocation of the patients.

The timeline of the assessment of the primary and secondary outcome measures is depicted in figure 1.

Intervention

The study was conducted between October 2014 and May 2016. Over a period of 16 weeks, participants received either music therapy or recreational therapy. All participants received their usual treatment while participating in the study and were not allowed to receive additional individual music therapy. Participants were free to leave the session or discontinue participation at any time. Each group consisted of three to five participants. The four participating centers had their own professionally trained music therapist and recreational therapist. They were all fully instructed to adhere to the study-protocol.

In the music therapy group, each of the 16 music therapy interventions lasted 60 minutes and was provided weekly. The music therapy approach focused on encouraging and engaging participants in expressive musical interaction [6]. The intervention was partly described in a protocol, a treatment guide in which the setting, goals and basic principles of the intervention were outlined, and the procedure itemized. The music therapy techniques aimed at achieving the goals were derived from the protocol "music therapy for Huntington's patients on improving and stimulating communication and self-expression" [25]. The music therapists were encouraged to be flexible while using the guidelines, allowing the "state-of-mind" of the participant, in combination with the therapist's own clinical experience, to be the guide. While the sessions were partly standardized without limiting the music therapists in their interactions, the intervention itself was to be applied according to the protocol: each session started with the same welcome song and ended with the same farewell song. Between these two songs, the music therapist was allowed to adjust the level of each intervention according to individual capacities. The music experiences could range from listening to music to playing or singing songs to free improvisation.

In the control group, recreational activities were offered under exactly the same circumstances as the afore-mentioned music therapy sessions. As in the intervention group, a treatment guide described the procedure for the control group. The main goal of the recreational activities was to enhance communication skills by way of encouraging and stimulating the patients to interact. The activities could vary from reading the newspaper, cooking, arts-and-crafts/handwork or puzzles/games. Musical activities, such as singing along or watching a music-video, were not allowed, nor was background music to be played during the activities. Participation in musical activities in the facility (such as attending an in-house music performance) was allowed. These activities are not considered to be music therapy and are open to all patients residing in the institution, regardless of participation in the study. Also, listening to music in the privacy of their own room was allowed for all participants throughout the study.

Statistical analysis

Sample size was determined based on the ICC of the primary outcome measurement(BOSH) [18]. We assumed that the values in the control group would not change very much over the course of the study, whereas those in the experimental group would improve by 25%. We further assumed an α of 0.05 and a ß of 0.20. Based on these assumptions, we came to the following sample size calculation:

- Social-cognitive original mean (SD) = 2.10 (1.58) and if we conservatively estimate a reduction in SD to 0.75, we would require an N of 30 per group for this subscale (for an effect size of 0.52 (moderate)).

For the data-analysis, we followed the same statistical procedure for all three (primary and secondary) outcome measures:
First we calculated the mean sum scores of the scale (see figure 2). The sum score of the baseline-values was then used as a covariate in the subsequent mixed model analysis as these baseline scores appeared to be different between the MT-group and the RT-group.

A linear mixed model with repeated measures was used to compare the four BOSH and PBA-s-scores of the experimental and the control group, fitting condition (MT or RT) and time variable (the assessment number) as fixed effects in the model.

As stratified randomization can lead to correlation between treatment arms, we adjusted for the stratification factor (i.e. the institution) in the analysis to obtain correct confidence intervals and p-values by fitting the institution code as a factor in our linear mixed model.

All data were gathered and stored in locked cabinets in the four different participating centers and entered into SPSS version 22 by an independent research assistant.

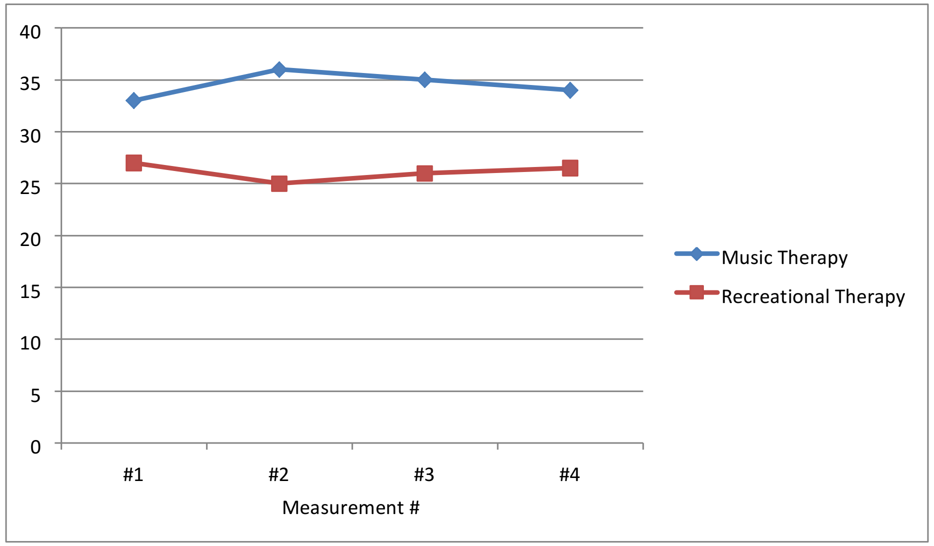

Fig. 2a Mean sum scores (range 15-60) of the social/cognitive domain of the BOSH for both conditions at each of the four time-points.

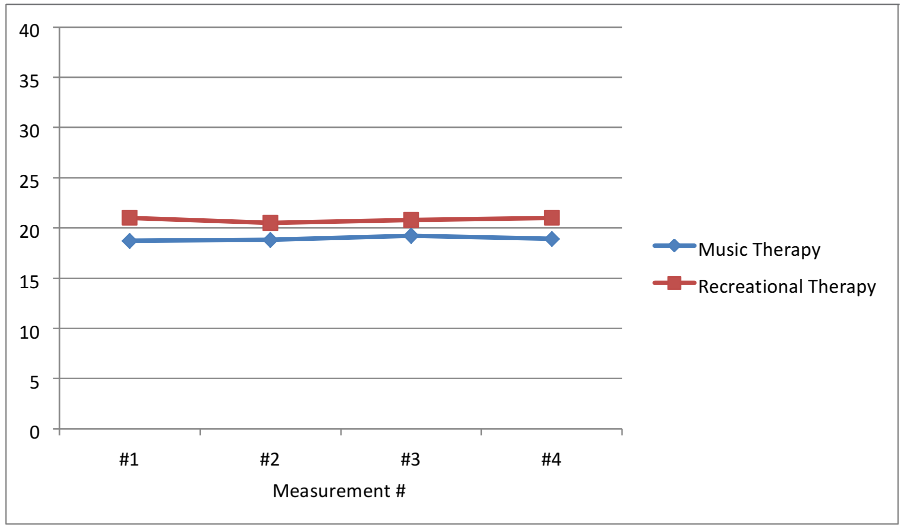

Fig. 2b Mean sum scores (range 12-48) of the mental rigidity/aggression- domain of the BOSH for both conditions at each of the four time-points.

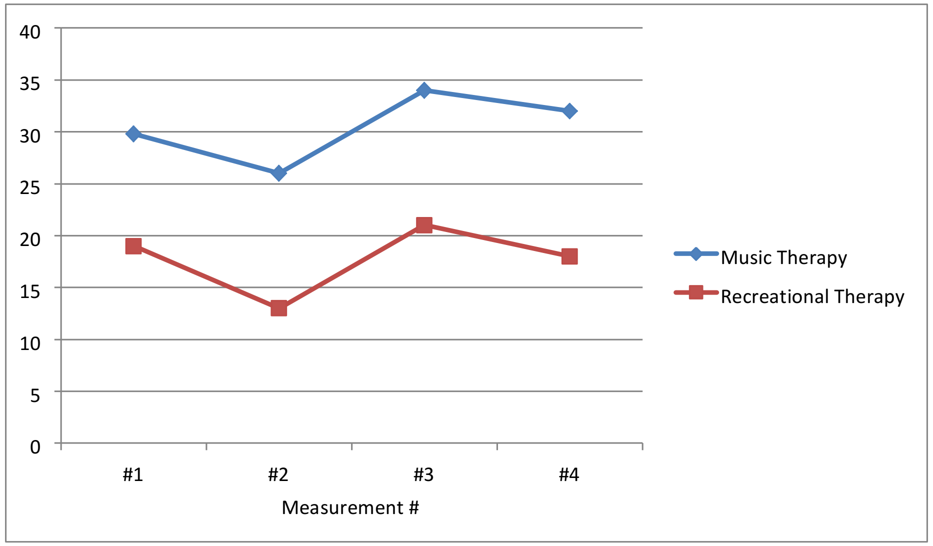

Fig. 2c Mean sum scores (range 0-176) of the severity/frequency scale of the PBAs for both conditions at each of the four time-points.

Results

A total of 187 residents from four different long-term care facilities were eligible to participate in the study. Of these, 124 residents were not included for various reasons: not meeting the inclusion criteria, refusing consent, medical advice or poor compliance. The remaining 63 participants were randomized to either music therapy (n=32) or recreational therapy (n=31). Of these, a total of 9 participants (5 from the MT group and 4 from the RT group) were lost to follow-up, due to death (n= 4), moving to another care-facility (n=1), or lack of motivation (n=4). This resulted in 54 participants remaining (27 randomized to MT and 27 to RT). See the flowchart in figure 1.

At baseline, the mean TFC-score of the MT-group (1.00) tended to be somewhat lower than that of the RT-group (1.90), indicating a lower functioning level of participants in the MT-group. However, this difference was not significant (p = .03). For all other characteristics (gender, age) the two groups did not differ significantly either.

For both conditions at each of the four time-points, the unadjusted mean sum scores of the social/cognitive subscale of the BOSH are shown in figure 2a, of the mental/rigidity/aggression subscale of the BOSH in figure 2b, and of the severity/frequency scale of the PBAs in figure 2c. Note that a lower score means improvement for all three outcome measures.

Linear mixed models analyses showed that

- the difference between conditions at the three post-baseline time points, after correction for the difference in baseline values, can assumed to be constant as there was no effect-modification (interaction) of these differences by time (see figure 2);
- the difference between the estimated means of the scores of the social/cognitive subscale of the BOSH between the two conditions (2.88) at the three post-baseline time points is significant at the .05 level (p = .042), with a beneficial effect for the control condition;
- the difference between the estimated means of the scores of the mental rigidity/aggression subscale of the BOSH between the two conditions (4.60) at the three post-baseline time points is not significant at the .05 level (p = .125);
- the difference between the estimated means of the scores of the severity/frequency scales of the PBA-s between the two conditions (-1.39) is not significant at the .05 level (p = .630).

See table 2.

When institute was added as a fixed effect in our model, there was no interaction effect between institute and condition, i.e. the difference between the means of the sum-scores of the two conditions did not depend on the institute for any of the three domains.

Table 2. Estimate of the fixed effects of the primary and secondary outcome measures

	Estimate	Significance	95% Confidence interval	
			Upper bound	Lower bound
SocCog[1] (Primary Outcome)	2.88	.042	.108	5.65
MentRigAggr[2] (Secondary Outcome)	4.60	.125	-1.32	10.52
PBAsSevFreq[3] (Secondary Outcome)	-1.39	.630	-7.16	4.38

[1] social/cognitive subscale of the Behavioural Observation Scale Huntington
[2] mental rigidity/aggression subscale of the Behavioural Observation Scale Huntington
[3] severity/frequency scale of the Problem Behaviours Assessment-short version

Discussion

In the present study we have looked for answers to the following three research questions:
1. Does MT improve expressive and communicative skills in people with HD?
2. Does MT reduce behavioral problems in patients with HD?

Music therapy offered to patients with Huntington's disease once weekly for a period of 16 weeks had no additional beneficial effect on improving expressive and communicative skills or on reducing behavioral problems when compared to recreational therapy. A slight clinical effect was found in the primary outcome measure (the social and cognitive subscale of the BOSH) in favor of recreational therapy. In our opinion, the clinical relevance of this outcome is negligible as the difference in outcome between the two conditions was very small. No significant effect could be found for the two secondary outcome measurements (the mental rigidity/aggression subscale of the BOSH and the severity/frequency scale of the PBA-s) in favor of MT or RT.

There seems to be a discrepancy between subjective (qualitative) positive evaluations that have been published and the objective (quantitative) outcome measures that are reported in this study. This is also highlighted in a comprehensive literature review [7]. Possible explanations of this apparent discrepancy are that this study is the first randomized controlled trial applying music therapy for patients in the advanced stage of Huntington's disease, involving a relatively large number of participants.

The strength of the study is three-fold:
First: The design: randomization took place separately in each participating facility. Anticipating the possibility of unbalanced and missing data, we decided to use a linear mixed model to analyze the results.

Second: The fact that we used an active condition in the control group, providing similar degrees of attention and group contact in both groups. Most studies to date have used "treatment as usual" as the control condition.

Third: The fact that on the one hand, the clinical method was clearly defined: both interventions were (partly) protocolled, guiding all therapists to conduct a similar and thus comparable procedure during the sessions. On the other hand, the therapists had the freedom to elaborate during each session as long as each of them aimed for the same goals.

It should also be mentioned that conducting an RCT with vulnerable late stage HD-patients is very challenging. The burden of participating in such studies is heavy, especially for the patients in the more advanced stages of the disease as in our study, who are more likely to drop out before completing the trial [1].

Several limitations of the present study may be the cause of the above-mentioned discrepancy between quantitative and qualitative evidence:

A. The vulnerability of the target population in relation to compliance with treatment.
Considering the low scores on both the MMSE and the TFC, the severity of the cognitive impairments at this stage of the disease is obvious. In the literature review [7], the HD-patients included in the studies were in the early or mid-stage of the disease, while in the present study, all participating patients were in the advanced stage.

Although participants were allocated to the groups by randomization, the scores of those in the music therapy group were somewhat lower in both the MMSE and the TFC, indicating a more severe functional and cognitive state in the MT-group. Adjustment for TFC-scores however did not provide different results, indicating that the functional difference was not a confounder.

The factors mentioned here might also explain the large number of sessions missed and hence the missing data (see table 1). The strength, however, of performing a mixed model technique is that it is less sensitive to missing data than "classical" techniques through its restricted maximum likelihood estimation of effects.

B. The sensitivity of the measurement tools for the advanced stage of the target population.
The assessment tools (BOSH and PBA-s) might not have been the most eligible, as they might not be sensitive enough to detect marginal clinical effects in the later stages of the disease. However, the tools that were available at the time of designing the study were expected to be not eligible to use in advanced stage patients (the target population of the presented study). The choice for the BOSH and the PBA-s was based on the expectation that the items of (the subscales of) these tools would detect changes in communication and expressiveness, as well as in behavior, see appendix 1. A good alternative for future studies might be the UHDRS-FAP (Unified Huntington's Disease rating Scale- For Advanced Patients) [26]. This is the only scale that detects decline in patients with a TFC-score ≤ 1. The UHDRS-FAP was developed in 2013 and appears to be more sensitive to change than the original UHDRS for cognitive and motor

domains. Also, a pilot validation study of the Music therapy Assessment Tool for Advanced Huntington's Disease (MATA-HD) has just finished in the UK [27]: preliminary data indicate that the MATA-HD is a promising tool for measuring patient's responses to music therapy interventions across psychological, physical, social and communication domains of functioning in patients with advanced HD. Neither tool was available yet when designing the present study.

Furthermore, validated measurement tools that are sensitive for emotional and social cognitive responses in dementia (see introduction) might be suitable to use in future studies with HD-patients.

C. The short-term effect of the intervention.
It would be quite valid to raise questions about the frequency and the time-points of the assessments. It is possible that the short-term effect of the intervention might not have been detected in the present study. In a comparable study which determined the effects of music therapy in reducing behavioral problems in elderly people with dementia, measurements were taken one hour before the session, and one, two and four hours after the session [28]. In our opinion this was not feasible in the present study due to the severity of the participants' condition.

D. Group-intervention versus individual intervention.
Group intervention, even though the group-size was small, might not have been the best option. In our opinion, contrary to Magee [19,20], at this late stage of the disease, individual therapy might be preferable.

Finally: when designing the study protocol we initially developed a third research question: 'does MT improve quality of life of patients with HD?'. We decided to omit this third question, as the relation between the primary and secondary outcome measures and improvement of the quality of life of patients with HD could not be evaluated in the present study with the assessment tools that were used. This third research question remains open for discussion. However, the lack of quantitative outcome measures supporting the beneficial effects of music therapy on communication and behavior in patients with HD does not implicate that music therapy does not have a beneficial effect on improving quality of life. When evaluating interventions that have the potential to improve quality of life, finding the best research designs and the best outcome measures for patients in the advanced stage of HD remains a major challenge.

Conclusion

This was the first study to assess the effect of group music therapy on HD patients in the advanced stages of the disease. The beneficial effects of music therapy, recorded in many, mainly qualitative case reports and studies, could not be confirmed with the design (i.e. RCT, group therapy vs individual therapy) and outcome measures that have been used in the present study. A comprehensive process-evaluation alongside the present effect evaluation is therefore performed. The outcome of this process evaluation is expected in the Spring of 2017 and will be published elsewhere. This will result in recommendations for future research to strengthen the (quantitative and qualitative) evidence for implementing music therapy in rehabilitation for persons with Huntington's Disease.

Ethical approval

The study has been approved by the Medical Ethics Review Committee of the Leiden University Medical Center, registration number P14.038, and by all four centers. The study has been registered in the Dutch Trial Register (NTR 4904).

Competing interests

None of the authors has any competing interests.

Authors' contributions

MBR is a neurological music therapist fellow. She drafted the protocol, analyzed the data and wrote the manuscript.
AV is a psychologist. She reviewed the manuscript.
RW is a physician and statistician. He contributed to the statistical analyses and reviewed the manuscript.
WA is elderly care physician and professor of institutional and elderly care medicine. He reviewed the manuscript.
RR is a neurologist and contributed to the development of the study design and reviewed the manuscript.
All authors have been involved in reviewing the manuscript, and have read and approved the final text.

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The participating centers were

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- De Riethorst Stromenland location Kloosterhoeve, Raamsdonksveer, The Netherlands
- Topaz Huntington Center Overduin, Katwijk, The Netherlands

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Appendices:

1. Second subscale of the BOSH, third subscale of the BOSH, PBA-s
2. Description of the procedures of the music therapy and the recreational therapy sessions

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APPENDIX 1:

<u>Behavior Observation Scale Huntington (BOSH) – second subscale (social/cognitive functioning)</u>

6. Ability to understand complex actions such as operating an electric wheelchair, a communicator, other electrical appliances, and so on
7. Voice control (control of sound and volume) and articulation
8. Intelligibility
9. Comprehensibility through nonverbal communication
10. Ability to understand verbal communication
11. Ability to understand nonverbal communication
12. Recollection of recent events important to patient (birthdays, trips, weddings)
12. Remembering appointments
13. Ability to occupy himself/herself, if necessary, using a diary
14. Ability to occupy himself/herself and participate in organized activities
15. Patient knows staff members and fellow inpatients by name
16. Emotionalism
17. Awareness of being ill
18. Seeking contact and receptiveness
19. Contact with family, friends, or fellow inpatients
20. Showing consideration for fellow inpatients

<u>Behavior Observation Scale Huntington (BOSH) – third subscale (mental rigidity and aggression)</u>

21. Degree to which verbal and physical aggression can be corrected
22. Tendency toward verbal and physical aggression
23. Patient tries to exceed the limits of standing agreements or house rules
24. Patient causes problems if a fixed routine is not adhered to
25. Patient accepts what you say
26. Patient is open to correction
27. Performance of specific activities is impeded because patient cannot dissociate from subjects or events that are not or are no longer relevant

28. Patient performs stereotypical, apparently aimless activities (such as walking and then sitting down again immediately), which take precedence over everything
29. Choking while eating or drinking
30. Eating and drinking
31. Voracity and insatiability
32. Bolting food

Problem Behaviours Assessment – short version

1. Depressed mood
2. Suicidal ideation
3. Anxiety
4. Irritability
5. Angry or aggressive behaviour
6. Lack of initiative (apathy)
7. Perseverative thinking or behaviour
8. Obsessive-compulsive behaviours
9. Delusions/paranoid thinking
10. Hallucinations
11. Disoriented behaviour

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APPENDIX 2:

Description of the procedures of the music therapy and the recreational therapy sessions

All participants (in both the experimental (intervention) group and the control group) will continue to receive treatment as usual. The intervention group will receive music therapy (MT-group). The control group will receive recreational therapy. The number of sessions (16) is equal in both groups, as are the day of the week and the time of the day at which the sessions will take place. Patients in both groups will participate in group interventions with three to five participants.

Intervention group

The music therapists committed to the study are professionally trained and have been specifically informed about the clinical method and its theoretical basis.

The main goal of the music therapy intervention is to enhance communication skills by way of encouraging and stimulating the patients in interaction. The music therapy approach applied in this study is focused on encouraging and engaging patients in expressive musical interaction. The role of the therapist is to use musical parameters and interventions to stimulate expressive and communicative skills. The degree of verbal reflection may vary; the therapist will, however, encourage the participants to express themselves. The therapeutic process is based on the mutual construction of meaning of emerging thoughts, images, emotional content and expressive qualities that often originate from the musical experience [10].

A treatment guide specifies the procedures. It outlines the setting, goals and basic principles of the intervention; Table 1 (the benefits of music therapy for neurodegenerative diseases) is used as guideline. The available music therapy techniques to target the set goals are derived from the protocol "music therapy for Huntington's patients on improving and stimulating communication and self-expression" [25]. However, the guidelines are to be administered flexibly according to the patient's state of mind and his needs at that very moment. The clinical expertise of the therapist will be the guide, providing the therapist with enough "space" for flexible adaptation within the treatment guide. Also, the patients music preference, especially because most of the treatment involves receptive music therapy, is very important. This is the reason why the protocol allows and encourages the music therapist to adjust their treatment by way of "tailor made" sessions, providing each of the participants with his or her music preference.

The process used in each session is standard while the content is flexible. The intervention will be provided at the same time of the same day of the week by a formally trained, experienced music therapist. The sessions will take place once weekly with a total of 16 sessions, lasting 45 minutes. They will be standardized without limiting the music therapists in their interactions. The intervention itself, however, will be (partly) applied according to a protocol. Each session starts with the same welcome song/musical piece and ends with the same farewell song/musical piece. In doing so, the participants become familiar with the start and the end of each session. In between these two songs/musical pieces, the music therapist adjusts the level of each intervention to individual capacities. After the welcome song, the music therapy sessions may be varied: the music experiences can range from listening to music to playing or singing songs to free improvisation. therapist has the freedom to determine what works best at that very moment for that specific patient. The participants will listen to music selected, sung or played by the therapist. Active participation in music activities by singing or playing a musical instrument will be stimulated as much as possible. The music will be selected by the music therapist to incite expressive and communication skills and to reduce agitation, based on musical parameters, such as rhythm, melody, harmony, dynamics, timbre. After each song/musical intervention, the therapist will encourage and stimulate the participants to reflect verbally on the music [25].

Besides the music therapy intervention during the whole study, participants are not allowed to receive additional individual music therapy.

All participants are allowed to leave the session at all times.

Control group

All activities will be provided by professionally trained recreational therapists who have been specifically informed about the study.

In the control group, recreational day activities will be offered under exactly the same circumstances as the music therapy sessions: a total of 16 weekly sessions, each lasting 45 minutes, every week at exactly the same time as the music therapy intervention. As in the intervention group, a treatment guide specifies the treatment procedures for the control group. In this guide, the setting and general goals are outlined. The main goal of the recreational activities is to enhance communication skills by way of encouraging and stimulating the patients in interaction..

The activities vary from reading the newspaper, cooking, arts-and-crafts/handwork or puzzles/games. Musical activities, such as singing along or watching a music-video are not allowed, nor will background-music be played. The recreational therapist is well instructed about and fully aware of this restriction. Besides that, during the whole study, participants from the control group are not allowed to receive music therapy. Both the physician who is responsible for the referrals and the music therapists are fully aware of this limitation. Participation in in regular musical activities however (such as watching a music video or attending a music-performance which takes place on the ward occasionally) is allowed. These activities are not considered to be music therapy and are open to all patients that reside in the institution, regardless of participation in the study. Also, listening to music in the privacy of their own room is allowed for all participants.

All participants are allowed to leave the session at all times.

The music therapy and the recreational day activities will be provided in separate rooms, away from the ward. Participants will be taken to the music therapy room or the activity room by the nursing staff. The music therapist and the recreational therapist make sure that they can start the moment all participants are in the room. After the session, the participants will be taken back to the ward by the nursing staff. The therapists will never leave a participant in the room unattended.

After each session, a short report of the activities will be written by both therapists, including an evaluation of each patient. Since a self-report from the patient himself is not feasible, the reports written by the therapists will be used for evaluation purposes and treatment fidelity.

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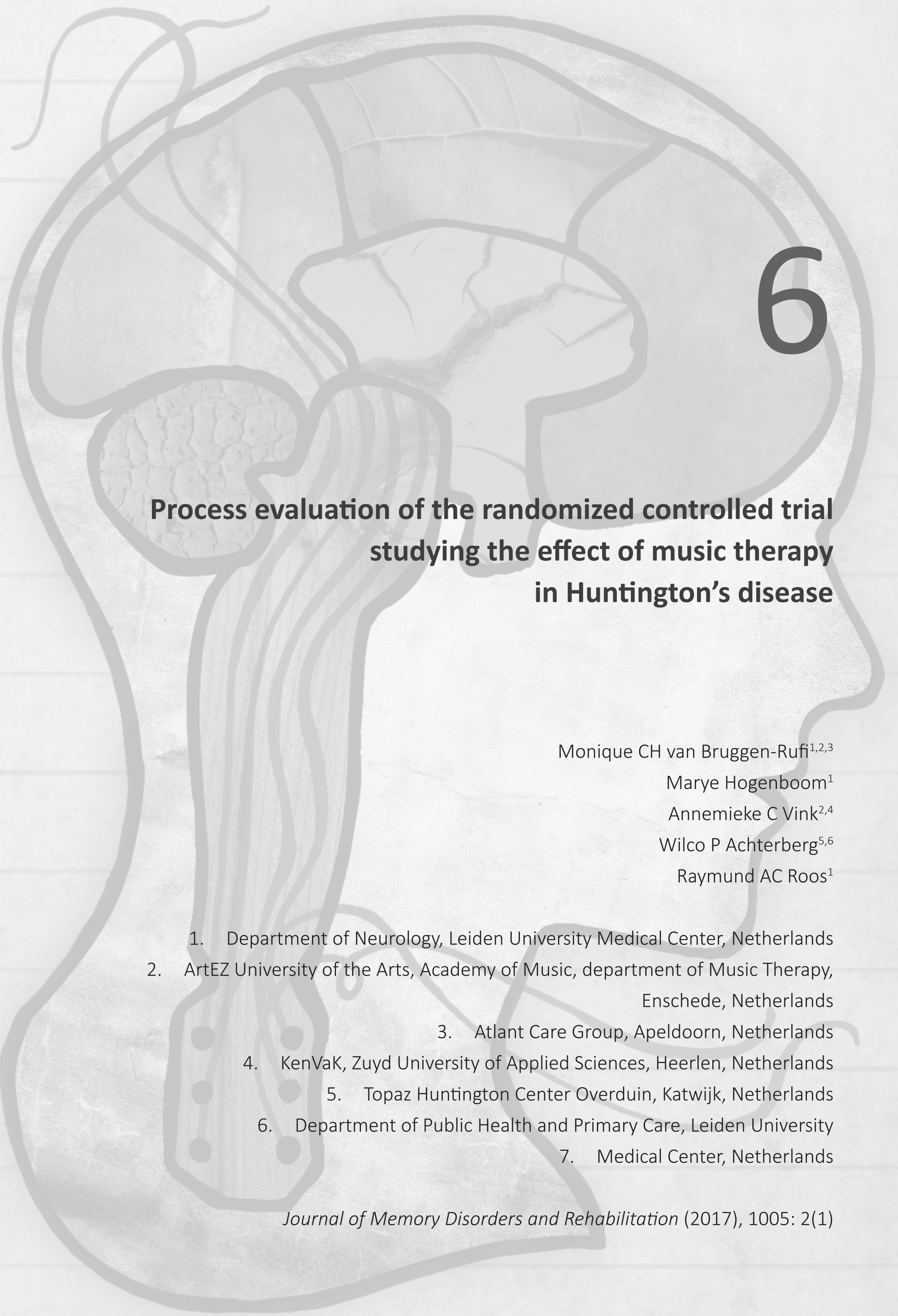
> *“With the right music, you either forget everything*
> *or you remember everything”*
>
> *Unknown*



6

Process evaluation of the randomized controlled trial studying the effect of music therapy in Huntington’s disease

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Abstract

Background/Introduction
This article reports the process evaluation of a multi-center randomized controlled trial in which the effect of music therapy in Huntington's disease (HD) was studied. The beneficial effects of this complex intervention, recorded in many, mainly qualitative case reports and studies, could not be confirmed with the design and outcome measures used in the present study. To find possible explanations for this discrepancy, we performed a comprehensive process-evaluation.

Aim
To evaluate the execution of this randomized controlled trial (RCT) by collecting information regarding (1) the study population, (2) the intervention and (3) the outcome measures. The evaluation will result in recommendations for future studies regarding study population, implementation and adjustment of the intervention and appropriate study design.

Method
A mixed model of qualitative and quantitative data was used. Qualitative data were analyzed following the guidelines of thematic analysis within the grounded theory and naturalistic inquiry. Quantitative data were derived from the evaluation forms and were accounted for in the analysis.

Results
The experience of twenty professionals was evaluated using an online survey, questionnaires, interviews, observation forms and field notes. The most obvious barrier was the severe cognitive decline of the study population in combination with circumstances within the participating centers, and the assessment tools that might not have been sensitive enough for the set goals of the RCT.

Conclusion
Performing a multi-center RCT studying the efficacy of music therapy with vulnerable patients in a long-term care facility is feasible, but challenging. No matter how complex the intervention and the study population, with the right study design, outcome measures and assessment tools, and with an unambiguous written protocol, and a continuous evaluation and monitoring throughout the whole study, barriers can be by-passed or avoided, and facilitators can be empowered. Suggestions are made for future research concerning the use of alternative designs (multiple single subject design study) and measurement tools (Goal Attainment Scale (GAS), Music Therapy Assessment Tool for Advanced HD (MATA HD)).

Introduction

This article reports the process evaluation of a randomized controlled trial (RCT) studying the effects of music therapy in patients with advanced stage Huntington's disease. An extensive description of the protocol (methods, randomization procedure, and intervention) and the results of this RCT are published elsewhere [1, 2]. Below is a short summary.

Music therapy is considered a complex intervention. These are interventions comprising multiple components acting independently or interdependently, and therefore difficult to develop, document, evaluate and reproduce. It is increasingly recognized that especially these kinds of interventions should be rigorously evaluated [3]. Documenting and evaluating each process step in detail, exploring the execution, implementation, receipt and setting of an intervention will help the interpretation of outcome parameters and designing future trials [4].

Huntington's disease (HD) is a progressive, neurodegenerative disease with autosomal dominant inheritance, characterized by motor disturbances, cognitive decline and behavioral and psychological symptoms and signs. These signs result in progressive functional decline [5] and a gradual loss of expressive and communicative skills. This combination leads to loss of quality of life [6].

Since there is no cure, all treatment is aimed at improving quality of life. One of these non-pharmaceutical treatments offered to patients with HD in long-term care facilities is music therapy. Music therapy is defined as "…the clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship…"[7]. Through music therapy an additional means of communication can be provided, enabling the patient to express his needs and emotions [8]. Furthermore, through music, contact can be established, especially as language deteriorates, such as for instance during the later stages of dementia [9].

The use and efficacy of music therapy in patients with Huntington's disease on a large scale has hardly been studied. Therefore, a multi-center single blind randomized controlled trial (RCT) has been conducted between October 2014 and May 2016 in four long-term care facilities specialized in Huntington's disease-care in The Netherlands [2]. The main goal of the RCT was to study the effect of music therapy on improving expressive and communication skills and behavior in patients with advanced HD. Sixty-three patients were randomised using center-stratified block-permuted randomisation. Two random groups were created. Over a period of 16 weeks, the experimental group was offered a weekly music therapy program according to a structured protocol, and the control group participated in weekly regular recreational therapy. Both therapies can be seen as complex intervention, difficult to develop, document, evaluate, and reproduce [10,11] (see box 1). In addition, both groups received usual care. The primary outcome measure to assess changes in expressive and communication skills was the second subscale (social cognitive functioning) of the Behaviour Observation Scale Huntington (BOSH) [12]. Changes in behavior were assessed by the third subscale (mental rigidity and aggression) of the BOSH and the Problem Behaviours Assessment-short version (PBA-s) [13]. The effect-evaluation showed that these outcomes did not improve in the MT group as compared to the control group [2].

Box 1: What makes an intervention complex [10,11]

- Number of interacting components within the experimental and control interventions
- Number and difficulty of behaviors required by those delivering or receiving the intervention
- Number of groups or organizational levels targeted by the intervention
- Number and variability of outcomes
- Degree of flexibility or tailoring of the intervention permitted

This article reports the process evaluation of the aforementioned randomized controlled trial. The aim of the study is to evaluate the execution of this RCT by collecting information regarding (1) the study population, (2) the intervention and (3) the outcome measures. The outcome will result in recommendations for future studies in regard to study design, study population, implementation and adjustment of the intervention and outcome measures.

This study design as well as the music therapy intervention can be seen as an example of a complex intervention [10,11] because:

- It is a multi-center trial: the trial took place in four different long term care facilities.
- All four institutes had their own therapists, psychologists, physicians, and nursing staff who were involved in the trial. All professionals had to be instructed separately.
- Two different measurement tools had to be assessed by many different assessors at four different moments in a 28-week timeframe. All assessors had to be trained.
- The participants receiving the intervention all were diagnosed with Huntington's disease in advanced stage, a disease with a wide spectrum of symptoms and signs.
- Interventions like music therapy are designed to be adapted to the specific needs of the patient ("tailor made") and to local circumstances. Therefore, a high flexibility-rate was demanded from the music therapists.

METHOD

The method as well as the results and implications of the present process evaluation are presented using the format that is based on the following three components [10]:

(1) The success rate of recruitment and quality of the study population;
(2) The quality of execution of the complex intervention, and;
(3) The process of acquisition of the evaluation data.
See for the related process measures of these three components box 2 [10].

Box 2: Process-evaluation components and related process measures of a complex intervention [10]

Process Components	**Process Measures**
Study population	1. Recruitment and selection rate 2. Barriers and facilitators in recruitment and selection process 3. Follow-up: attrition rate 4. Barriers and facilitators for follow-up
Multiple components	1. Quality of delivery of the interventional components 2. Barriers and facilitators for delivery of interventional components 3. Adherence to interventional components 4. Barriers and facilitators for adherence to interventional components 5. Experience of participants and instructors with intervention components
Evaluation data	1. Outcome measures: coverage of interventional components 2. completeness of data collection 3. Barriers and facilitators for data collection

Participants

Due to the vulnerability of the patients with HD in the advanced stage, we did not involve them in the process-evaluation: the burden of being exposed to additional questionnaires was an important consideration. Observation forms filled out by the therapists after each session were consulted to determine the patient's compliance and experience.

We used a purposive sampling strategy to select 20 professionals who had been involved in the execution of the trial. In doing this, we made sure that each group of professionals and each of the four participating centers were equally represented. Participating professionals were one team per site, consisting of a site monitor, a music therapist, a recreational therapist, a BOSH-assessor, and a PBA-s-assessor.

Data collection

A mixed method of qualitative and quantitative data collection was used to analyze the responses obtained from:

- Online survey of monitors, assessors and nursing staff and therapists;
- Evaluation forms filled out by music therapists and recreational therapists after each session;
- Interviews with one of each of the monitors, assessors, nursing staff and therapists;
- Notes taken during contact with monitors and research assistant.

Online survey of monitors, assessors, nursing staff and therapists

An online survey was sent to all 20 participating professionals. Each of the three process components mentioned above was assessed in the questionnaire that consisted of ten open questions about the study population, the quality of execution of the complex intervention, and the process of acquisition of the evaluation data.

Evaluation forms filled out by music therapists and recreational therapists after each session

Evaluation forms were filled out by the eight therapists involved in the study (four music therapists and four recreational therapists) after each session. These forms provided both qualitative and quantitative data about the treatment compliance of the patients, about disturbing factors prior to or during the intervention, and were used to check what activities and which techniques were used during the sessions and if this matched with the protocol.

Interviews with the monitors, assessors, nursing staff, and therapists

In addition to the questionnaires, we used face-to-face semi-structured interviews with four other professionals that were involved in the execution of the study: one BOSH-assessor, one PBA-assessor, one music therapist and one recreational therapist. They were chosen by way of convenience sampling.

The three components mentioned above (study population, complex intervention and data-evaluation) were the guideline during the (semi-structured) interviews.

Notes taken during contact with monitors and research assistant

Furthermore, the four monitors of each participating center had contact with the principal researcher (MvBR) on a regular base throughout the whole study. This ensured the progress of the study, the adherence of the protocol and the data collection (i.e. random check of the raw scores in the data base). The frequency and the intensity of this contact differed between the sites. Also, the research assistant (MH) visited the four participating centers on a regular basis, checking the raw scores, and entering all collected data into SPSS version 22. Site notes of all her visits, phases of data collection and data preparation were also included in the present process evaluation.

Procedure Data collection

Guidelines of two methods were followed: the naturalistic inquiry [14] and the thematic analysis in accordance with the grounded theory of Glaser & Strauss [15]. The first is a method that emphasizes the trustworthiness of the study, while the second is an analytical approach used most frequently in grounded theory studies whereby theoretical insights are generated from qualitative data (inductive process) [16].

Trustworthiness

To ensure credibility and trustworthiness we used the following procedures:

a) Triangulation

We ensured methodological and data triangulation by using different methods of data collection (online survey, questionnaires, observation forms, interviews and site notes).

b) Confirmability

During the analysis, the research assistant (MH) examined the analysis process and records for accuracy (confirmability). The interpretations of the data and the preliminary results were presented and discussed with the principal researchers' supervisors (AV, WA, RR) Their objective feedback was used to finalize the conclusions of the study.

Analysis

The analysis was conducted by the principal researcher (MvBR). The three components mentioned above [10] (study population, complex interventions and data-evaluation) were the guideline throughout the whole analysis procedure.

The themes and concepts were derived from the data by using the open coding system: different categories were identified and codes that described the same themes were clustered or deducted (see figure 1a, 1b and 1c "Categories and Themes"). A content analysis was performed according to the constant comparison method, based on the grounded theory of Glaser & Strauss [15]. Data were extensively collected, coded and organized. The whole process of constant comparison leads to general conclusion(s) which can logically be derived from the data [17,18].

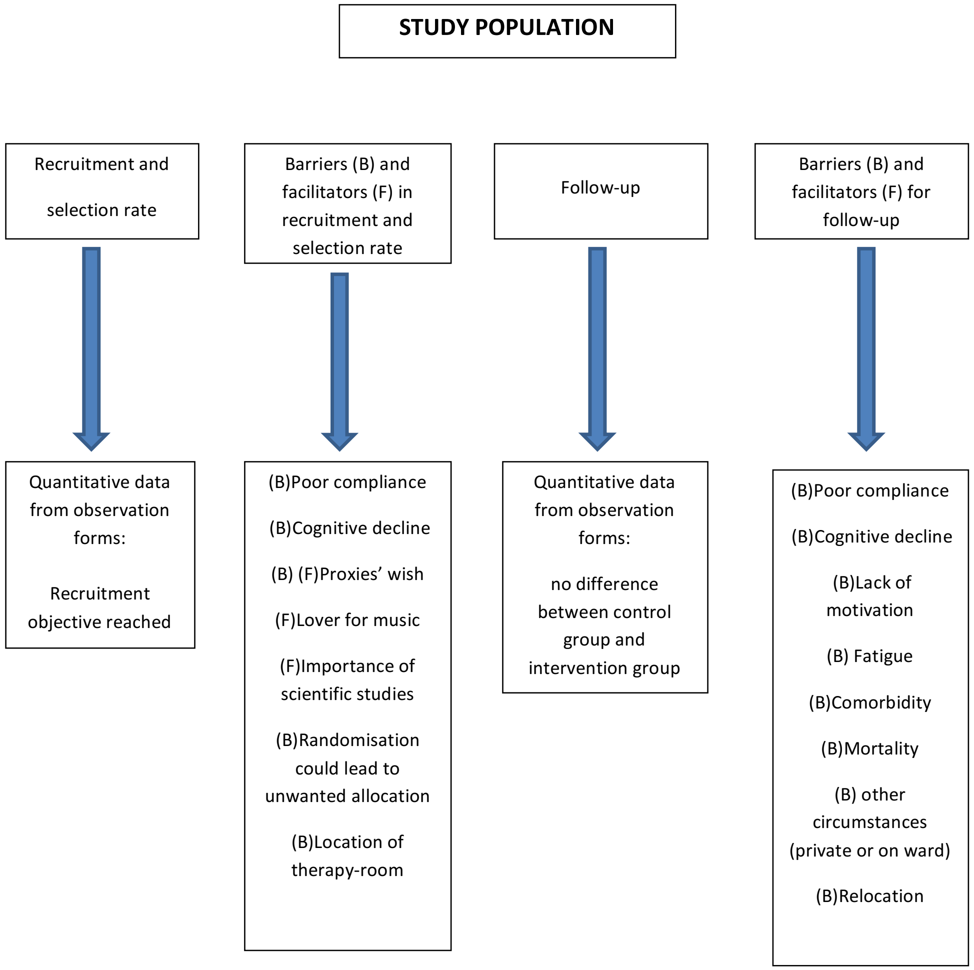

Figure 1a: Categories and themes study population

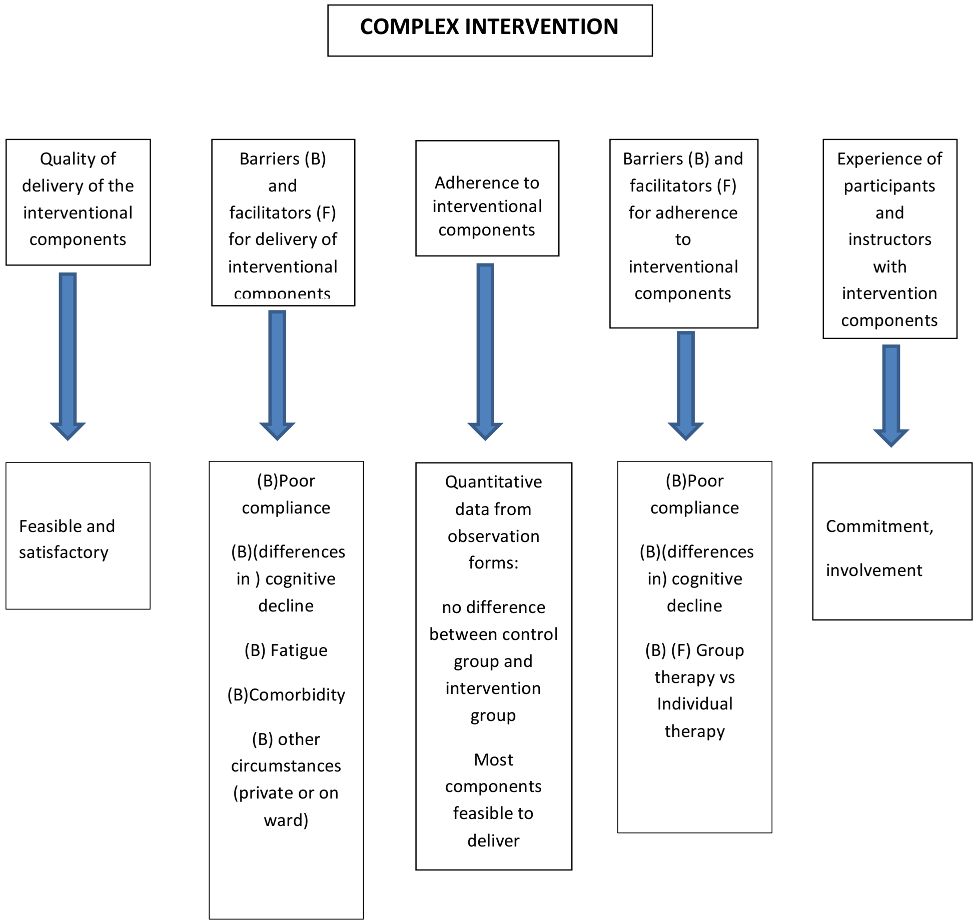

Figure 1b: Categories and themes complex intervention

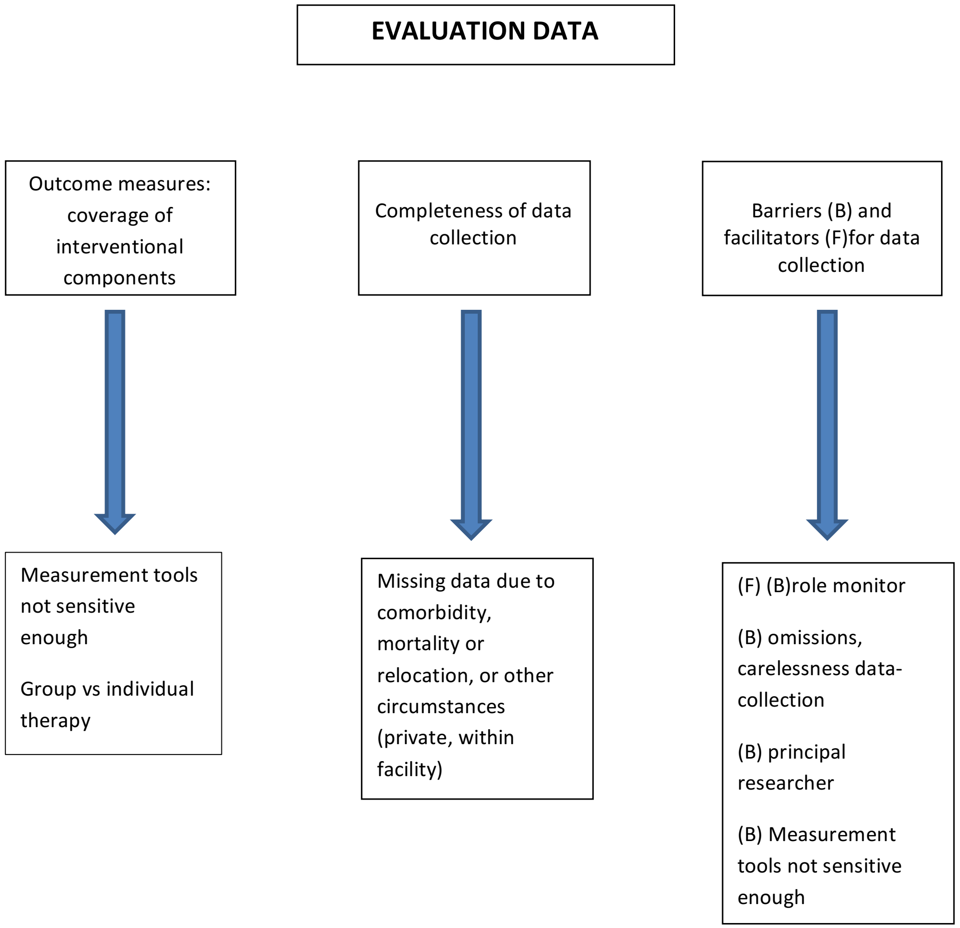

Figure 1c: Categories and themes evaluation data

Results

Below, the results of the online survey (n = 19), the interviews (n = 4), the evaluation forms (n = 8) and the site notes (n = 5) are presented, using the format as depicted in box 2 [10]. See also Table 1 (demographic and clinical characteristics of the study population specified per institution).

A. Study population

1. Recruitment and selection rate

A total of 187 patients were eligible to participate in the trial (see figure 2 flowchart). 124 of them declined participation due to refusing consent (n= 95), not meeting the inclusion criteria (n=14), poor compliance (n=10) or medical advice (n=5). Most of the recruitment was done by the nursing staff. This process was complicated and time consuming because most of the study's target population, patients in the advanced stage of HD, had poor insight and could not fully understand the purpose, the process and the possible risks and benefits of the study. In most cases, their proxies (next of kin or legal guardian) had to be informed as well. This happened both through information-meetings with the principal researcher, or by one-on-one meetings or telephone-calls by either the principal researcher or the nursing staff. Besides that, a written document that gave a comprehensive explanation about the study's protocol was handed out to all eligible patients and their proxies.

Based on the statistical power calculation [1] we needed a minimum of 60 patients. 63 Patients or their proxies signed the informed consent: the recruitment objective was reached.

2. Barriers and facilitators in recruitment and selection process

The most important reasons for participation was the willingness to dedicate time and effort to scientific research. Also, the love for music was a great motivator to sign up. The most important reason why (the proxies of) eligible patients declined participation was the heavy burden to participate in scientific trials. Another hindrance was the chance to be allocated, through randomization, in the control group instead of the music therapy group: some patients would refuse to participate in the latter. In the discussion section below we will elaborate on this topic.

Furthermore, in one of the participating centers, the room where the intervention was to take place was too small for patients in wheelchairs or beds, reason why some patients had to be excluded for participation beforehand.

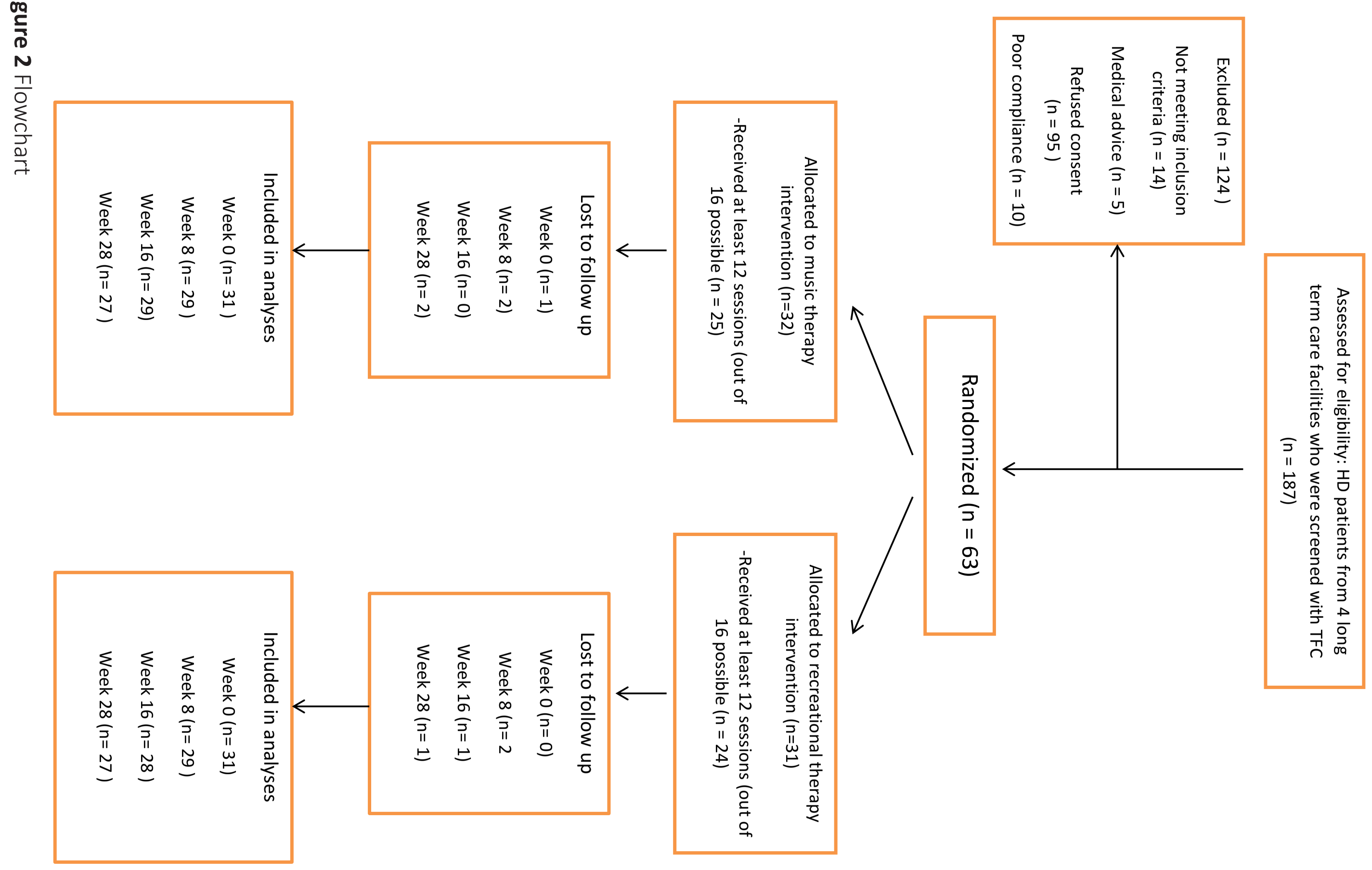

Figure 2 Flowchart

Table 1. Demographic and clinical characteristics of the study population specified per institution

	Inst. 1 MT (n = 9)	Inst. 1 RT (n = 9)	Inst. 2 MT (n = 4)	Inst.2 RT (n = 4)	Inst.3 MT (n = 11)	Inst.3 RT (n = 10)	Inst.4 MT (n = 8)	Inst.4 RT (n = 8)	Total MT (n = 32)	Total RT (n = 31)
Number of sessions										
- attended/max	90/144	102/144	58/64	55/64	166/176	146/160	96/128	80/128	410/512	383/496
- missed (%)	54 (37,5%)	42 (29%)	6 (9,4%)	9 (14%)	10 (5,7%)	14 (8,8%)	32 (25%)	48 (37,5%)	102 (19,9%)	113 (22,8%)
n (%) men	1 (11,1%)	1 (11,1%)	1 (25,0%)	1 (25,0%)	4 (36,4%)	4 (40,0%)	4 (50%)	4 (50%)	10 (50%)	10 (50%)
n (%) women	8 (88,9%)	8 (88,9%)	3 (75,0%)	3 (75,0%)	7 (63,6%)	6 (60,0%)	4 (50%)	4 (50%)	22 (51,2%)	21 (48,8%)
Mean age (years)	56	49	52	55	57	53	54	61	55	55
Mean TFC-score at baseline	0,22	1,88	0,75	1,75	1,09	2,33	1,88	1,5	0,99	1,86
Mean MMSE-score										
- at baseline	17,0 (n=3)	20,4 (n=7)	10,0 (n=3)	20,0 (n=3)	14,5 (n=9)	16,7 (n=10)	21,0 (n=2)	20,0 (n=1)	15,6 (n=17)	19,3 (n=26)
- after session 16	16,3 (n=3)	20,1 (n=7)	9,0 (n=3)	22,2 (n=4)	13,2 (n=9)	14,4 (n=10)	23,0 (n=2)	none	15,4 (n=19)	18,9 (n=21)
No. of patients (%) who received psychotropic medication throughout the duration of the trial (week 0 – week 28)	7 (78%)	7 (78%)	2 (50%)	2 (50%)	11 (100%)	10 (100%)	5 (63%)	4 (50%)	25 (73%)	23 (70%)
- antipsychotics	5	6	2	1	9	7	3	3	19	17
- antidepressants	6	2	2	0	5	5	5	4	18	18
- anxiolytics	5	3	2	1	8	4	4	4	19	12
- hypnotics	2	0	1	1	5	4	0	2	8	7
- anti-epileptics	0	1	0	0	2	2	0	1	2	4

Inst. = Institution, MT = Music Therapy, RT = Recreational Therapy

3. Follow-up: attrition rate
Based on the quantitative data, the number of missed intervention-sessions in the experimental group (102/512) and in the control group (113/496) as well as missed assessments in the experimental group (19/256) and the control group (13/248) was practically equal. See also result C2.

4. Barriers and facilitators for follow-up
Reasons to miss sessions were: relocation to another facility (mentioned 4 times), mortality (3), lack of motivation (2), fatigue (1), comorbidity (1) or private circumstances (1).

B. Multiple components of the complex intervention
1. Quality of delivery of the interventional components
All eight therapists, who were extensively instructed before the start of the study and who followed the same protocol, stated that the feasibility and the satisfactory of delivering the intervention components were dependent on the differences in the cognitive state of the participating patients. For those patient whose cognition was not severely affected, the sessions could be tailor made. For the others, however, delivering the planned components was not feasible in many occasions.

2. Barriers and facilitators for delivery of interventional components
The most important barrier for delivery and to fully benefit from the intervention, mentioned by all eight participating therapists, was the cognitive decline of the patients. Other barriers that were mentioned were equal to the reasons mentioned above why sessions were missed (see A4).

An important barrier to deliver the intervention was the absence of the patients, due to the circumstances within the nursing homes: non-availability of the nursing staff to transport participants from the ward to the therapy room, broken elevators, or community-events (i.e. a concert or showing a movie) at the same time of the intervention. In one of the participating centers an extensive renovation was taking place at the same time as the study. This caused enormous noise pollution for both the experimental and control group.

Based on the quantitative data derived from the observation forms, from the experimental group (MT), 22% of the participants followed fewer than 12 out of 16 sessions (n=7). For the control group (RT) this percentage was 23 (see table 1 and figure 2) (n=7). An attendance of > 75% can be accounted for in the analyses of the outcome measures.

3. Adherence to interventional components
In both the experimental and control group, the interventional components were feasible to deliver to those patients who were actively involved. See B1.

4. Barriers and facilitators for adherence to interventional components
As mentioned above (see B2), the most obvious barrier for adherence was the low cognitive state some of the patients were in (mentioned by all eight therapists). Also, circumstances within the facility itself were important barriers for adherence.

5. Experience of participating therapists with intervention components
As mentioned above, the patients themselves did not receive questionnaires, hence they were not involved in the process-evaluation. According to the eight therapists who filled out the observation forms after each session, the patients with higher functioning cognition benefitted from the intervention, in that they enjoyed the sessions and that their communication and social interaction seemed to improve.

All eight therapists felt a great commitment and involvement in the execution of the study. The protocol they had to follow was feasible, with enough opportunity to tailor it to meet the patient’s needs. As mentioned above, the biggest challenge for the therapists was the patients’ different cognitive state within the group. The overall opinion of the therapists was that the group size was small enough to warrant personal attention, despite this difference, while at the same time the group dynamic stimulated the social interaction of the patients.

C. Evaluation data
1. Outcome measures: coverage of interventional components
To make sure that all assessments took place at the four different timepoints, in the week prior to the assessment weeks (at baseline, week 8, 16 and 28), the monitors sent a reminder to all assessors. Afterwards, the monitors checked if all the measurements had taken place.

2. Completeness of data collection
The Behaviour Observation Scale Huntington (BOSH) [12] was considered easy to administer by the nursing staff. No instruction was needed prior to the first assessment. However, if two answers were filled out instead of one when the assessors were not convinced about the answer, the least beneficial one was entered into the statistical program. This happened 56 times (0,8%).

The assessors who administered the Problem Behaviours Assessment- short version (PBA-s) [13] had to follow a mandatory instruction-course, which they found very helpful. The frequency of both measurements (every 8 weeks, 3 times in total and a follow-up assessment after 12 weeks) was considered feasible.

For the experimental group, 7 BOSH-assessments and 12 PBA-s-assessments were missed. For the control group these numbers were 8 for the BOSH and 5 for the PBA-s-assessments.

3. Barriers and facilitators for data collection
The frequency of both measurements (every 8 weeks, 3 times in total and a follow-up assessment after 12 weeks) was considered feasible but time-consuming for all assessors.

All four assessors that filled out the online survey stated that the PBA-s was more challenging to administer with the patients that were cognitively more declined. Besides that, for this tool a caregiver (nurse or proxy) had to be present to help answering the questions, which caused some more organization in planning. The assessors found the scoring of the PBA-s difficult, also due to the cognitive state of most of the patients. The mandatory training that they followed prior the study was considered very helpful.

Of the four participants who had administered the BOSH, one found the tool not sensitive enough for the more advanced patients. According to the assessors that filled out the survey, most important reasons why data were missing were participants moving to hospitals or other nursing homes or death.

Finally, the research-assistant, who was responsible for the data-input, encountered inconsistencies in the scoring or the collection of the data in two of the facilities. These omissions were not always picked up by the monitors who were responsible for the final check of the data before input into SPSS, and who otherwise could have instructed the assessors to be more accurate when filling out the forms.

Discussion and implications

Barriers and facilitators of the study population

Results from the process evaluation indicate that some patients refused to participate once they were allocated to the control group and not to the music therapy group. The information about the trial has to be unambiguous that no changes between allocation can be made once the patient is randomized.

Most RCT's use usual care or no treatment as control condition [19]. The present study used an active control condition providing similar amounts of attention and group contact for both groups.

When conducting an RCT, the presence or absence of the treatment must be the only difference between the treatment and control groups in order to prove that any therapy works. While this is almost never the case when comparing music therapy to other therapies [20] recreational therapy was chosen as the control condition because being a complex, multi-faceted intervention as is music therapy, recreational therapy to us seemed to be the most appropriate control intervention to make the two groups as homogeneous in set-up and personal attention and thus as comparable as possible. The study-protocol unambiguously stated that no music activities were to be provided in the control group [2]. Apart from the intervention being compared, the groups were treated in an identical manner (i.e. day of the week, time of day, same "warm-up" and "cool-down" routine) and the same outcome data was obtained from all groups. Since the groups were randomly assigned and treated identically, apart from the intervention received, any differences in the outcomes are attributed to the difference in intervention [21,22].

However, randomization may not be appropriate if patients have a strong treatment preference. If they do participate, their motivation to remain in the study may drop significantly after learning that they have been assigned to the control group [21]. This was the case in the present study.

Besides that, the cognitive problems, the lack of insight and the unawareness/anosognosia, known to patients with HD, often lead to poor treatment compliance [23, 24].

Furthermore, there seemed to be a discrepancy between the proxies' expectation and the patients' ability or willingness to participate in the study. This implicates that more clearness has to be given, specifically to the proxies, about compliance to treatment and the burden to participate in the trial, and that inclusion of participants should specifically address appropriateness for participation, including physical and cognitive limitations [10].

Despite having executed a block-permuted randomization to allocate the participating patients, a difference in cognitive function in each group could not be avoided. This seemed to have been the most obvious limitation for the professionals to work with. Adjusting the baseline scores (TFC, MMSE) in the inclusion criteria could have avoided this difference. Classifying/dividing the groups on the basis of their baseline scores, however, will lead to non-homogeneous study-groups, and is therefore not desirable, nor is changing the cut-off score in the inclusion criteria, since the target group of this RCT are the more advanced HD-patients.

Delivery of the intervention

Process evaluation of the complex intervention in this study show that adherence and compliance leaves much to be desired, mostly due to comorbidity, mortality, relocation and circumstances on the ward where participants reside or the location of the therapy room in relation to the ward.
The protocol should be clear about the location where the interventions are to take place; the treatment location should be close to the ward and accessible for all patients. A special consideration has to be given to caregivers' availability to bring participants to and from the intervention room. Also, more emphasis should be placed on the importance of compliance, so that planning other events on the ward at the same time of the intervention will be avoided. The most important barrier for implementation of the intervention was the frailty of the participants. The signs and symptoms of patients with HD are mostly multifactorial by cause and include cognitive decline. Besides, many patients are receiving psychotropic medication (see table 1), resulting in a state of low awareness of their surroundings.

The most important challenge for implementation of the intervention was the fact that the trial took place in four different facilities, each with its own therapist. Even though all therapists followed the same protocol, aiming for the same endpoints, the methods that were used varied in each house. The uniqueness of music therapy, however, i.e. the tailor-made interventions, allow this variety. The process-evaluation indicated that most therapists were satisfied with the delivery of their intervention, given the limitations they encountered as mentioned above.

Evaluation of the outcome measures

The process evaluation identified some limitations of the collection, evaluation and analyses of the outcome measures.

Firstly, due to the fact that the patients were excluded for participation in the present evaluation, determining their reactions to the intervention is purely based on the perception of the therapists, hence subjective and possibly biased.

The BOSH [12] is an observation form that is completely filled out by caretakers, while the PBA-s [13] has to be filled out with the help of patients and proxies. The number of missed measurements however were almost the same for the BOSH as for the PBA-s.

There are indications that the measurement tools that were used might not have fully matched the intervention outcomes (improvement of communicative and expressive skills and behavioral changes). In future designs, adjusting the outcome measures to anticipated goals is desirable.

Strength and limitations

The strength of the presented process-evaluation is, that the participating professionals, nor the principle researcher, had any knowledge about the results of the effect-study (the RCT): these results were deliberately withheld until initial data collection and analysis of this process-evaluation were complete, in order to prevent it from influencing the research findings. The process evaluation identified a valuable facilitator in the fact that each participating center had a monitor, a point of contact attached to the study. This was very beneficial for the process of collection and input of the data.

The subjectivity of the interviewees and the persons surveyed can be seen both as a limitation and as a strength of the present study. On the one hand they were to give answers concerning and on behalf of the participating patients, which could have led to bias. On the other hand, in qualitative research it is the subjectivity that matters the most, as social desirable responses are avoided.

Scoring the MMSE [25] at baseline and after the last session (week 16) was considered extremely difficult, due to the severe cognitive state the patients were in. Besides, the scoring was not consistent: some assessors (2) scored 0 where others (3) scored 99 (meaning the score is missing). These missing data were set to zero to overcome this inconsistency in the scores between the houses. This may have led to a distorted image of the MMSE-outcomes. Instructions hereabout must have been better described in the protocol.

Finally, all participating professionals stated that they felt involved in and committed to both the process evaluation and the effect-study. At the same time, however, the contact with the principal researcher was sometimes laborious, due to the fact that the latter was not often present/visible on site. Most of the contact had to be maintained through internet.

Conclusion and recommendations for future studies

Based on the results of the process-evaluation, the limitations in the present study are

- The cognitive state of the patients: the highly fluctuating physical and emotional responses to the intervention, and the diverse demographical, psychosocial and musical backgrounds of the patients, mean that randomization is likely to be ineffective in distributing confounders evenly between groups.

- The use of quality of life outcome did not necessarily capture respondents' characteristic voices reflecting whether the experience was important to them. Furthermore, the treatment goal was the same for all participating patients: improving communicative and expressive skills.
- The music therapy protocol could not be standardized, as music therapists tailor their approach according to patient's need.

- For future study designs, the following possibilities can be taken into consideration to avoid these barriers and limitations:
- Individual therapy sessions: the power of music therapy lies in the fact that the sessions can be tailor-made, meeting the individual needs of each patient [1, 2]. Taking the differences in cognitive state of the group-members into consideration, individual therapy to deliver the planned intervention components is recommended.

- Using the Goal Attainment Scale (GAS) as the primary 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 [26].

- Using the Music therapy Assessment Tool for Advanced Huntington's Disease (MATA-HD) as the secondary assessment tool. A pilot validation study of this newly developed tool has just finished in the UK [27]: 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.

- Furthermore, validated measurement tools that are sensitive for emotional and social cognitive responses in dementia might be suitable to use in future studies with HD-patients.

- 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 [28].

The demands for evidence of treatment efficacy and effectiveness are placing increased pressure on the field of music therapy. Although the dialogue of clinical effectiveness in music therapy should not be dominated by the biomedical hierarchical model of evidence-based practice, "...despite the challenges of meeting all key design demands typical of an RCT, it is possible to design rigorous music therapy RCTs that accurately estimate music therapy treatment benefits..." (Bradt, 2012, p. 120) [21].

Performing a multi-center RCT studying the efficacy of music therapy with vulnerable patients in a long-term care facility is feasible but challenging, if certain conditions are met and adjustments made. No matter how complex the intervention and the study population, with an unambiguous written protocol, the right study design, 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.

When evaluating interventions that have the potential to improve quality of life, finding the best research designs and the best outcome measures for patients in the advanced stage of HD remains a major challenge. The biggest challenge for the music therapy researcher is to integrate different study-designs and to learn from the experiences of previous complex intervention studies. This asks for all multidisciplinary team members surrounding the patient with Huntington's disease to be willing to learn, to cooperate and to be creative [29].

Competing interests

None of the authors has any competing interests.

Authors' contributions

MB is a neurological music therapist fellow. She developed the study design and drafted the manuscript.
MH is a psychologist. She contributed to drafting (part of) the manuscript.
AV is a psychologist. She reviewed the manuscript.
WA is elderly care physician and professor of institutional and elderly care medicine. He contributed to the development of the study design and reviewed the manuscript.
RR is a neurologist and contributed to the development of the study design and reviewed the manuscript.

All authors have been involved in reviewing the manuscript, and have read and approved the final text.

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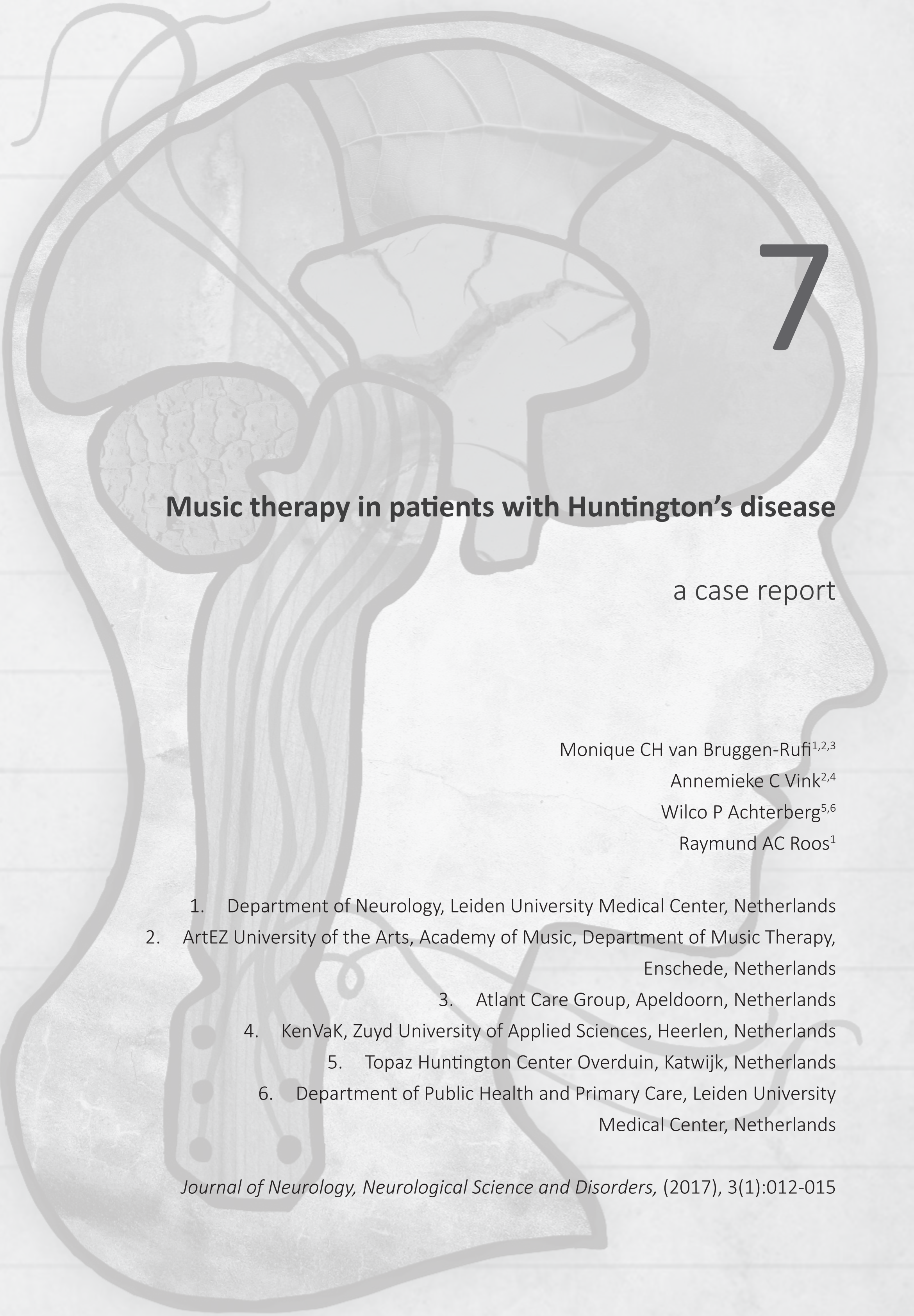
“Mijn geheugen staat in notenschrift te lezen,
elke herinnering kent zijn eigen lied,
elke goede, elke slechte periode,
onlosmakelijk verbonden met muziek”

Jan Rot (1957 - Uit: Mijn Geheugen, theatershow “Rot is liefde” 1993)



7

Music therapy in patients with Huntington’s disease

a case report

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Abstract

This chapter reports about 2 patients with Huntington's Disease who benefit greatly from music therapy while they are struggling with behavioral and emotional problems, due to the advanced stage of the disease. Huntington's disease (HD) is an inherited neuropsychiatric disease with progressive neural degeneration of the basal ganglia and gradual atrophy of the frontal and temporal cortex. Symptoms are progressive and include motor, emotional and cognitive disturbance. There is as yet no cure for HD, nor can its progress be reversed or slowed down. All treatment is aimed at improving quality of life.

Music therapy is a non-pharmacological intervention to improve communication skills, reducing behavioral problems and thus leading to a better quality of life in patients with HD. There is little knowledge on how music therapy may contribute to improve the QoL in HD. This case report provides greater insight into how to treat patients with HD, especially in the advanced stage of the disease.

Keywords: Huntington's disease, quality of life, music therapy, case report

Case reports

Huntington's disease (HD) is an inherited neuropsychiatric disease with progressive neural degeneration of the basal ganglia and gradual atrophy of frontal and temporal cortex [1]. Symptoms are progressive and include motor, emotional and cognitive disturbance. Despite the increase in number of therapeutic trials over the last 20 years, there is as yet no cure for HD, nor can its progress be reversed or slowed down [2,3].

Many of the patients present with language abilities that are inadequate to enable them to fully or sensitively express their feelings verbally. Dysarthria, dyspraxia, or aphasia result in poor articulation of words or difficulties in expressing language [4]. While speech itself is severely impaired, the thinking process of persons with HD, especially in the later stages, is often severely delayed. Also, poor insight, lack of awareness and denial, all due to cognitive decline associated with HD, imply that it is extremely difficult to create a coherent and meaningful therapeutic relationship. In addition, persons presenting with rigid thought processes may have difficulty considering alternative viewpoints, solutions, or situations. Finally, many of the patients have a low self-awareness due to the use of psychotropic medication [1,2,3,4]. As long as there is no cure for HD, the emphasis of many of the treatments is on improving quality of life [3]. One of these non-pharmaceutical treatments offered to patients with HD in long-term care facilities is music therapy [5].

The American Music Therapy Association (AMTA) defines music therapy as follows:
"Music therapy is the clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program" [6].

Music therapy uses music experiences and patient-therapist relationships in order to effect therapeutic change. Music therapists are part of the multidisciplinary team and participate in interdisciplinary treatment planning, ongoing evaluation, and follow-up [6]. They assess emotional well-being, physical health, social functioning, communication abilities, and cognitive skills through musical responses. Music therapists design music sessions for individuals and groups based on client needs using music improvisation, receptive music listening, song writing, lyric discussion, music and imagery, music performance, and learning through music [7].

Applying music therapy to persons with Huntington's disease is challenging, especially in the later stages of the disease, because of the aforementioned deficiencies. The following two case reports illustrate the finding that music therapy can be successfully applied in persons with HD to help them with self-expression. The first report tells the story of a person with HD in whom music turns out to be the trigger for him to open up and show the man that he really is, as opposed to the patient with severe behavioral problems whom nurses are afraid to approach. The second report tells the story of another person with HD, whose lack of verbal communication hinders him from showing remorse towards a caregiver whom he has physically abused. Through therapeutic song-writing, he is offered the opportunity to rewrite the lyrics of a familiar song, personalizing it to his own experience.

Person A

A 64-year-old man in the late stage of Huntington disease was admitted to the long-term care facility. Because of severe behavioral problems, aggression, agitation and sexual disinhibition, he was treated with psychotropic drugs, the main side-effect being that he slept most of the day. Despite the medication, the negative behavior towards the nursing staff continued. Furthermore, female nurses inadvertently triggered inappropriate sexual behavior. This resulted in a situation where most female nurses became afraid to approach him. His daily care was always carried out by at least two nurses, preferably one of them male. He could no longer express himself verbally, and so during his outbursts he would scream loudly and his involuntary movements would get worse.

One of the few personal items he brought with him, was his guitar. A phone call to his daughter revealed that in his younger years, he had been a pretty good “rock-and-roll” guitarist. According to his daughter, music had always been his one and only outlet. Taking all these facts into account, it was decided to start with music therapy to see if music could be the trigger for him to open up and express himself, with the aim of improving his behavior.

During my first visit, he was sitting in a wheelchair. Abiding by the instructions from the caregivers on the ward, the door of his room was left open for reasons of safety. Apart from greeting him and introducing myself, I did not talk much with him for the remainder of this first session that only lasted 15 minutes. I played my guitar and sang some songs that I thought would please him. Over the next few weeks, I slowly increased the duration of my visit and my guitar playing, and he seemed to get used to me gradually. I based my song-choices on the information I had about him: his age, the city where he was brought up, and knowing a little bit about his musical taste. As expected, there was no verbal reaction, but he seemed to calm down somewhat, showing fewer unwanted movements (chorea) and listening attentively to the songs.

I continued this procedure for the next three sessions, building trust and trying to create a safe environment. During the 4th session he requested a song that I had played for him in one of the previous sessions by mentioning the title of the song verbally. From that moment on I started a conversation about music. This first conversation, although very laborious, was the turning point in our therapy-sessions. He actually initiated talking about his love for music, and he started singing along with the lyrics that he was familiar with: I left out some words in the lyrics and he filled in the blanks. Obviously he was enjoying the sessions. After each song we talked about the lyrics, the artists, and the times when this particular song was a top-chart hit. We continued like this in weekly sessions.

A couple of weeks later I decided to involve his own guitar in the session. I placed the guitar on his lap, and he held it tight against his chest. Although he could not play it himself anymore, I could see that he enjoyed just holding the instrument. When at the end of the session I returned the guitar to its case, I noticed a small piece of paper inside. Although it was almost illegible, the title of a song had been noted. It was a fairly obscure instrumental piece for the guitar, but I happened to know it well. During the next session I started to play this particular song; he lit up and started to cry. From that moment on he would ask me to play this particular song every session.

In the meantime, I decided to compile a CD with all the familiar songs that we played together. I advised the nursing staff to play this CD whenever he was getting agitated, or during stressful moments of the day (like bathing).

I also videotaped him during the music therapy sessions to show my colleagues the “other side” of this person. This video footage brought about major changes in how the nurses on the ward would look at him. From that moment on, he was no longer the patient that nurses were afraid to take care of, nor was he the patient who was always alone in his room, isolated from the rest of the residents. He became involved in community events on the ward. Whenever it got too crowded for him, or whenever he showed signs of being too stressed, the nurses took him back to his room and left him to listen to a compilation CD of one of his favorite artists from “way back when”.

When he passed away two years later, his daughter asked me to play a couple of his favorite songs during the funeral ceremony and people could watch the video footage of him singing along.

The next case report describes another person in the advanced stage of Huntington's Disease. For him, the song-writing method has proven beneficial on previous occasions. Song-writing in music therapy is a method whereby the therapeutic intervention consists of the process and product of writing a song with the client. Baker and Wigram [8] present a provisional definition: 'The process of creating, notating and/or recording lyrics and music by the client and therapist within a therapeutic relationship to address psychosocial, emotional, cognitive and communication needs of the client' (Baker and Wigram, 2005, p.16).

The therapeutic effect is achieved through the client's creation, performance and/or recording of his or her own song. The therapist's role is to facilitate this process, ensuring that the clients create a composition that they feel they can own and that expresses their personal needs, feelings and thoughts. The product is something that the client can revisit, share with others, and that can be evidence of self-expression [8].

Experience tells us that it is better to use only familiar and preferred songs, rather than creating a completely new song. Because of the cognitive decline during the advanced stage, creating a completely new song might be a bridge too far. Also, by using a familiar melody line, any anxiety about the person's musical capacity to perform the work will be minimized. "…And while no song that is created is entirely novel, each song typically tells a story in an original way…"(Marade (2007) in Baker, 2015, p.61, [9].

The case report below resembles that of many persons with HD who present with communication problems, cognitive impairments and rigidity/compulsive behavior.

Person B
A 58-year-old man with Huntington's disease who had been institutionalized for three years in the long-term care facility, was chosen to join a small group of fellow residents at a 4-day summer-camp.

After one day, the physician of the facility received a phone call from one of his caregivers, telling him that the man had completely lost it. He had shown aggressive and agitated behavior and had physically attacked one of the nurses. The reason for this outburst was because he was told not to smoke in his bedroom, and having ignored this, his cigarettes were taken away. He was sent home the next day as his behavior had not improved, despite medication to calm him. Upon arrival in the nursing home, he was still very agitated. The psychologist who met with him did not manage to talk any sense into him. He did not seem to understand that his behavior was intolerable, nor did he show any remorse for having abused the nurse. He kept screaming and was very upset that he had been sent home.

The physician asked me if I could possibly calm him by playing his favorite music or his self-made songs.

I had known him for over a year by this time; he had been receiving individual music therapy once every week. He is known for not being able to show or express his emotions verbally, although he does have the urge to do so. Music therapy has proven beneficial for him. One of the methods that we often use is analyzing or writing song lyrics to improve communication and expression.

When he came to me, the first thing we did was just listen to some of his old-time favorites while I played along on my guitar. We didn't talk at first, we just enjoyed listening to the music together. After a couple of songs, I started talking about what actually happened. As expected, he could not find the right words to express himself. I then grabbed my guitar and started playing a well-known Dutch song. We talked about the metaphoric meaning of these lyrics, how your thinking gets clearer if you let go of negative and angry feelings. But I also took part of the lyrics literally and "translated" this into how his nicotine-addiction and compulsion for smoking cigarettes had taken over at the summer-camp, the reason why he went completely out of his mind. During our conversation he opened up, and I showed empathy when we started talking about what had happened. At the same time, however, we talked about the fact that his behavior could not be tolerated. He told me that he realized this, and that he was very sorry about what had happened, and that he felt very sorry for the nurse he attacked. He wanted to apologize to her, but he did not know how.

I suggested that we could rewrite this particular song in his own lyrics to express his regrets. He seemed to like this idea. I formatted what he had just said to me into new lyrics, making sure to use exactly the wording that he used, without changing it a bit. My only job was to make his words fit into the cadence of the song so he could sing along.

After a while, he thought the lyrics were "perfect". We sang the song a couple of times, and when he was completely satisfied I suggested that we could record the song. We did so the next day, and I burned the song on several CDs, giving him the opportunity to give one to the nurse whom he had attacked. For him, this was the only way to show his regrets and apologize to her. For the nurse, this was the best way to realize that it was the patient who had attacked her, but it was the person who had created a song for her to show his regret and bury the hatchet.

The two stories above are examples of persons with HD who benefit from music therapy.
As the ability to communicate and express oneself deteriorates over time, music therapy could play an important role in the treatment of persons with HD in all phases of the disease [10]. By providing an additional means of communication, thus enabling the patient to express emotions, “(…) meaning is conveyed through the combination of lyrics and music. Lyrics clearly have a capacity to communicate, in a concrete way, the events that are core to the song. But music can also be key in conveying intended meaning…” (Baker, 2015, p.75 [4).

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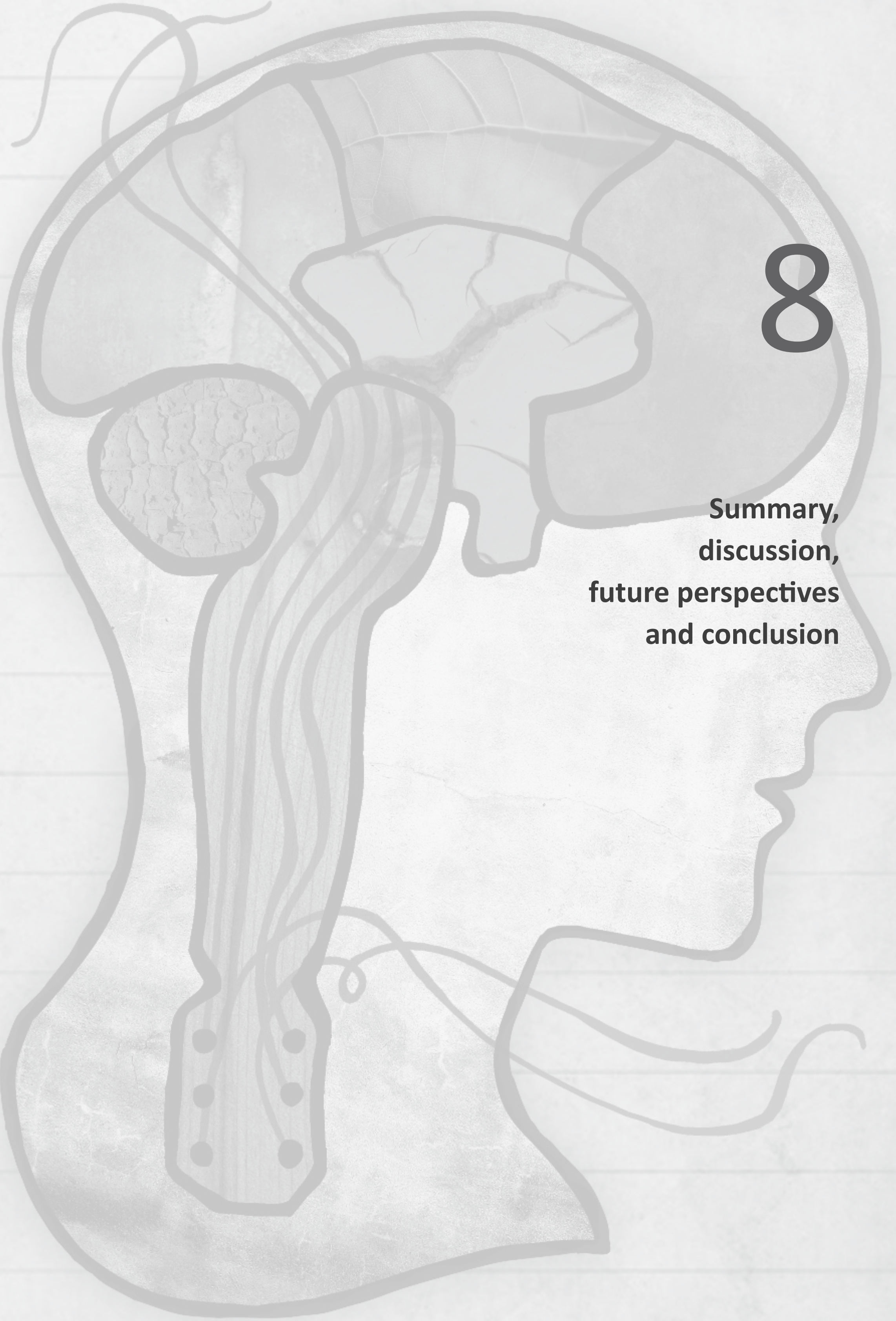
> *“Musik ist die schönste und zugleich die einzige Sprache,*
> *die überall auf dieser Welt verstanden wird”*
>
> *Johann Wolfgang von Goethe (1749 – 1832)*



8

Summary, discussion, future perspectives and conclusion

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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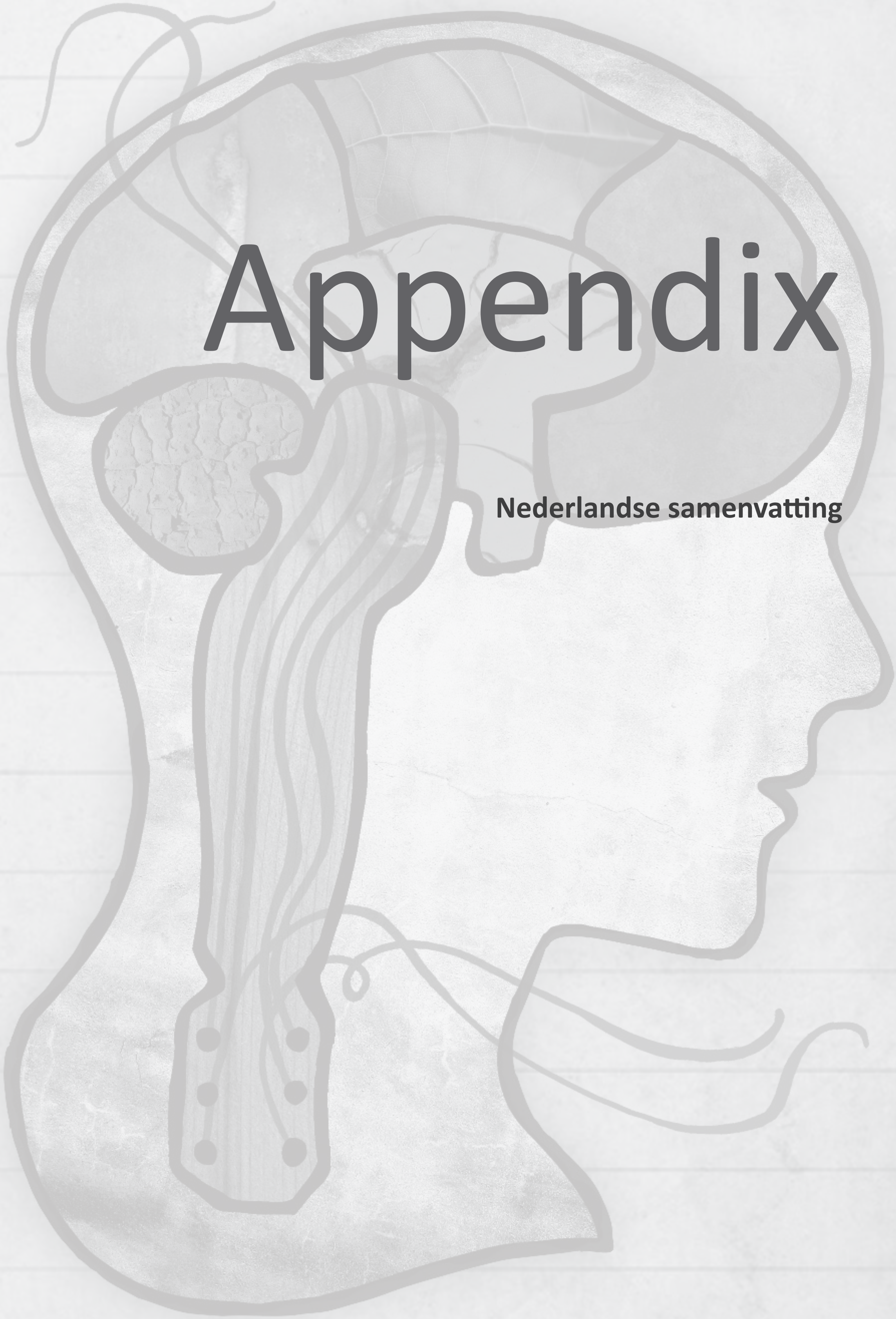
Appendix

Nederlandse samenvatting



Nederlandse samenvatting

De Ziekte van Huntington (ZvH) is een aangeboren, erfelijke, progressieve, neurodegeneratieve aandoening die wordt gekenmerkt door motorische, cognitieve en psychiatrische problematiek. De motorische beperkingen bestaan voornamelijk uit ongewilde bewegingen. De cognitieve veranderingen hebben voornamelijk betrekking op concentratie, geheugen, executieve functies, en het verwerven van nieuwe informatie. Emotionele stoornissen dienen zich vaak al voor de motorische en cognitieve problemen aan. Depressie, irritatie, impulsiviteit en angst zijn veel voorkomende symptomen [1-3].

Als gevolg van de fysieke en cognitieve achteruitgang gaan ook de communicatieve vaardigheden achteruit. Een soms snelle achteruitgang van deelname in het alledaagse leven en het kunnen omgaan met situaties die bij het leven horen is hier weer het gevolg van [4]. De zelfstandigheid van de patiënt komt hiermee in het gedrang, hetgeen vaak leidt tot een toename van gedragsproblemen. Zo vermindert de kwaliteit van leven (KvL) naarmate de ziekte vordert. Zolang er nog geen genezing voor de ziekte is, ligt de nadruk op de zorg *(care versus cure)* voor patiënten met de ZvH, met als specifieke doel het in stand houden en verbeteren van de kwaliteit van leven [4].

Muziektherapie is een niet-medicamenteuze interventie die mogelijk gunstige effecten heeft op het verbeteren van de communicatieve en expressieve vaardigheden voor patiënten met de ZvH. Verondersteld wordt, dat verbetering van genoemde vaardigheden zal leiden tot verbetering van het gedrag, hetgeen weer leidt tot algehele verbetering van de KvL van patiënten met de ZvH [5].

De algemene doelstelling van dit proefschrift was om te bepalen of deze veronderstelling bevestigd kan worden middels het uitvoeren van een experimenteel kwantitatief onderzoek. De eerste doelstelling was om middels een literatuuronderzoek te achterhalen wat de stand van zaken is m.b.t. kennis van muziektherapie voor patiënten met de ZvH (**Hoofdstuk 2**). Dit onderzoek bracht een schaarste aan het licht over genoemd onderwerp. De meeste artikelen betreffen kleinschalige, observationele studies. Doelstellingen en in te zetten methodieken in relatie tot de verschillende stadia van de ziekte zijn in deze artikelen niet nauwkeurig omschreven. Deze conclusie bevestigde onze aanname dat een onderzoek naar de effectiviteit van muziektherapie bij deze patiëntenpopulatie nodig is.

Vervolgens voerden we een focusgroep-studie uit om te onderzoeken of zes Huntington-ervaringsdeskundigen vanuit verschillende klinische disciplines een mogelijke waardevolle rol voor de muziektherapeut weggelegd zagen om de KvL van patiënten met de ZvH te verbeteren. Uit de resultaten van deze studie, beschreven in **hoofdstuk 3**, komt naar voren dat psychosociale aspecten de KvL het meest beïnvloeden. Gevoel van veiligheid, vertrouwen en structuur waren de kwalificaties die het meest genoemd werden. De focusgroep-deelnemers waren van mening dat muziektherapie een belangrijke rol kan spelen in de behandeling van patiënten met de ZvH wanneer het vermogen om te communiceren en zichzelf uit te drukken minder wordt naarmate de ziekte vordert.

De in hoofdstuk 2 en 3 beschreven inzichten vanuit de literatuur en van de focusgroep-deelnemers werden vervolgens gebruikt om een experimenteel onderzoek naar de effecten van muziektherapie op te zetten. Het hoofddoel van dit onderzoek was het verbeteren van de KvL van patiënten met de ZvH door het verbeteren van communicatieve vaardigheden. We ontwikkelden een gerandomiseerd, gecontroleerd onderzoeksdesign (randomized controlled trial=RCT). Dit was de eerste RCT waarbij muziektherapie met een groot aantal patiënten in het gevorderde stadium van de ZvH werd uitgevoerd. Het design van deze studie wordt beschreven in **hoofdstuk 4.**

De resultaten van deze enkelvoudig-geblindeerde, multicenter RCT staan beschreven in **hoofdstuk 5**. Drieënzestig patiënten verblijvend in vier verschillende verpleeghuizen voor langdurige zorg in Nederland, allen gespecialiseerd in de zorg voor patiënten met de ZvH, werden middels randomisatie aan de interventiegroep (muziektherapie) of aan de controlegroep (activiteitenbegeleiding) toegewezen. Beide groepen hadden 16 maal een wekelijkse sessie. De primaire uitkomstmaat waren de communicatieve- en expressieve vaardigheden. De secundaire uitkomstmaat was het probleemgedrag. Metingen vonden plaats op baseline en vervolgens na 8, 16 en 28 weken. Hierbij werd gebruik gemaakt van de Gedrags Observatie Schaal voor Huntington (GOSH) [6] en de Problem Behaviours Assessment-short meetschaal(P-BA-s) [7]. Om de scores van de twee groepen met elkaar te vergelijken werd gebruik gemaakt van een statistische techniek volgens het “linear mixed model with repeated measures”-model.

De gunstige effecten van muziektherapie, zoals gerapporteerd in vele kwalitatieve onderzoeken en case-reports, konden met de door ons gekozen uitkomstmaten en meetinstrumenten niet bevestigd worden.

Tegelijkertijd bereidden we een uitgebreide procesevaluatie voor om te onderzoeken hoe de RCT was uitgevoerd en om hiermee de resultaten van de studie tegen het licht te houden. Deze evaluatie, beschreven in **hoofdstuk 6**, bracht verschillende struikelblokken en beperkingen van de studie aan het licht. Deze beperkingen betroffen (1) de karakteristieken van de onderzoekspopulatie, (2) de studie-methode en de uitkomstmaten, en (3) de behandeldoelen. In de onderstaande discussie wordt hierop ingegaan en worden aanbevelingen voor de praktijk en toekomstige studies gedaan.

Vanwege de kwetsbaarheid van de onderzoekspopulatie was de patiënt zelf in geen van de hiervoor genoemde kwalitatieve onderzoeken (focusgroep en procesevaluatie) direct betrokken. Om die reden hebben we in **hoofdstuk 7** in een case-report twee patiënten beschreven waarbij muziektherapie succesvol wordt ingezet. De patiënt krijgt een stem en een gezicht. Tegelijkertijd wordt een inkijk gegeven in de dagelijkse praktijk van de muziektherapeut.

Onderzoeksopzet
Wanneer de effectiviteit van interventies in de gezondheidszorg moeten worden geëvalueerd, wordt de RCT in het algemeen beschouwd als de “gouden standaard”.

Dit is het eerste onderzoek naar de effecten van muziektherapie bij patiënten in het vergevorderde stadium van de ZvH. In veel RCT’s wordt de interventie vergeleken met een controlegroep waarin geen interventie wordt aangeboden of waarbij de interventie wordt vergeleken met de standaard aangeboden zorg. In deze studie kreeg de controlegroep activiteitenbegeleiding aangeboden onder dezelfde omstandigheden en volgens hetzelfde protocol als de muziektherapiegroep.

Uit de procesevaluatie die werd uitgevoerd kwamen de volgende beperkingen naar voren:

1. Door de klinische verscheidenheid van de ZvH en de karakteristieken van de onderzoekspopulatie is het aannemelijk dat, ondanks randomisatie, geen evenredige verdeling van verstorende variabelen (confounders) tussen de beide groepen werd bereikt [9].
2. Omdat de studie plaats vond in vier verschillende zorginstellingen hebben we besloten om een gestratificeerde gepermuteerde blok-randomisatie uit te voeren, waarbij elke deelnemende zorginstelling een apart stratum vormde. Hiermee beoogden we verschillen tussen de centra onderling te voorkomen [10].

De groepsgrootte van minimaal drie en maximaal vijf werd bepaald op basis van de haalbaarheid en de bereidwilligheid van de patiënt om deel te nemen. De cognitieve achteruitgang, de sterk fluctuerende fysieke en emotionele reactie op de behandeling en de diverse demografische, psychosociale en muzikale achtergrond van de patiënt waren hierin leidend.

3. De vooropgestelde behandeldoelen (verbetering van de communicatieve en expressieve vaardigheden) waren dezelfde voor alle deelnemende patiënten.
4. Er zijn aanwijzingen dat de gebruikte meetinstrumenten niet sensitief genoeg waren om veranderingen te detecteren in de primaire en secondaire uitkomstmaten (communicatieve en expressieve vaardigheden en gedrag).
5. Onderstaand volgt een gedetailleerde uitweiding over de bovengenoemde beperkingen.

In de definitie van muziektherapie van de American Music Therapy Association (AMTA) [4,5] staat expliciet geschreven dat behandeldoelen moeten worden toegespitst op het individu, daarbij rekening houdend met en aangepast aan de vermogens van dit individu. De keuze van dezelfde behandeldoelen en uitkomstmaten voor elke deelnemende patiënt conflicteert met deze definitie.

De uitkomstmaten werden gekozen op basis van de aanname dat verbetering van communicatieve en expressieve vaardigheden van de patiënt leidt tot verandering van het gedrag, hetgeen uiteindelijk leidt tot verbetering van de KvL [5].

De keuze van de GOSH en de PBA-s als meetinstrumenten was gebaseerd op de verwachting dat de items van deze instrumenten veranderingen in de gekozen uitkomstmaten zouden kunnen detecteren [8]. De assessoren die deelnamen aan de procesevaluatie waren echter van mening dat dit, gezien de (vaak slechte) cognitieve staat waarin de patiënten verkeerden, niet het geval was [11]. Deze mening is in overeenstemming met wat in de literatuur staat beschreven over de GOSH en de PBA-s [6,12]. Daarnaast was bij de onderzoekspopulatie een hoog bodem-effect te verwachten [13].

Er is een tekort aan ziekte-specifieke gestandaardiseerde meetinstrumenten om consistente en betrouwbare informatie betreffende de klinische effecten van interventies van de ziekte te verzamelen. Dit gegeven reflecteert wellicht de schaarste aan experimentele studies naar de effecten van niet-medicamenteuze interventies bij patiënten met de ZvH [12].

Van het huidige meetinstrument dat wordt gebruikt voor klinische evaluaties, de Unified Huntington’s Disease Rating Scale (UHDRS), wordt verondersteld dat deze de gevoeligheid mist voor de marginale klinische effecten, met name op het gebied van cognitieve en psychiatrische symptomen in het vergevorderde stadium van de ziekte [14]. Als antwoord hierop werd in 2013 een nieuwe meetschaal ontwikkeld die gevoeliger lijkt te zijn voor veranderingen binnen de cognitieve en motorische domeinen. Deze nieuwe schaal, de UHDRS-FAP (For Advanced Patients) is de enige schaal die achteruitgang detecteert bij patiënten met een TFC (Total Functional Capacity)-score ≤ 1, hetgeen duidt op een zeer lage cognitieve functionaliteit. Het instrument was nog niet gevalideerd ten tijde van het ontwerpen en uitvoeren van de onderhavige studie.

Recent werd een ziekte-specifiek meetinstrument voor muziektherapie ontwikkeld voor patienten in het gevorderde stadium van de ZvH: de Music therapy Assessment Tool for Advanced HD (MATA-HD) [12]. Of er een relatie bestaat tussen het muzikaal gedrag en de muzikale gevoeligheid van patiënten in het vergevorderde stadium van de ZvH en eigenschappen op het fysieke, psychologische en sociale vlak, heeft men tot op heden nog niet kunnen aantonen [12]. Een meetinstrument als de MATA-HD dat zowel muzikaal als niet muzikaal gedrag in kaart kan brengen, kan de oplossing zijn om een dergelijke relatie aan te tonen. De voorlopige resultaten geven aanwijzingen dat de MATA-HD een veelbelovend instrument is om de reacties van patiënten in het gevorderd stadium van de ZvH op muziektherapie-interventies te meten, en om aan de hand hiervan een uitspraak te kunnen doen omtrent het functioneren op psychologisch, fysiek, sociaal en communicatief vlak. De MATA-HD, die in de nabije toekomst nog gevalideerd moet worden (zie ook “future perspectives”), was nog niet beschikbaar ten tijde van het ontwerpen en uitvoeren van de onderhavige studie.

Conform de hiervoor genoemde definitie van muziektherapie is het wenselijk om de uitkomstmaten af stemmen op de individuele doelen. Daarnaast bemoeilijkt het bodemeffect bij patiënten in het gevorderde stadium van de ZvH van de genoemde meetinstrumenten deze te evalueren.

In dit licht bezien is de Goal Attainment Scale (GAS) [15] een geschikt meetinstrument: de GAS maakt gebruikt van een mathematische techniek die het bereiken van individuele doelen, die voor elk persoon die deelneemt in het onderzoek zijn vastgesteld, kwantificeert [16]. Hierbij moet opgemerkt worden dat het vaststellen van individuele doelen uiterst moeizaam kan zijn voor patiënten met de ZvH gezien het slecht ziekte-inzicht en het feit dat ze zich niet bewust zijn van hun conditie als gevolg van de cognitieve achteruitgang [5].

Verbetering van de onderzoeksopzet

De dialoog aangaande de klinische effectiviteit van muziektherapie moet niet gedomineerd worden door het biomedische hiërarchische model van de Evidence Based Practice (EBP). Volgens Bradt [16] is het mogelijk een strikte RCT te ontwikkelen die een accurate inschatting maakt van de voordelen van de muziek-therapeutische behandeling, mits aan bepaalde condities en aanpassingen wordt voldaan. Hoe complex de interventie en de onderzoekspopulatie ook is, met een eenduidig protocol, zorgvuldig gekozen uitkomstmaten en meetinstrumenten en een voortdurende evaluatie en monitoring gedurende het hele onderzoek kunnen struikelblokken worden voorkomen, en kunnen facilitatoren worden verbeterd [16].

Verschillende onderzoeksvragen vergen verschillende types onderzoeksmethodieken en evidentie [16]. Experimentele studies met kwantitatieve uitkomsten blijven belangrijk voor clinici en beleidsmakers. Echter, de kwantitatieve uitkomsten alleen geven onvoldoende informatie om tot een goede inschatting te komen van de effecten van een complexe interventie en om te bepalen welke uitwerking deze effecten hebben op de patiënt.

Wanneer men een complexe interventie ontwikkelt, is het belangrijk om met de context en de omstandigheden waarin de interventie wordt uitgevoerd rekening te houden. Vaak is observationeel of kwalitatief onderzoek voorafgaande aan de RCT noodzakelijk om duidelijk in kaart te brengen welke aspecten van de problemen relevant adequaat zijn om de doelen te bereiken [17].

Deze adviezen zijn in de huidige studie grotendeels opgevolgd: voorafgaand aan de RCT werd een uitgebreide literatuurstudie uitgevoerd [4], gevolgd door een kwalitatieve focusgroep-studie [5]. Aansluitend aan de RCT werd een procesevaluatie uitgevoerd, waarbij gebruik werd gemaakt van een combinatie van zowel kwalitatieve als kwantitatieve onderzoeksgegevens [11]. Aanbevelingen voor verbeteringen of aanpassingen voor de klinische praktijk en toekomstige onderzoeken volgen hieronder.

Toekomstperspectieven

De volgende mogelijkheden kunnen in overweging genomen worden om struikelblokken en beperkingen die in de huidige studie werden tegengekomen, te voorkomen.

- Uitvoeren van een pilotstudie of haalbaarheidsstudie [16]: in een pilotstudie kunnen kwesties als werving en selectie, uitval en therapietrouw van de deelnemers verkend worden. Tevens kunnen voorlopige gegevens over doeltreffendheid van de interventie worden verkregen. Tijdens deze pilotfase worden het behandelplan, het protocol, en eventuele trainingsschema's ontwikkeld.

- Individuele therapiesessies: de zorg voor kwetsbare patiënten met de ZvH vraagt om een individuele benadering om aan de complexe behoeftes van deze patiënten tegemoet te komen. Om de geplande interventie-componenten te kunnen aanbieden verdient individuele therapie de voorkeur boven groepstherapie gezien de onderling vaak grote verschillen in cognitieve staat van de patiënten.

- Meetinstrumenten: de kracht van muziektherapie ligt in het feit dat de sessies op maat gesneden kunnen worden om daarmee de individueel opgezette doelen van elke patiënt te behalen [4,5]. Het gebruik van het hiervoor genoemde GAS meetinstrument [15] om deze doelen te bepalen is aan te bevelen. Een mogelijk ander goed alternatief voor toekomstig onderzoek is het gebruik (na validatie) van de eveneens hiervoor genoemde MATA-HD [12] en de UHDRS-FAP [14].

- Het ontwerpen van multipele n=1 studies; dit is een ontwerp dat vaak wordt gebruikt in bepaalde vakgebieden binnen de psychologie en gedragswetenschappen waarin het subject zijn eigen controle is in plaats van een ander individu. Dit soort onderzoek is uiterst flexibel en benadrukt de individuele verschillen in reacties op interventie-effecten op verschillende domeinen [18]. Met n=1 studies doorgrond je het veranderingsproces van patiënten met betrekking tot de complexiteit van muziektherapie [19].

- Het betrekken van mantelzorgers: in toekomstige studies is de overweging om familieleden en mantelzorgers in het onderzoek te betrekken de moeite waard, omdat dit de communicatie tussen hen en de patiënt ook buiten de muziektherapie-sessies ten goede komt. Dit is niet alleen een uiterst wenselijk resultaat dat ongetwijfeld leidt tot verbetering van de KvL voor zowel de patiënt maar ook de mantelzorger [5], maar ook zal de inbreng van zowel de patiënt als de mantelzorger een waardevolle bron zijn om toekomstige klinische studies richting te helpen geven [20].

De gunstige effecten van muziektherapie voor patiënten met de ZvH konden in het onderhavige onderzoek niet aangetoond worden middels het design en de gebruikte uitkomstmaten [8].

Dit impliceert dat ofwel muziektherapie niet effectief is, of de gekozen uitkomstmaten (communicatieve en expressieve vaardigheden en probleemgedrag) zijn niet geschikt om de effectiviteit aan te tonen. Ondanks de complexiteit van zowel de onderzoekspopulatie alsook de interventie, is het haalbaar om een RCT uit te voeren. Om de effectiviteit van de interventie te kunnen aantonen moet de RCT worden voorafgegaan, vergezeld of aangevuld door andere observationele of kwalitatieve studies en moeten de meest geschikte en beschikbare uitkomstmaten en meetinstrumenten worden gebruikt.

Conclusie

Wanneer de effectiviteit van interventies die de potentie hebben om de KvL te verbeteren geëvalueerd moet worden, is het vinden van de meest geschikte onderzoeksopzet en uitkomstmaten een hele uitdaging. Voor de muziektherapie-onderzoeker ligt deze uitdaging vooral in het vinden van alternatieve studieontwerpen en in het leren vanuit ervaringen van andere onderzoeken waar complexe interventies bij gemoeid waren. Dit vergt van het multidisciplinaire team rondom de patiënt met de ZvH de bereidwilligheid om te leren, samen te werken en om creatief te zijn [17].

In een poging om een bijdrage te leveren aan de evidentie van muziektherapie en uitgaande van de hiervoor genoemde aanname dat deze methodiek wordt beschouwd als de gouden standaard wanneer de effectiviteit van gezondheidszorg-interventies aangetoond moet worden, hebben we gekozen voor de RCT-methodiek in het onderhavige onderzoek. Gebleken is dat het uitvoeren van een multi-center RCT naar de effecten van muziektherapie bij kwetsbare patiënten die in een faciliteit voor langdurige zorg verblijven haalbaar maar zeer uitdagend is.

Echter, in de alledaagse praktijk van de muziektherapeut worden de strikte regels die gelden voor de RCT, waar de te onderzoeken interventie gestandaardiseerd moet worden om de experimentele groep met de controlegroep te kunnen vergelijken, beschouwd als hindernissen die moeten worden genomen [9,21]. Deze strikte regels conflicteren met wat er in de definitie van muziektherapie staat geschreven, namelijk dat behandeldoelen moeten worden aangepast aan het functieniveau van de patiënt teneinde deze individuele doelen te kunnen behalen. De toegevoegde waarde van muziektherapie is dat de interventie kan worden aangepast aan de individuele behoeftes en mogelijkheden van de patiënt. De geïndividualiseerde wijze waarop muziektherapie ingrijpt op elk patiënt is wat de therapie effectief maakt. Het is daarom niet de *inhoud* die gestandaardiseerd zou moeten worden, maar de *functie* van de interventie. Zodoende staat het de therapeut vrij om elke denkbare techniek of methode volgens een gestandaardiseerd protocol te integreren teneinde specifieke doelen te bereiken [9,21].

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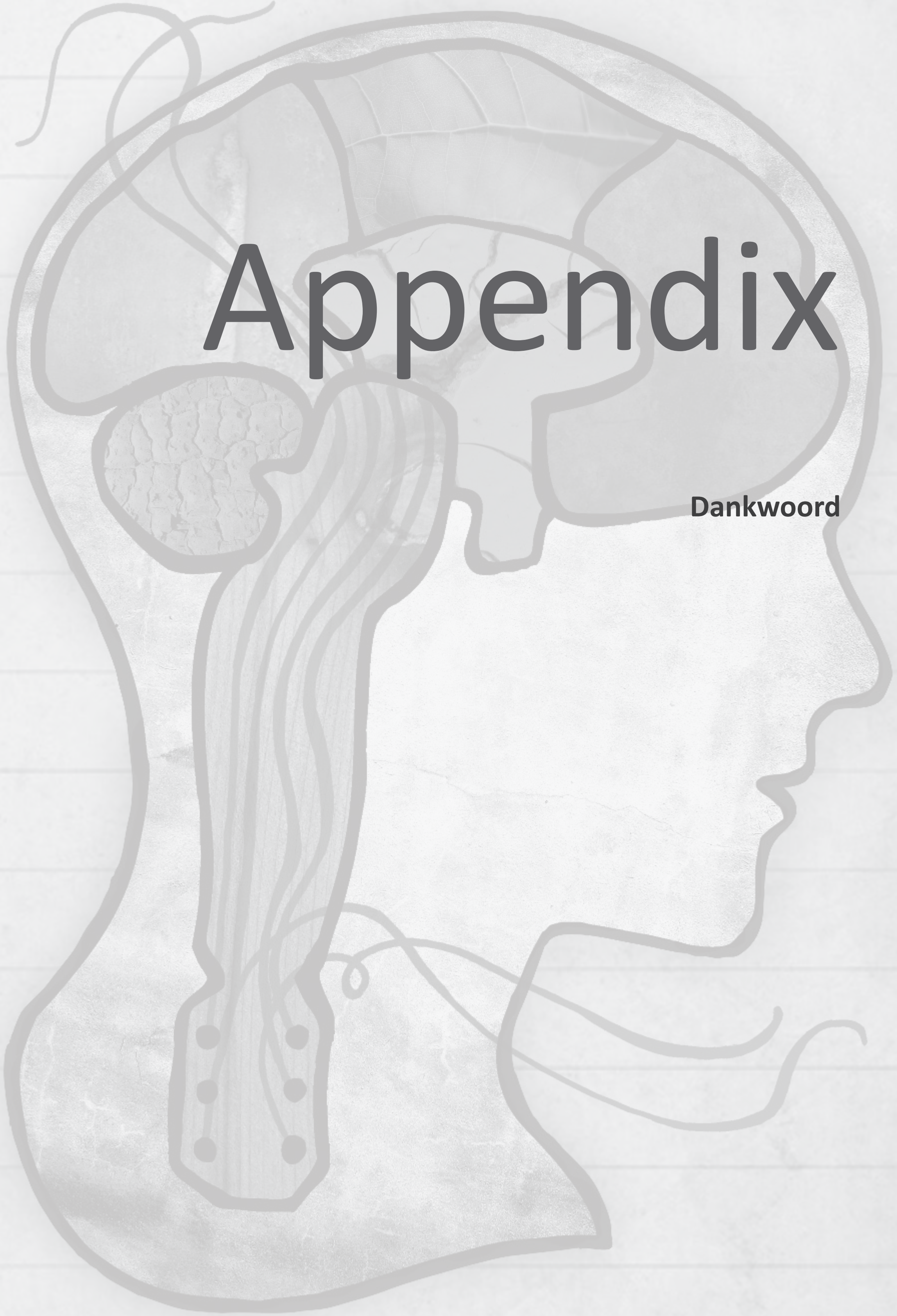

Appendix

Dankwoord

Dankwoord

Ik dank in de eerste plaats alle patiënten en hun familieleden voor hun bereidwilligheid om mee te werken aan dit onderzoek.

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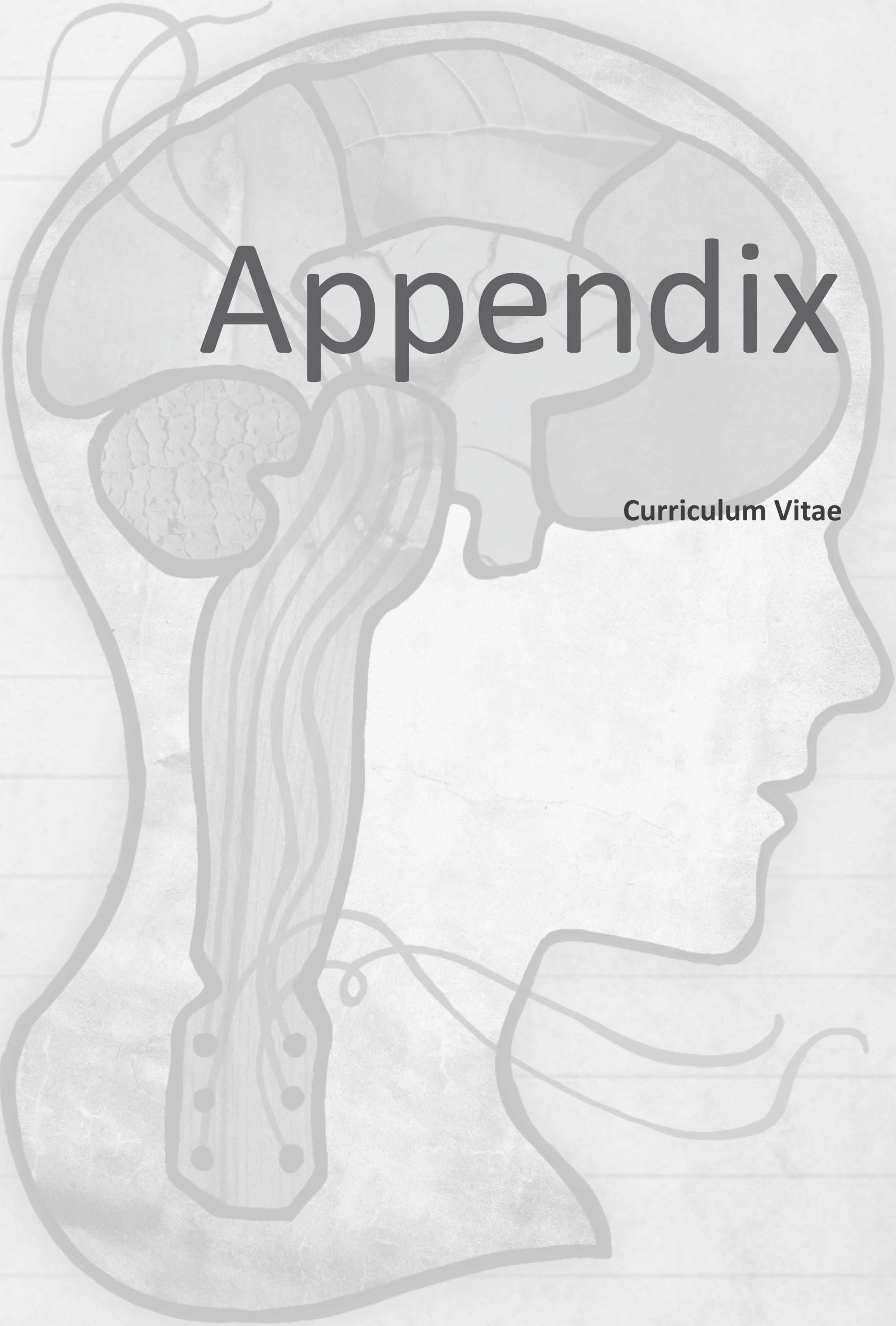
Wichita Falls, Texas, USA, oktober 2017.



Appendix

Curriculum Vitae

Curriculum Vitae

Monique van Bruggen-Rufi werd geboren op 16 april 1962 te Ede. Na het eindexamen Gymnasium β aan het Marnix College te Ede in 1980 werkte ze achtereenvolgens als operatie-assistente i.o. in het Bronovo ziekenhuis te ’s Gravenhage en als medisch secretaresse/spreekuur-assistente op verschillende poliklinieken (orthopedie, reumatologie, neurologie, psychologie) in het Medisch Spectrum Twente te Enschede.

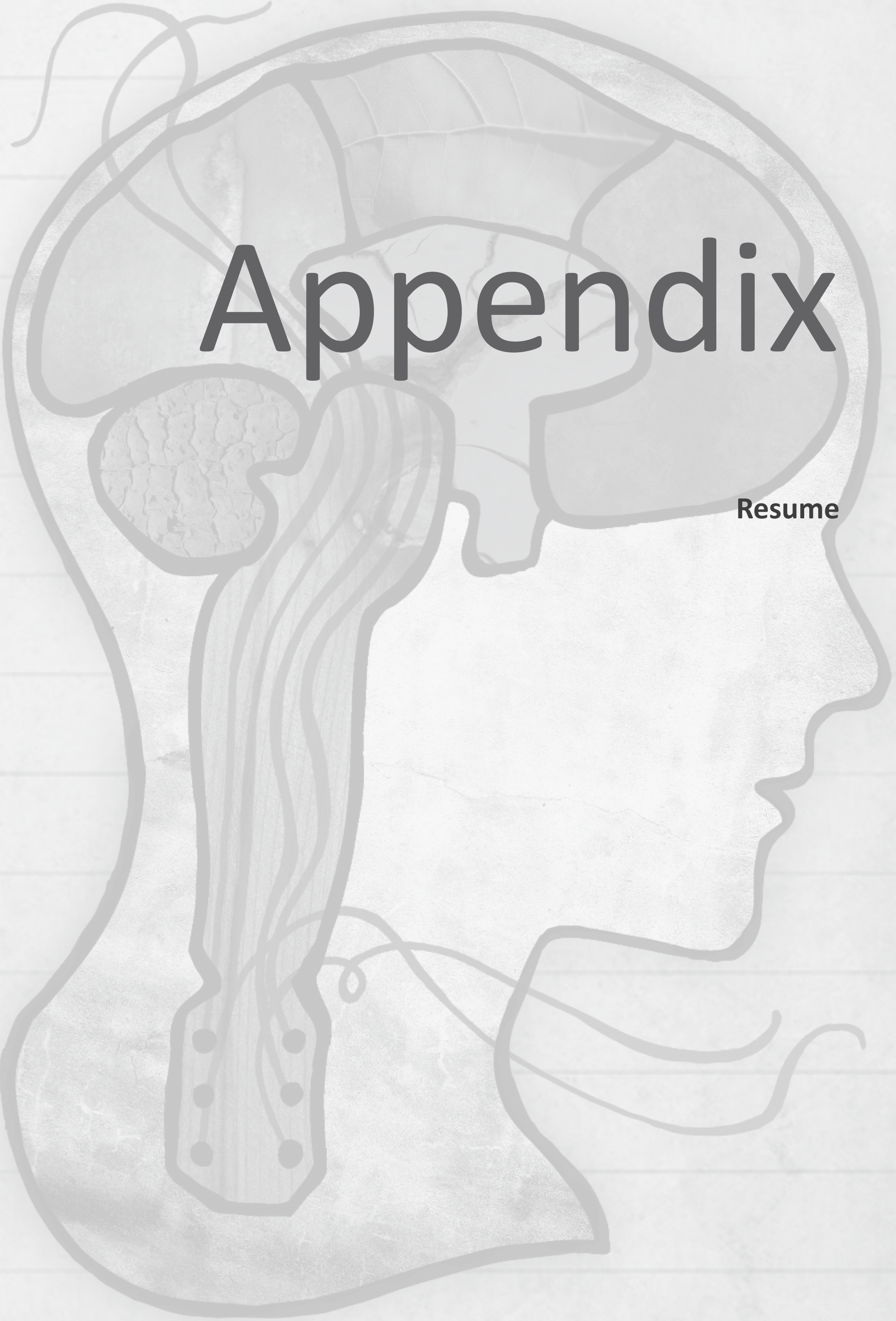
In 2001 besloot Monique alsnog een jeugddroom te vervullen en deed toelatingsexamen klassiek gitaar aan het Conservatorium te Enschede. Zij studeerde alhier in 2006 af als muziektherapeute. In datzelfde jaar begon ze te werken bij Atlant Zorggroep te Apeldoorn, dezelfde zorginstelling waar ze in 2004 tijdens haar stage voor het eerst kennis maakte met mensen die aan de ziekte van Huntington lijden.

Vervolgens studeerde Monique van 2008 tot 2010 aan de Hogeschool Zuyd te Heerlen bij Henk Smeijsters, alwaar ze haar Master of Music Therapy-graad behaalde. In 2010 en 2011 volgde ze de training tot Neurologisch Muziek Therapeut-Fellow (NMT-F) bij Prof. Michael Thaut aan de Colorado State University in de VS. In 2012 begon ze haar promotie-traject aan het Leids Universitair Medisch Centrum te Leiden bij Prof. Raymund Roos, neuroloog, gespecialiseerd in de Ziekte van Huntington. Later sloten Prof. Wilco Achterberg en Dr. Annemieke Vink zich aan als respectievelijk tweede promotor en co-promotor.

Monique is senior geregistreerd muziektherapeute en docente aan de Bachelor en Master muziektherapie-opleiding van ArtEZ University of the Arts, Academy of Music, Department of Music Therapy in Enschede, en onderzoeker bij Atlant Zorggroep te Apeldoorn. Daarnaast is ze zelfstandig gevestigd en geeft ze in deze hoedanigheid gitaarlessen en muziektherapie.
Monique is sinds 1982 getrouwd met haar jeugdliefde Leo van Bruggen. Samen hebben zij twee kinderen: Mark (1988) en Wendy (1989).

Appendix

Resume



Resume

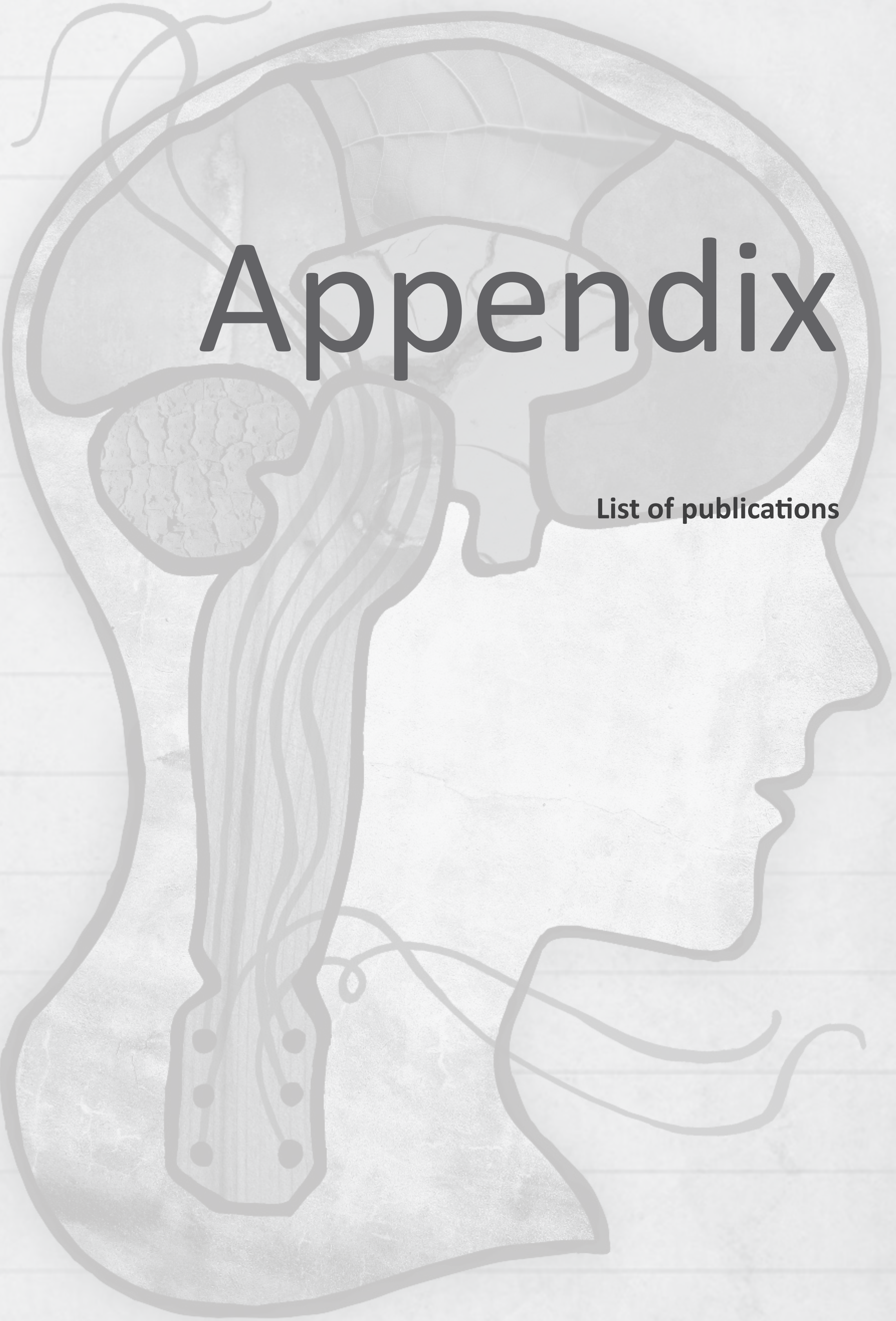
Monique van Bruggen-Rufi was born in Ede, The Netherlands, on April 16, 1962. She attended Marnix College in Ede (Gymnasium β) from 1974 till 1980. After graduation she started an in-service-training to become a surgical assistant at Bronovo Hospital in The Hague, followed by different positions (medical secretary/physician's assistant) in different (outdoor)clinics (orthopedic surgery, rheumatology, neurology, psychology) at Medical Spectrum Twente in Enschede, The Netherlands.

In 2001 Monique decided to follow a long-desired dream and auditioned for studying classical guitar at the Conservatory School of Music in Enschede. Here she graduated as a music therapist in 2006. In the same year she started her career as a music therapist at Atlant Zorggroep Apeldoorn, the long term care facility where she first started working with patients with Huntington's disease during her internship in 2004.

From 2008 till 2010 Monique studied at the University of Applied Science in Heerlen with Henk Smeijsters, where she earned her Master's degree in Music Therapy in 2010. In 2010 and 2011 she was trained to become a Neurologic Music Therapist-Fellow (NMT-F) at the Colorado State University in de US with Prof. Michael Thaut. In 2012 she started as a PhD-candidate at the Leiden University Medical Center in Leiden with Prof. Raymund Roos, Head of the Neurology Department and specialized in Huntington's Disease. Prof. Wilco Achterberg and Dr. Annemieke Vink joined the team shortly after.

Monique is a lecturer at the Bachelor and Master program at the ArtEZ University of the Arts, Academy of Music, Department of Music Therapy in Enschede, The Netherlands, and researcher at Atlant Zorggroep Apeldoorn, The Netherlands. She is partly self-employed as a music therapist and a guitar teacher in her private practice.

Monique has been married with her high-school-sweetheart Leo van Bruggen since 1982. They have a son (Mark, 1988) and a daughter (Wendy, 1989).



Appendix

List of publications

List of publications

Bruggen-Rufi, C.H.M. van, Hogenboom M., Vink A.C., Achterberg W.P., Roos R.A.C. (2017). Process Evaluation of a Randomized Controlled Trial Studying the effect of music therapy in patients with Huntington’s Disease. Journal of Memory Disorders and Rehabilitation 2(1): 1005

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