267th ENMC International Workshop:

Psychological Interventions for Improving Quality of Life in Slowly Progressive Neuromuscular Disorders.

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Abstract

This workshop aimed to develop recommendations for psychological interventions to support people living with slowly progressive neuromuscular disorders (NMD). The workshop comprised clinicians, researchers, people living with NMD and their relatives. First, participants considered the key psychological challenges presented by NMD and the impact of NMD on relationships and mental health. Later, several psychological approaches for enhancing well-being in NMD were described. The results of randomised controlled trials of Cognitive Behaviour Therapy and Acceptance and Commitment Therapy for improving fatigue, quality of life, and mood in adults with NMD were examined. Then the group considered ways to adapt therapies for cognitive impairments or neurodevelopmental differences that occur in some NMD, alongside ways to support children and adolescents with NMD and their family members. Based on the evidence from randomised controlled trials, carefully conducted observational studies, and the coherence of these data with the experience of those living with NMD, the group recommends that psychological interventions should be embedded in the routine clinical care offered to people living with NMD.

Keywords: neuromuscular disorders; psychological interventions; mental well-being; cognitive behavioral therapy; acceptance and commitment therapy

1. Introduction

The ENMC workshop on psychological interventions for improving quality of life (QoL) in slowly progressive neuromuscular disorders (NMD) occurred on May 20th, 2022, in Hoofddorp, The Netherlands. This workshop gathered a group of 27 participants, comprising patient and caregiver representatives with different types of NMD and expert healthcare professionals and researchers (neurologists, paediatric neurologists, psychologists, physical- and occupational therapists, rehabilitation physicians, and psychiatrists.)

The workshop aimed to develop guidelines for supporting psychological well-being and QoL in people living with NMD and their family members and caregivers. The group considered:

- The lived experience of NMD
- Relevant past and ongoing research on psychological aspects of NMD
- Current clinical practice across Europe regarding psychological interventions for people living with NMD

We hoped this work would consolidate a network of patients, healthcare professionals, and researchers interested in psychological interventions for improving QoL in NMD.

2. Background

Although there is much variation between individuals, on average having a NMD negatively impacts QoL [1]. People with NMD, together with their family, have to periodically adapt their daily activities as symptoms progress and manage accompanying emotions, like frustration and anxiety [2] Indeed, 75% of people with NMD experience challenging emotions as a part of living with a NMD [3]. In some cases - for example as part of Duchenne muscular dystrophy or myotonic dystrophy type 1 (DM1) - NMD also involves cognitive changes or neurodevelopmental or psychiatric disorders.

Studies consistently show that psychological factors, like illness perceptions, coping methods, and psychological flexibility, explain significant proportions of the variance in QoL and mood, over and above measures of disease severity [1,4,5]. This suggests that interventions targeted at psychological factors could improve outcomes such as mood and QoL, even where disease severity is high [6]. Therefore, this workshop considered the evidence for such interventions, and how these can be used in clinical practice.

3. Living with a slowly progressive neuromuscular disorder

The psychosocial challenges of living with a NMD

The workshop began by examining the lived experience of NMD. Four people who have a diagnosis of NMD shared their perspectives on the main psychosocial challenges. To supplement these presentations, data was presented from a survey of psychosocial needs and the barriers to accessing psychological intervention that was circulated to people living with NMD, their relatives and health care professionals in advance of the workshop. The questionnaire was completed by 198 people living with NMD, 49 close relatives, and 29 health care professionals from eight different countries (Italy 56%, Brazil 21%, Netherlands 15%, Germany 3%, Portugal 3%, Bulgaria 1%, France 1% and Canada 0.3%). There were more than 40 different NMD diagnoses, mostly facioscapulohumeral muscular dystrophy (FSHD) (40%), Charcot-Marie-Tooth disease (24%), Mitochondrial Myopathy (6%), Limb-Girdle Muscular Dystrophy (LGMD) (4%) or Duchenne Muscular Dystrophy (4%).

The presentations from the patient representatives and the results of the questionnaire identified some common psychosocial challenges, which can be broadly divided into three spheres (physical, social, and emotional), which are described in Table 1.

Results from the questionnaire suggested that psychosocial challenges differ across each stage of the disease. In the early stages, even before diagnosis, patients may experience vague symptoms such as pain and fatigue, even wondering if they are "imagining the symptoms." At the point of diagnosis, professionals recommended paying particular attention to the communication of the diagnosis and corresponding psychoeducation and family guidance. It was recommended that patients and relatives are informed of psychological support possibilities, such as support groups or psychological interventions.

Immediately following diagnosis the most common psychosocial challenges experienced by patients are a lack of information about the disease, difficulty accepting the disease, changes to relationships and daily life activities such as work, and difficulties accepting assistive devices. Patients also reported a range of emotional experiences involving feelings of isolation, fear of the future, sadness, anger, and guilt (e.g., about heredity or towards the impact on partners.)

The psychological challenges of the later stages are characterised by managing the emotions that occur with significant changes in physical functioning e.g., the first time using a wheelchair or not being able to reach the top of your head. The professionals who responded to the questionnaire stressed that the support in this stage should be individualised to the person and their needs, symptoms, and personal situation. They also highlighted the importance of adequate communication between the multidisciplinary team and the patient and their relatives and performing regular monitoring for mood.

Barriers to psychological support

Respondents described significant barriers to accessing psychological support. Barriers often consisted of unpleasant emotional responses to the idea of accessing psychological support, such as shame and fear. Others mentioned logistical barriers such as lack of information, difficulty accessing specialised professionals, accessibility, time, and finances.

Role of caregivers

The group of attending expert patients and relatives emphasised that NMD affects not only the person living with the condition but also close family members. Caregivers face challenges in adapting their roles within the relationship as NMD progresses. One particular challenge is the need to approach the relationship in a way that balances autonomy and dependency. This is not always intuitive, and family members can feel helpless when dealing with this situation. Therefore, caregivers may also benefit from psychological support.

4. Key contributors to psychosocial well-being in NMD

In the next part of the workshop, attendees presented research describing key contributors to psychosocial well-being in NMD, and the implications for intervention methods.

Adults with NMD

Pain and fatigue

Pain and fatigue contribute to QoL and mood in NMD [7–10]. These are complex symptoms that are influenced by a range of factors depending on the person. Therefore, a multidimensional and personalised model of pain is required. Both aerobic exercise and cognitive behavioural therapy have been found to decrease experienced fatigue in FSHD and DM1 [11,12]. Some practical advice for adequate coping with the persistent symptoms of pain and fatigue includes: exercise the relatively strong muscles, spare the relatively weak muscles, make use of assistive devices e.g., walking aids, smartwatches, etc. and avoid eccentric exercise and overuse. Next, make sure to start low in exercise intensity to build up muscle

strength gradually and to build confidence and go slowly but consistently towards increasing the exercise.

Sexuality

Sexual health is understood as physical, mental, and social well-being in relation to sexuality. In chronic illnesses, 72% of patients describe issues with their sexuality [13], so it is crucial to address sexuality in healthcare. Symptoms of NMD, such as muscle weakness, pain and fatigue, can affect participation in sexual activities. Two guidelines are available for occupational and physical therapists, respectively. These guidelines offer recommendations on discussing sexuality with clients, assessing sexuality issues and interventions [14,15]. Sexuality interventions should be multidisciplinary - because each team member has relevant expertise to contribute. Interventions in occupational therapy include, for example, recommendations on positioning, energy conservation techniques, and adapting sexual devices.

Cognitive symptoms in DM1

Cognitive impairment in adults with DM1 is well recognized. A reduced IQ and domain-specific cognitive impairments have been identified, affecting mainly frontotemporal (attention, language, memory impairment) and frontoparietal pathways (executive functioning and visuoconstruction) [16–24]. Additionally, social cognition has also been studied in DM1, and it is suggested that while patients don't show difficulties in social cognition tasks that demand higher cognitive processes, such as Theory of Mind, they perform worse on less cognitively demanding social cognition tasks, such as facial emotion recognition [25]. This cognitive impairment could be reflected in the observed functional disability and dependency in daily activities [26,27]. On average people with cognitive symptoms show lower social engagement, more psychosocial problems, and poorer psychosocial well-being [28,29].

In addition to the cognitive involvement of DM1, interest has been raised in the ageing process of this patient group. People with DM1 usually present signs and symptoms typically seen in ageing (cataracts, baldness, diabetes, or cardiac arrhythmia) earlier than expected. Therefore, an accelerated ageing hypothesis has been suggested for this disease. Longitudinal cognitive studies have been conducted in DM1 to clarify the existence of an accelerated cognitive decline. Most of the studies observed a progressive decline, this decline is domain-specific rather than global [30,31]. Visuoconstruction is probably the most vulnerable cognitive domain to the passage of time [32].

The mentioned cognitive and behavioural features may have an impact on psychological well-being, and therefore it is important to take them into consideration when providing psychological support. Likewise, fatigue and daytime sleepiness are frequent central nervous system (CNS) symptoms in DM1, and are important sources of discomfort and complaints in patients.

Also apathy is common in people with DM1 [33], with a pooled prevalence of 55% [34]. Apathy is defined as a lack of motivation, initiative, interests, and awareness or difficulties that may impact the provision of healthcare (non-compliance with the treatment) and on the well-being of family (source of burden). Apathy is associated with a lower QoL and decreased level of independence and participation [35,36].

People with DM1 may experience depressive symptoms associated with specific situations related to the condition (diagnosis, evolution, etc.). Nevertheless, in NMD, in general, brief periods of sadness in certain situations are normal, and a period of adaptation is sometimes needed. Still, when these symptoms are distressing, persistent, and affecting daily functioning, treatment is highly recommended.

Approach to treatment of emotional disturbances in DM1

DM1 related factors might have an impact on their psychological well-being, such as nutritional deficiency, medication side effects, quality of sleep, respiratory defects, endocrine dysfunction, etc. These medical conditions should be considered during the intervention process.

Although it is not always necessary, the most used medications for major depression are selective serotonin reuptake inhibitors and selective norepinephrine reuptake inhibitors. Psychostimulants might also be helpful for symptoms such as daytime sleepiness, attention deficit, or fatigue.

As described later in this article, psychological interventions can be delivered in many different ways (individual, couple therapy, family, group) and with different approaches and techniques. Also, where cognitive impairment occurs, neuropsychological intervention might be helpful to reduce functional impairment.

Children and youths with NMD

Assessment of behavioural and neuropsychiatric functioning in boys and young men with Duchenne and Becker muscular dystrophy

In the last two decades interest in studying learning and behaviour problems in children and youths with Duchenne and Becker muscular dystrophy (DMD and BMD, respectively) has increased. These children tend to show altered brain morphology (reduced grey matter volumes and reduced integrity in connectivity.) Neurocognitive functioning may be impaired (automatization, attention, and working memory deficits) resulting in learning difficulties (dyslexia, dyscalculia), and behavioural problems as well as affective functioning (anxiety, depression) and neuropsychiatric disorders (Attention Deficit and Hyperactivity Disorder [ADHD], Autism Spectrum Disorder [ASD], Obsessive Compulsive disorder). Therefore, these children's functioning and psychological adjustment should be systematically assessed.

However, it is important to keep in mind that instruments should be administered with caution, preferably multi-method and multi-informant [37].

Cognitive involvement in children with DM1

Children and adolescents with a diagnosis of DM1, can be classified into three paediatric phenotypes regarding the age of symptom onset: congenital (at birth – 1 year), childhood (1-10 years) and juvenile-onset (10-20 years). As in adults, CNS involvement is common in the paediatric forms of the disease, but with certain distinctive features. Cognitive impairment is one of the CNS symptoms, and its severity depends on the age of onset (the earlier, the more severe impairment), which can vary from severe intellectual disability to subtle neurocognitive deficits. Therefore, paediatric DM1 could be understood as a neurodevelopmental disorder [38].

Mild to severe intellectual disability has been reported in the congenital phenotype, and lower intelligence and specific cognitive impairment in the childhood and juvenile forms of DM1 [39–41]. The cognitive profile of these children is generally characterised by deficits in attention, memory, visuospatial, and executive functioning [42–45], together with poorer social cognition [25,46,47]. Additionally, certain comorbidities such as ADHD, social communication deficits, ASD, and/or learning disabilities (dyslexia and/or dyspraxia) have been described in children with DM1 [40–43,46,48,49]. Concerning the progression of cognitive deficits during childhood, a 7-year follow-up study in patients with congenital and childhood DM1 reported no decline in cognitive abilities. Nevertheless, while children with the childhood phenotype had a positive evolution in adaptive behaviour during these years, a deterioration in adaptive behaviour, socialisation and daily living standard scores was shown in children with the severe congenital DM1 phenotype [41].

In addition to cognitive dysfunction, other neurodevelopmental, behavioural, sleep and emotional symptoms (anxiety, depression) have been reported in DM1, and are needed to be

considered for intervention. Consensus-based care recommendations including potential treatments for the neurodevelopmental management of paediatric DM1 have been published [49].

Mental health in children and youth with NMD

NMD symptoms can compromise autonomy in daily life activities [50,51]. Therefore, children and youth with NMD may require direct assistance (medical, physical, and emotional care). Parents may also benefit from help to support their child into independence. Diminished independence is one of the potential stressors both for patients and their caregivers [52–55]. A study conducted with boys with DMD, described that those patients that had distal deletion (vs proximal), used a wheelchair, or suffered from intellectual disability, were more likely to present with emotional and behavioural problems, such as anxiety and depression [56]. Nevertheless, these are not the only factors that have an impact on their psychological adaptation, well-being and QoL. Fortunately, the coping strategies used by both patients and their relatives could moderate the relationship between illness and psychological adjustment. The study of Tesei et al. (2020)[57],showed that avoidant coping strategies of both patients and parents predicted increased emotional/behavioural problems. On the contrary, positive reinterpretation and acceptance are considered to be more adaptive in the context of chronic illness.

Considering the potential impact of adaptive coping strategies on psychological well-being, interventions targeting both parents and patients, aimed at discouraging the use of avoidant coping and, promoting the use of adaptive coping (i.e., positive reinterpretation, acceptance, problem-solving for situations that are controllable) could reduce anxiety and depression and, more generally, psychological distress among children living with NMD.

Needs of mothers of boys with DMD

Stress in mothers to boys with DMD is elevated, possibly due to increased behavioural problems, particularly in social interactions, rather than only due to the physical demands and to cope with the severe disease condition alone. Therefore, caring for a person with DMD can be associated with a substantial burden, impaired QoL, and mental health problems [58]. Additionally, neuropsychological studies have shown that mothers, as a group, perform poorer than healthy controls on attention, executive functions, memory, and visuospatial tasks [59]. Mothers carrying the DMD mutation seem to be particularly vulnerable from a cognitive perspective.

This highlights the advice that caregivers of patients with DMD should be screened for emotional and/or cognitive problems. Support to caregivers could be beneficial for the family's mental health and for the patients. In addition, mothers showing signs of cognitive dysfunction should be supported with specific strategies to cope with planning and decision-making difficulties.

5. Psychological support and interventions in NMD

The evidence base and clinical application of several psychological therapies for NMD was also discussed.

Cognitive behavioural therapy in FSHD and DM1

Cognitive behaviour therapy (CBT) aims to change dysfunctional cognitions and behaviour. It is an individualised treatment, because cognition and behaviour are different in every individual. CBT is based on the principle that psychological problems are, partially, based on unhelpful ways of thinking and behaviours. Therefore people suffering from psychological problems can learn better ways of coping, which relieves their psychological symptoms. Different strategies to change the thinking pattern are: learning to recognize one’s cognitive distortions and then to reevaluate them in light of reality, gaining a better understanding of the

behaviour and motivation of others, using problem-solving skills to cope with difficult situations, and learning to develop a greater sense of confidence in one's own abilities.

In a study by Voet et al. (2019) [60], people with FSHD received CBT 2-3 times a week for 16 weeks. A positive effect was found for experienced fatigue, social participation, physical activity, sleep quality, and even disease progression. Also, in the OPTIMISTIC trial, where CBT was given to 225 people with DM1 patients with severe fatigue, increased values in the 6-minute walking test (6MWT) and physical activity and a decrease in the level of fatigue and daytime sleepiness and a deceleration of disease progression was found [12]. The clinical application of group-based CBT intervention for FSHD and DM1 in an inpatient rehabilitation setting was described in the study of Okkersen et al. (2018)[12]. Treatment involved six modules encouraging key skills in coping, cognitions towards pain, fatigue, activity, catastrophizing, sleep, social support, and negative social interactions. Every patient received two group sessions during the first week of rehabilitation and a final session in the last week before discharge of the patients. Results showed a significant reduction of general fatigue, mental fatigue, and physical fatigue symptoms, and an increase in motivation for physical activity. At 2-6 weeks post-discharge, most participants felt less burdened (96%) with increased daily activity levels (92%). Other relevant studies were also presented [61,62].

Neuromuscular discussion groups

The implementation of NMD discussion groups within the rehabilitation setting was described. These groups provide a forum for people facing the same difficulties to support each other and share experiences and coping strategies. An exploration of participants' experiences of discussion groups at the University Hospital Saint-Luc Brussels was presented. Two key treatment mechanisms were identified: a) patients feeling understood via sharing experiences with other patients who are facing similar situations, b) sharing effective coping strategies. The

impact and mechanisms of discussion groups at a German Rehabilitation Clinic (Klinik Hoher Meißner) were also explored. Here, groups discussed coping strategies, communication strategies and acceptance of aids and help. Physician-led group information sessions were seen as useful for providing information about the disease and have also been utilised at the German Rehabilitation Clinic. These lectures are focused on answering common questions (e.g., what is muscular atrophy, and why is it sometimes so difficult to get a diagnosis). Information is provided on sources of support, such as patient registries, neuromuscular centres, and self-help organisations. Information is also provided on recent research (e.g., medications and gene therapy) and on practical things such as driving a car or exercise training with NMD.

Acceptance and Commitment Therapy

In the workshop the results of a randomised controlled trial of Acceptance and Commitment Therapy (ACT) for improving QoL and mood were presented [63]. In this trial, 155 people living with a range of NMD (mainly FSHD, LGMD and Inclusion Body Myositis (IBM)) were randomised to either usual care or a brief remotely-delivered guided self-help ACT intervention. Significantly greater post-intervention improvements in QoL and mood of moderate effect size were apparent in the intervention group and were maintained at six months post-randomization.

ACT takes a different approach from traditional cognitive behaviour therapies - focusing first on helping people to 'live well' and to engage more fully in meaningful activities. ACT does this by encouraging a quality within behaviour called psychological flexibility, which can be defined as "the capacity to persist or to change behaviour in a way that 1) includes conscious and open contact with thoughts and feelings (openness), 2) appreciates what the situation affords (awareness), and 3) serves one's goals and values (engagement)" [64].

Many intervention methods can be used to encourage psychological flexibility. These typically include conversations designed to help participants connect with their overarching goals and

values (e.g., kindness, creativity, etc.) and to enact activities that reflect these values. Other techniques are then used to help reduce the impact of competing sources of influence over behaviour – such as negative thoughts or uncomfortable feelings. For example, variations of mindfulness practice can help people notice they can observe their thoughts and feelings instead of acting on them. Perspective-taking exercises can help people approach themselves in more self-compassionate ways.

Relaxation methods and mindfulness

Relaxation and mindfulness are techniques that are often included in interventions like CBT and ACT. Combined, such interventions could have potential benefits on the psychological consequences of NMD. Relaxation can be achieved through meditation, autogenic- or, where applicable, muscle- relaxation, as well as deep breathing. Mindfulness aims to purposely bring one's attention in the present moment without evaluation. Both techniques can be used to prevent or reduce stress, anxiety, and pain in the general population or specific diseases. Except as part of CBT or ACT [65], we are not aware of any trials of such techniques in isolation in NMD. However, a randomised clinical trial with people with amyotrophic lateral sclerosis (ALS) patients found significant improvements in QoL, anxiety, depression, and interaction with people and the environment following mindfulness training [66]. Relaxation and mindfulness should be explored further as promising techniques to prevent stress and anxiety or to help individuals to cope with emotional disturbances, especially in combination with other interventions (i.e., with cognitive behavioural therapy). However, in some NMD where weakness in the breathing muscles is present, relaxation may have an adverse effect and will increase anxiety. In this case, it should not be offered.

Contextual Approach to NMD

In this workshop, the Contextual Approach - as developed by the psychiatrist Iván Böszörményi-Nagy - [67] to cope with NMD was presented. This is an explicitly systemic

framework that focuses on the individual's relationships with their family, friendship and work groups. It consists of four dimensions that impact on the person's functioning: facts, about what 'is'; psychology, about thinking and feeling; interactions between people; and the relational ethics, about what does and does not contribute to the relationship. The first three dimensions may be included in interventions like CBT and ACT. The fourth dimension may be more unique to the contextual approach. It involves constructs such as loyalty, acknowledgement and the balance of giving and receiving in relationships.This approach can be used to improve QoL and mood via seeing people with NMD within their systems of family, friends, work colleagues etc.

Resilience and the capability approach

The final talk on psychological approaches to improving well-being in NMD emphasised that a shift in emphasis may be required in our approach to treatments, towards helping our patients focus on capability. Treatment approaches focusing on curing the disease might leave the present patients alone in trying to find a good life with the disease. Therefore, the question arises, "do we, as clinicians/researchers, help patients to have a good life with the disease?". An example of how this can be facilitated is by shifting the focus away from the disease, towards the current experience of illness. Treating patients is not only about suppressing the 'negative' symptoms of the disease but also about improving health and improving resilience.

This approach to treatment is sometimes termed a 'capability approach', a concept developed by the Nobel prize Laureate Amarthya Sen [68]. Within the capability approach clinicians might focus on creating opportunities for people to be and do things they value and find personally meaningful.

6. Recommendations

The opportunities for psychological support/treatments were highlighted during the workshop. Evidence from randomised controlled trials shows that such treatments can improve QoL, mood, and fatigue [2,12,61–63,65]**.** Consequently, the group made several recommendations:

- **Psychological interventions should be embedded in the routine clinical care offered to people with NMD.**

  While not all people with NMD will require or want psychological support, all individuals with NMD should be able to access psychological support. For example, evidence based approaches such as CBT or ACT.

- **Individualise the psychological treatment to a person's situation.**

  Where psychological support is indicated, providers should first assess each person as an individual - carefully considering their personal circumstances, coping methods, values, etc.

- **Consider the involvement of family members/caregivers.**

  Psychological interventions could also be helpful for the families/relatives of those living with NMD, who also face psychosocial challenges due to the condition.

- **Consider barriers to accessing psychological support.**

  Due to the accessibility problems related to the disease, E-Health and remote therapy could reduce the barriers to participating in psychological support. Other barriers for people with NMD, like shame and fear, should also be addressed.

- **More research is required on psychological interventions for NMD**.

  Alongside research on disease-modifying treatments, it is also important to develop research projects that seek for a better QoL for people living with NMD. Both patients and professionals agreed on the importance of these topics in future research. [6].

To continue sharing up-to-date evidence, best clinical practices and to promote collaboration on research programs, the members of the 267th ENMC International Workshop plan to set up a network of patients, healthcare professionals, and researchers with expertise in psychological support in NMD, called INSPIRE (International NeuromuScular disorder Psychosocial InteRvention nEtwork.).

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References

[1] Graham CD, Rose MR, Grunfeld EA, Kyle SD, Weinman J. A systematic review of quality of life in adults with muscle disease. J Neurol 2011;258:1581–92. https://doi.org/10.1007/s00415-011-6062-5.

[2] Graham CD, Simmons Z, Stuart SR, Rose MR. The potential of psychological interventions to improve quality of life and mood in muscle disorders: Psychological Interventions for Muscle Disorders. Muscle Nerve 2015;52:131–6. https://doi.org/10.1002/mus.24487.

[3] Padua L, Shy ME, Aprile I, Cavallaro T, Pareyson D, Quattrone A, et al. Correlation between clinical/neurophysiological findings and quality of life in Charcot-Marie-Tooth type 1A. J Peripher Nerv Syst 2008;13:64–70. https://doi.org/10.1111/j.1529-8027.2008.00159.x.

[4] Graham CD, Weinman J, Sadjadi R, Chalder T, Petty R, Hanna MG, et al. A multicentre postal survey investigating the contribution of illness perceptions, coping and optimism to quality of life and mood in adults with muscle disease. Clin Rehabil 2014;28:508–19. https://doi.org/10.1177/0269215513511340.

[5] Graham CD, Gouick J, Ferreira N, Gillanders D. The influence of psychological flexibility on life satisfaction and mood in muscle disorders. Rehabilitation Psychology 2016;61:210–7. https://doi.org/10.1037/rep0000092.

[6] Nierse CJ, Abma TA, Horemans AMC, van Engelen BGM. Research priorities of patients with neuromuscular disease. Disability and Rehabilitation 2013;35:405–12. https://doi.org/10.3109/09638288.2012.694964.

[7] Jensen MP, Abresch RT, Carter GT, McDonald CM. Chronic pain in persons with neuromuscular disease. Arch Phys Med Rehabil 2005;86:1155–63. https://doi.org/10.1016/j.apmr.2004.11.028.

[8] Jensen MP, Hoffman AJ, Stoelb BL, Abresch RT, Carter GT, McDonald CM. Chronic pain in persons with myotonic dystrophy and facioscapulohumeral dystrophy. Arch Phys Med Rehabil 2008;89:320–8. https://doi.org/10.1016/j.apmr.2007.08.153.

[9] Laberge L, Dauvilliers Y, Bégin P, Richer L, Jean S, Mathieu J. Fatigue and daytime sleepiness in patients with myotonic dystrophy type 1: to lump or split? Neuromuscul Disord 2009;19:397–402. https://doi.org/10.1016/j.nmd.2009.03.007.

[10] Miró J, Raichle KA, Carter GT, O'Brien SA, Abresch RT, McDonald CM, et al. Impact of biopsychosocial factors on chronic pain in persons with myotonic and facioscapulohumeral muscular dystrophy. Am J Hosp Palliat Care 2009;26:308–19. https://doi.org/10.1177/1049909109335146.

[11] Koopman F, Brehm M, Beelen A, Voet N, Bleijenberg G, Geurts A, et al. Cognitive behavioural therapy for reducing fatigue in post-polio syndrome and in facioscapulohumeral dystrophy: A comparison. J Rehabil Med 2017;49:585–90. https://doi.org/10.2340/16501977-2247.

[12] Okkersen K, Jimenez-Moreno C, Wenninger S, Daidj F, Glennon J, Cumming S, et al. Cognitive behavioural therapy with optional graded exercise therapy in patients with severe fatigue with myotonic dystrophy type 1: a multicentre, single-blind, randomised trial. The Lancet Neurology 2018;17:671–80. https://doi.org/10.1016/S1474-4422(18)30203-5.

[13] Haboubi NHJ, Lincoln N. Views of health professionals on discussing sexual issues with patients. Disabil Rehabil 2003;25:291–6. https://doi.org/10.1080/0963828021000031188.

[14] Levine SB. *Sexual Function in People with Disability and Chronic Illness: A Health Professional's Guide* . Edited by Marca L. Sipski and Craig J. Alexander. Journal of Sex Education and Therapy 1998;23:171–2. https://doi.org/10.1080/01614576.1998.11074230.

[15] Muslemani S. Guide de pratique en ergothérapie – Favoriser la sexualité et la vie amoureuse des adultes présentant une maladie neuromusculaire. Groupe de recherche interdisciplinaire sur les maladies neuromusculaires (GRIMN); 2019.

[16] D'Angelo MG, Bresolin N. Report of the 95th European Neuromuscular Centre (ENMC) sponsored International Workshop Cognitive Impairment in Neuromuscular Disorders, Naarden, The Netherlands, 13-15 July 2001. Neuromuscular Disorders 2003;13:72–9. https://doi.org/10.1016/S0960-8966(02)00155-4.

[17] Gaul C, Schmidt T, Windisch G, Wieser T, Müller T, Vielhaber S, et al. Subtle cognitive dysfunction in adult onset myotonic dystrophy type 1 (DM1) and type 2 (DM2). Neurology 2006;67:350–2. https://doi.org/10.1212/01.wnl.0000225180.27833.c1.

[18] Meola G, Sansone V, Perani D, Scarone S, Cappa S, Dragoni C, et al. Executive dysfunction and avoidant personality trait in myotonic dystrophy type 1 (DM-1) and in proximal myotonic myopathy (PROMM/DM-2). Neuromuscular Disorders 2003;13:813–21. https://doi.org/10.1016/S0960-8966(03)00137-8.

[19] Minnerop M, Weber B, Schoene-Bake J-C, Roeske S, Mirbach S, Anspach C, et al. The brain in myotonic dystrophy 1 and 2: evidence for a predominant white matter disease. Brain 2011;134:3530–46. https://doi.org/10.1093/brain/awr299.

[20] Modoni A, Silvestri G, Grazia Pomponi M, Mangiola F, Tonali PA, Marra C. Characterization of the Pattern of Cognitive Impairment in Myotonic Dystrophy Type 1. Arch Neurol 2004;61. https://doi.org/10.1001/archneur.61.12.1943.

[21] Okkersen K, Buskes M, Groenewoud J, Kessels RPC, Knoop H, Engelen B van, et al. The cognitive profile of myotonic dystrophy type 1: A systematic review and meta-analysis. Cortex 2017;95:143–55. https://doi.org/10.1016/j.cortex.2017.08.008.

[22] Peric S, Mandic-Stojmenovic G, Stefanova E, Savic-Pavicevic D, Pesovic J, Ilic V, et al. Frontostriatal dysexecutive syndrome: A core cognitive feature of myotonic dystrophy type 2. Journal of Neurology 2015;262:142–8. https://doi.org/10.1007/s00415-014-7545-y.

[23] Romeo V, Pegoraro E, Ferrati C, Squarzanti F, Sorarù G, Palmieri A, et al. Brain involvement in myotonic dystrophies: neuroimaging and neuropsychological comparative study in DM1 and DM2. J Neurol 2010;257:1246–55. https://doi.org/10.1007/s00415-010-5498-3.

[24] Sistiaga A, Urreta I, Jodar M, Cobo AM, Emparanza J, Otaegui D, et al. Cognitive/personality pattern and triplet expansion size in adult myotonic dystrophy type 1 (DM1): CTG repeats, cognition and personality in DM1. Psychological Medicine 2010;40:487–95. https://doi.org/10.1017/S0033291709990602.

[25] Labayru G, Arenzana I, Aliri J, Zulaica M, Munain ALD, Sistiaga AA. Social cognition in myotonic dystrophy type 1: Specific or secondary impairment? PLoS ONE 2018;13:1–11. https://doi.org/10.1371/journal.pone.0204227.

[26] Muslemani S, Gagnon C, Gallais B. Instrumental activities of daily living in adults with the DM1 childhood phenotype: going beyond motor impairments. Neuromuscul Disord 2022;32:313–20. https://doi.org/10.1016/j.nmd.2022.02.004.

[27] Tremblay M, Muslemani S, Côté I, Gagnon C, Fortin J, Gallais B. Accomplishment of instrumental activities of daily living and its relationship with cognitive functions in adults with myotonic dystrophy type 1 childhood phenotype: an exploratory study. BMC Psychology 2021;9:56. https://doi.org/10.1186/s40359-021-00562-1.

[28] Axford MM, Pearson CE. Illuminating CNS and cognitive issues in myotonic dystrophy: Workshop report. Neuromuscular Disorders 2013;23:370–4. https://doi.org/10.1016/j.nmd.2013.01.003.

[29] Bugiardini E, Meola G, Alvarez C, Angeard N, Bassez G, Day JW, et al. Consensus on cerebral involvement in myotonic dystrophy. Workshop report: May 24-27, 2013, Ferrere (AT), Italy. Neuromuscular Disorders 2014;24:445–52. https://doi.org/10.1016/j.nmd.2014.01.013.

[30] Gallais B, Gagnon C, Mathieu J, Richer L. Cognitive decline over time in adults with myotonic dystrophy type 1: A 9-year longitudinal study. Neuromuscular Disorders 2017;27:61–72. https://doi.org/10.1016/j.nmd.2016.10.003.

[31] Winblad S, Samuelsson L, Lindberg C, Meola G. Cognition in myotonic dystrophy type 1: a 5-year follow-up study. European Journal of Neurology 2016;23:1471–6. https://doi.org/10.1111/ene.13062.

[32] Labayru G, Aliri J, Zulaica M, López de Munain A, Sistiaga A. Age-related cognitive decline in myotonic dystrophy type 1: An 11-year longitudinal follow-up study. Journal of Neuropsychology 2020;14:121–34. https://doi.org/10.1111/jnp.12192.

[33] Gallais B, Montreuil M, Gargiulo M, Eymard B, Gagnon C, Laberge L. Prevalence and correlates of apathy in myotonic dystrophy type 1. BMC Neurol 2015;15:148. https://doi.org/10.1186/s12883-015-0401-6.

[34] Velden BG van der, Okkersen K, Kessels RP, Groenewoud J, Engelen B van, Knoop H, et al. Affective symptoms and apathy in myotonic dystrophy type 1 a systematic review and meta-analysis. Journal of Affective Disorders 2019;250:260–9. https://doi.org/10.1016/j.jad.2019.03.036.

[35] Fujino H, Shingaki H, Suwazono S, Ueda Y, Wada C, Nakayama T, et al. Cognitive impairment and quality of life in patients with myotonic dystrophy type 1. Muscle and Nerve 2018;57:742–8. https://doi.org/10.1002/mus.26022.

[36] Van Heugten C, Meuleman S, Hellebrekers D, Kruitwagen-van Reenen E, Visser-Meily J. Participation and the Role of Neuropsychological Functioning in Myotonic Dystrophy Type 1. JND 2018;5:205–14. https://doi.org/10.3233/JND-170246.

[37] Hellebrekers DMJ, Lionarons JM, Faber CG, Klinkenberg S, Vles JSH, Hendriksen JGM. Instruments for the Assessment of Behavioral and Psychosocial Functioning in Duchenne and Becker Muscular Dystrophy; a Systematic Review of the Literature. Journal of Pediatric Psychology 2019;44:1205–23. https://doi.org/10.1093/jpepsy/jsz062.

[38] Angeard N. A neurodevelopmental approach to myotonic dystrophy type 1. Developmental Medicine & Child Neurology 2019;61:1126–1126. https://doi.org/10.1111/DMCN.14194.

[39] Angeard N, Gargiulo M, Jacquette A, Radvanyi H, Eymard B, Héron D. Cognitive profile in childhood myotonic dystrophy type 1: is there a global impairment? Neuromuscul Disord 2007;17:451–8. https://doi.org/10.1016/j.nmd.2007.02.012.

[40] Lagrue E, Dogan C, De Antonio M, Audic F, Bach N, Barnerias C, et al. A large multicenter study of pediatric myotonic dystrophy type 1 for evidence-based management. Neurology 2019;92:e852–65. https://doi.org/10.1212/WNL.0000000000006948.

[41] Lindeblad G, Kroksmark AK, Ekström AB. Cognitive and adaptive functioning in congenital and childhood forms of myotonic dystrophy type 1: a longitudinal study. Developmental Medicine and Child Neurology 2019;61:1214–20. https://doi.org/10.1111/dmcn.14161.

[42] Angeard N, Jacquette A, Gargiulo M, Radvanyi H, Moutier S, Eymard B, et al. A new window on neurocognitive dysfunction in the childhood form of myotonic dystrophy type 1 (DM1). Neuromuscul Disord 2011;21:468–76. https://doi.org/10.1016/j.nmd.2011.04.009.

[43] Douniol M, Jacquette A, Cohen D, Bodeau N, Rachidi L, Angeard N, et al. Psychiatric and cognitive phenotype of childhood myotonic dystrophy type 1. Dev Med Child Neurol 2012;54:905–11. https://doi.org/10.1111/j.1469-8749.2012.04379.x.

[44] Sweere DJJ, Pel JJM, Kooiker MJG, van Dijk JP, van Gemert EJJM, Hurks PPM, et al. Clinical Utility of Eye Tracking in Assessing Distractibility in Children with Neurological Disorders or

ADHD: A Cross-Sectional Study. Brain Sci 2022;12:1369. https://doi.org/10.3390/brainsci12101369.

[45] Wozniak JR, Mueller BA, Bell CJ, Muetzel RL, Lim KO, Day JW. Diffusion tensor imaging reveals widespread white matter abnormalities in children and adolescents with myotonic dystrophy type 1. Journal of Neurology 2013;260:1122–31. https://doi.org/10.1007/s00415-012-6771-4.

[46] Angeard N, Huerta E, Jacquette A, Cohen D, Xavier J, Gargiulo M, et al. Childhood-onset form of myotonic dystrophy type 1 and autism spectrum disorder: Is there comorbidity? Neuromuscul Disord 2018;28:216–21. https://doi.org/10.1016/j.nmd.2017.12.006.

[47] Leddy S, Cercignani M, Serra L, Bozzali M. Social cognition in type 1 myotonic dystrophy - A mini review. Cortex 2021;142:389–99. https://doi.org/10.1016/j.cortex.2021.05.004.

[48] Ekström A-B, Hakenäs-Plate L, Samuelsson L, Tulinius M, Wentz E. Autism spectrum conditons in myotonic dystrophy type 1: A study on 57 individuals with congenital and childhood forms. Am J Med Genet 2008;147B:918–26. https://doi.org/10.1002/ajmg.b.30698.

[49] Johnson NE, Aldana EZ, Angeard N, Ashizawa T, Berggren KN, Marini-Bettolo C, et al. Consensus-based care recommendations for congenital and childhood-onset myotonic dystrophy type 1. Neurology: Clinical Practice 2019;9:443–54. https://doi.org/10.1212/CPJ.0000000000000646.

[50] Mercuri E, Muntoni F. Muscular dystrophies. Lancet 2013;381:845–60. https://doi.org/10.1016/S0140-6736(12)61897-2.

[51] Straub V, Bertoli M. Where do we stand in trial readiness for autosomal recessive limb girdle muscular dystrophies? Neuromuscul Disord 2016;26:111–25. https://doi.org/10.1016/j.nmd.2015.11.012.

[52] Latimer R, Street N, Conway KC, James K, Cunniff C, Oleszek J, et al. Secondary Conditions Among Males With Duchenne or Becker Muscular Dystrophy. J Child Neurol 2017;32:663–70. https://doi.org/10.1177/0883073817701368.

[53] Magliano L, D'Angelo MG, Vita G, Pane M, D'Amico A, Balottin U, et al. Psychological and practical difficulties among parents and healthy siblings of children with Duchenne vs. Becker muscular dystrophy: an Italian comparative study. Acta Myol 2014;33:136–43.

[54] Miladi N, Bourguignon JP, Hentati F. Cognitive and psychological profile of a Tunisian population of limb girdle muscular dystrophy. Neuromuscul Disord 1999;9:352–4. https://doi.org/10.1016/s0960-8966(99)00006-1.

[55] Pousada T, Groba B, Nieto-Riveiro L, Pazos A, Díez E, Pereira J. Determining the burden of the family caregivers of people with neuromuscular diseases who use a wheelchair. Medicine (Baltimore) 2018;97:e11039. https://doi.org/10.1097/MD.0000000000011039.

[56] Colombo P, Nobile M, Tesei A, Civati F, Gandossini S, Mani E, et al. Assessing mental health in boys with Duchenne muscular dystrophy: Emotional, behavioural and neurodevelopmental profile in an Italian clinical sample. Eur J Paediatr Neurol 2017;21:639–47. https://doi.org/10.1016/j.ejpn.2017.02.007.

[57] Tesei A, Nobile M, Colombo P, Civati F, Gandossini S, Mani E, et al. Mental health and coping strategies in families of children and young adults with muscular dystrophies. J Neurol 2020;267:2054–69. https://doi.org/10.1007/s00415-020-09792-6.

[58] Landfeldt E, Edström J, Buccella F, Kirschner J, Lochmüller H. Duchenne muscular dystrophy and caregiver burden: a systematic review. Dev Med Child Neurol 2018;60:987–96. https://doi.org/10.1111/dmcn.13934.

[59] Demirci H, Durmus H, Toksoy G, Uslu A, Parman Y, Hanagasi H. Cognition of the mothers of patients with Duchenne muscular dystrophy. Muscle & Nerve 2020;62:710–6. https://doi.org/10.1002/mus.27057.

[60] Voet NB, van der Kooi EL, van Engelen BG, Geurts AC. Strength training and aerobic exercise training for muscle disease. Cochrane Database Syst Rev 2019;12:CD003907. https://doi.org/10.1002/14651858.CD003907.pub5.

[61] Voet N, Bleijenberg G, Hendriks J, de Groot I, Padberg G, van Engelen B, et al. Both aerobic exercise and cognitive-behavioral therapy reduce chronic fatigue in FSHD: an RCT. Neurology 2014;83:1914–22. https://doi.org/10.1212/WNL.0000000000001008.

[62] Voet NBM, Bleijenberg G, Padberg GW, van Engelen BGM, Geurts ACH. Effect of aerobic exercise training and cognitive behavioural therapy on reduction of chronic fatigue in patients with facioscapulohumeral dystrophy: protocol of the FACTS-2-FSHD trial. BMC Neurol 2010;10:56. https://doi.org/10.1186/1471-2377-10-56.

[63] Rose M, Graham CD, O'Connell N, Vari C, Edwards V, Taylor E, McCracken LM, Radunovic A, Rakowicz W, Norton S and Chalder T, 2022. A randomised controlled trial of acceptance and commitment therapy for improving quality of life in people with muscle diseases. Psychological medicine, pp.1-14.

[64] McCracken LM, Morley S. The Psychological Flexibility Model: A Basis for Integration and Progress in Psychological Approaches to Chronic Pain Management. The Journal of Pain 2014;15:221–34. https://doi.org/10.1016/j.jpain.2013.10.014.

[65] Rose MR, Norton S, Vari C, Edwards V, McCracken L, Graham CD, et al. Acceptance and Commitment Therapy for Muscle Disease (ACTMus): protocol for a two-arm randomised controlled trial of a brief guided self-help ACT programme for improving quality of life in people with muscle diseases. BMJ Open 2018;8:e022083. https://doi.org/10.1136/bmjopen-2018-022083.

[66] Pagnini F, Marconi A, Tagliaferri A, Manzoni GM, Gatto R, Fabiani V, et al. Meditation training for people with amyotrophic lateral sclerosis: a randomized clinical trial. Eur J Neurol 2017;24:578–86. https://doi.org/10.1111/ene.13246.

[67] Goldenthal P. Doing contextual therapy: An integrated model for working with individuals, couples, and families. W W Norton & Co.; 1996.

[68] Saito M. Amartya Sen's Capability Approach to Education: A Critical Exploration. J Philosophy of Education 2003;37:17–33. https://doi.org/10.1111/1467-9752.3701002.