"Activity limitations in patients with neuromuscular disorders"

Vandervelde, Laure

Abstract
Assessment in patients with NMD consists principally of measures of motor impairment since they are well known by clinicians and their measures do not require much equipment. The conventional treatments in patients with NMD are above-all focused on the diminution of motor impairments by maintaining or improving joint mobility, muscle strength and endurance. Nevertheless, a reduction of motor impairments does not directly lead to a higher ability in performing daily activities. Therefore, activity limitations should be measured specifically. A new scale of activity limitations was first developed in children and adults with NMD. The use of the Rasch model provided a scale to assess the fundamental psychometric qualities. Secondly, relationships between motor impairments and activity limitations were investigated to verify the assumption that reduced motor impairments do not necessarily lead to higher activity levels. Finally, to complete the investigation of psychometric qualities, a …

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Activity limitations in patients with neuromuscular disorders

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# Contents

INTRODUCTION..............................................................................................................1

CHAPTER 1:
ACTIVLIM: A RASCH-BUILT MEASURE OF ACTIVITY LIMITATIONS IN PATIENTS WITH NEUROMUSCULAR DISORDERS................................................................................................................. 19

1.1. DEVELOPMENT AND VALIDATION OF THE ACTIVLIM QUESTIONNAIRE.............................................................................................................................. 19

1.2. ACTIVLIM IN CHILDREN WITH NMD: WHY A QUESTIONNAIRE COMPLETED BY THE CHILD’S PARENTS.................................................................................. 40

1.3. COMPARISON BETWEEN SELF-REPORTED AND OBSERVED DIFFICULTY IN ADULTS WITH NMD................................................................................................. 49

CHAPTER 2:
MOTOR IMPAIRMENTS AND THEIR RELATIONSHIPS WITH ACTIVITY LIMITATIONS IN PATIENTS WITH NMD.............. 59

CHAPTER 3:
RESPONSIVENESS STUDY OF THE ACTIVLIM QUESTIONNAIRE.................................................................................................................. 81

DISCUSSION AND PERSPECTIVES.............................................................................. 95

REFERENCES................................................................................................................. 105

APPENDICES................................................................................................................ 117
Introduction

Putting on a T-shirt, taking a shower, going downstairs or getting in a car are basic tasks performed everyday, sometimes even without thought. These tasks in the areas of personal care, mobility, and home maintenance are called *activities of daily living* in the rehabilitation field (Andren & Grimby, 2004, Coster et al., 2004). These activities are actually a combination of several movements requiring a minimum level of motor control and muscle strength (Buchner et al., 1996). Disorders of motor function could lead to disruption in the movement execution and, therefore, to some difficulties in the achievement of basic daily activities. One source of such disorders is neuromuscular disorder.

Neuromuscular disorders: A disruption of motor function

Neuromuscular disorders (NMD) are “a heterogeneous group of acquired or hereditary diseases of the motor unit, including motor neuron diseases, disorders of the peripheral nerves, neuromuscular transmission disorders, and muscle diseases” (McDonald, 2002, Cup et al., 2007). There are approximately 600 different NMD that can affect both children and adults (Cup et al., 2007). The principal and most common deficit of NMD consists of a deterioration of motor function, which is often of a degenerative nature. Nevertheless, the rate of progression, the clinical features, and the pathophysiology vary considerably from one NMD to another (Fowler et al., 1995, Ozsarlak et al., 2001, Hogrel et al., 2006). In Belgium, patients with NMD receive multidisciplinary and individual care by neuromuscular centres. The most prevalent NMD encountered in those centres are Duchenne, Becker, limb-girdle and facio-scapulo-humeral muscular dystrophies, myotonic dystrophies, hereditary neuropathies, spinal muscular atrophies, and amyotrophic lateral sclerosis.

Many muscular dystrophies result from the inefficient or non-production of a muscle protein due to gene abnormalities and lead to progressive muscle atrophy and weakness (Emery, 1998). Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) are inherited X-linked recessive diseases characterized by skeletal muscle and variable myocardial involvement (Emery, 1998, McDonald...
et al., 1995a, McDonald et al., 1995b). The muscle weakness is predominant in the proximal muscle groups of the upper and lower limbs. In patients with DMD, the disease onset occurs before the age of five, and the progression is generally fatal in the second decade of life for untreated patients (Emery, 1998). However, quality of life and patient comfort can be improved by appropriate physiotherapeutic and medical treatment of the DMD symptoms, for instance, by the use of nocturnal ventilation (Eagle et al., 2007, Manzur et al., 2008). Consequently, these patients can now live beyond the age of 30. Patients with BMD have a later onset and a slower rate of progression, which often defines BMD as a mild type of DMD (McDonald et al., 1995a). Limb-girdle muscular dystrophies (LGMD) include disorders with autosomal dominant and recessive inheritance characterized by weakness of the shoulder and/or pelvic girdle muscles, with variable rates of progression (McDonald et al., 1995c). Facio-scapulo-humeral muscular dystrophy (FSHD), on the other hand, is a slowly progressing disorder with early involvement of facial and shoulder musculature. Finally, myotonic dystrophy (MD) is an autosomal dominant, multisystemic disorder, which can range from asymptomatic deficits in case of adult form of the MD to severe deficits in the case of the congenital form of the MD (Johnson et al., 1995). The principal clinical features of MD include progressive muscle weakness, myotonia (i.e., difficulty in relaxing the muscle after voluntary contraction), cardiac conduction defects, cataracts, baldness and endocrine disorders (Schara & Schoser, 2006).

Hereditary neuropathies (HN), the most frequent of which is Charcot-Marie-Tooth neuropathy (CMT), affect motor and/or sensory peripheral nerves (Pareyson, 2004). This neuropathy is usually responsible for distal muscle weakness and atrophy that mainly involves intrinsic hand and foot muscles. Distal sensory loss, skeletal deformities such as pes cavus, and absent tendon reflexes are also clinical signs of HN. Finally, the disease course of HN is very slowly progressive.

Spinal muscular atrophies (SMA) and amyotrophic lateral sclerosis (ALS) are both disorders of the motor neurons located in the anterior horn of the spinal cord. SMA represents a heterogeneous group of disorders with different modes of inheritance (Wirth et al., 2006). Nevertheless, most patients are affected by the autosomal recessive form characterized by progressive weakness and atrophy in proximal muscle groups of the upper and lower limbs. The clinical course ranges
from early onset, with death before the age of two, to nearly asymptomatic, with a normal adult life characterized by only mild weakness (Wang et al., 2007). ALS is one of the most progressive NMDs, with 50% of patients dying within 3 years of onset (Mitchell & Borasio, 2007). The etiology is unknown for most ALS cases; onset is typically between the ages of 40 and 60 years. The clinical features are related to the level of motor neuron degeneration: bulbar involvement with difficulties in speech and swallowing, cervical involvement with muscle weakness in upper limbs, and lumbar involvement with muscle weakness in lower limbs (Mitchell & Borasio, 2007). Moreover, some motor neurons of the central nervous system are also involved in ALS, which typically leads to spasticity (Ashworth et al., 2006).

Although NMDs affect different parts of the motor unit, they all share progressive muscle weakness and atrophy with resulting deficits of motor function. No curative treatment allowing total motor function recovery is currently available for patients with hereditary or degenerative NMDs (Bertini et al., 2005, Foster et al., 2006, Reilly et al., 2006, Talbot, 2007). As a result, daily activities requiring the use of upper and/or lower limbs are difficult or even impossible for these patients. For instance, boys with DMD generally lose their ability to walk in early adolescence (Manzur et al., 2008), leading to dependence in daily activities such as going upstairs or taking a bath. Additionally, patients with HN may suffer weakness and atrophy of their hand muscles, which leads in this case to dependence in manual daily activities such as grasping a glass of water or cutting meat (Vinci et al., 2005). Finally, foot drop in patients with distal weakness could influence the patients’ balance and gait pattern with some consequences to the ability to step out of a bathtub or to walk outdoors on uneven floor for instance (Stackley et al., 2007).

While NMDs are accompanied by a wide variety of functional deficits, common difficulties in performing daily activities can be showed by the patients, whatever their clinical features or rate of progression, and whatever the location and the severity of the deficits. Ability to perform activities is defined as a part of the functioning of the patient (WHO, 2001). The functioning of a subject is described from a perspective of the body, the individual and society by the International Classification of Functioning, disability and Health (ICF) proposed by the World Organisation (WHO). Consequently, to put the difficulties in performing daily
activities into the context of a theoretical framework, it is important to first describe and evaluate the impact of NMDs on functioning of the patients using the ICF.

The International Classification of Functioning, Disability, and Health

In 2001, the World Health Organization (WHO) developed the International Classification of Functioning, Disability, and Health (ICF), a standard language and conceptual framework to describe an individual’s health and functioning (WHO, 2001). The ICF attempts to provide a concept of health from a biological, individual and social perspective by defining three components of functioning: (1) body functions and structures (body dimension), (2) activity (individual dimension), and participation (social dimension). Body functions refer to physiological and psychological function of the body systems, and body structures are anatomical parts of the body such as organs, limbs and their components. Activity is defined as the achievement of a task or an action important for the patient’s everyday life. Finally, participation refers to the patient’s involvement in life situations, such as taking part in social activities. Problems or difficulties a patient may have in each component are: impairments, activity limitations, and participation restrictions. These negative aspects of functioning are summarized under the umbrella term of “disability” (WHO, 2001). Impairments are defects, significant deviations or losses in body functions and structures; activity limitations refer to difficulties a patient may experience in executing activities of daily living; and participation restrictions are problems a patient may have during involvement in life situations.

The impact of NMDs on body functions and structures is quite obvious, since the NMDs are defined as disorders of the motor unit, which is itself a body structure (McDonald, 2002). The deterioration of any part of the motor unit could affect other body structures, such as limbs and their components (e.g., muscles, joints, bones,…). Moreover, NMDs can also affect several body functions (e.g., cardiac and respiratory functions). Impairments in motor function constitute the main problem in patients with NMD (McDonald, 2002). Nevertheless, the location and severity of motor impairments vary widely according to the etiology of the
disease, since the origin of the muscle weakness, its pathophysiology, and the related symptoms depend on the type of NMD (Hogrel et al., 2006). Impaired motor function principally manifests by muscle weakness and atrophy. However, some other impairments such as diminution in mobility (e.g., active and passive range of motion), skeletal deformities (e.g., scoliosis), a decrease in respiratory functions, or sensory impairment by virtue of peripheral sensory nerve degeneration could also be present in patients with NMDs (Fowler et al., 1995). As these supplementary impairments are not found in every NMD, they are not studied in the present work. Nevertheless, all these impairments (weakness, loss of sensitivity, bone deformities…) could have an impact on the activity and participation in patients with NMD. Indeed, a restricted respiratory function could impede the achievement of daily activities requiring endurance or more oxygen consumption such as walking several hundred meters or walking upstairs (Simonds, 2006). A diminution of the range of motion in the shoulders for instance could hinder the achievement of large movements, required in activities such as putting on a T-shirt.

NMD can therefore limit daily activities requiring the use of upper and/or lower limbs, such as walking, going upstairs, dressing the lower and upper body, or carrying a grocery bag. The activity component refers to a patient’s ability to use his limbs in executing such daily activities (WHO, 2001), and is different from motor function. The former relates to the patient’s movements as performed with the intent of a specific activity, while the latter refers to an analytical task without a specific purpose.

Finally, NMD may also restrict the participation of the patient in familial life, work or school life, and leisure activities. For instance, a wheelchair-bound patient could face restrictions to attending some cultural or sports places, participating in home maintenance or having relationships with peers outside his/her family unit.

Figure 1 summarizes the impact of NMD on a patient’s functioning in terms of body, individual and social components. The ICF also illustrates the dynamic interactions between each of these components. However, these interactions are specific and not always straightforward. For instance, two patients with the same level of impairments will not necessarily have the same level of...
Figure 1: Impact of neuromuscular disorders on patient motor functioning, according to the ICF dimensions (adapted from WHO, 2001).
activity or participation. Indeed, patients with muscle weakness can develop compensatory strategies that allow them to complete daily activities or participate in social life. Likewise, patients with normal muscle strength could be limited in the achievement of daily activities because of a lack of muscle endurance or pain. Overall, the functioning of the three components is an interaction between the health condition and contextual factors that represent the complete background of the patient’s life (WHO, 2001). The contextual factors include environmental and personal factors that could have a positive or a negative influence on achievement of daily activities, on performance as a member of society, and on body functions and structure (Law, 1993; Schneider et al., 2003). Environmental factors are external to patients and constitute the physical and social environment in which the patients live. They represent the immediate environment of the patients, such as home, workplace or school settings (e.g., family, colleagues, and physical and material features of the environment), but also the social structures, services and systems in the society (e.g., nursing at home services, social security, and transportation services). Personal factors include features such as gender, lifestyle, age, motivation, and personality. For instance, the use of assistive devices may reduce activity limitations, or inaccessible buildings may restrict the patient’s participation in social and cultural life (WHO, 2001).

To infer activity limitations from one or more impairments, or participation restrictions from activity limitations, often seems consistent. However, it is important to evaluate each component separately and thereafter examine potential relations and causal links between them. Motor impairments are often assessed and studied in patients with NMDs by using muscle strength measures (Brooke et al., 1981; Haigh et al., 2001); meanwhile, few instruments are available to measure daily activities and social participation in patients with NMD. Nevertheless, a relevant and useful measurement instrument should present good psychometric qualities (Herndon, 1997). Basic psychometric qualities include reliability, validity, responsiveness, unidimensionality, and linearity. Reliability is a property that describes how consistent the instrument is (Frisbie, 1989) and how reproducible the scores are. An individual whose condition has not changed should receive the same score by different examiners (inter-rater reliability) or by the same examiner (intra-rater reliability). In the case of self-reporting scales, the same patient should also
provide the same responses twice (test-retest reliability). Validity is defined as the ability of an instrument to actually measure what it purports to measure (Messick, 1989). The content of the instrument (e.g., items, scoring procedure, etc.) usually relies on expert judgments (content validity). The results of the instrument should be coincide with results of another relevant test (concurrent validity), or, in the absence of a gold standard, the results should be associated with a widely used test that is theoretically related (construct validity). As for responsiveness, the instrument should detect important changes over time, even at some minimal threshold (De Bruin et al., 1997). A measurement instrument is unidimensional when it measures only one variable without being influenced by other factors (e.g., gender, language community or type of NMD) or itself influencing the measurement (Bond & Fox, 2001, Wright & Linacre, 1989). Finally, an instrument is linear when the measurement unit is constant throughout the scale, so that intervals between two graduations represent the same amount of a variable (Wright & Linacre, 1989).

The first objective of this present work is therefore to develop a scale of activity limitations with good psychometric qualities in patients with NMDs. This scale will be a common measure of activity limitations in all patients with NMDs. Indeed, as previously mentioned, the NMDs share several deficits such as progressive muscle weakness and atrophy with resulting difficulties in performing daily activities. The measure of activity limitations should represent a common variable to all patients with NMDs allowing quantitative comparisons between different diagnosis groups in terms of activity limitations or simply allowing the use of a single scale to follow patients in neuromuscular centres. Moreover, as NMD are of a degenerative nature, this scale will be common to children and adults in order to follow the patients from childhood to adulthood. Nevertheless, assessing children with DMD and adults with HN on a common scale could be quite unusual for clinicians. To achieve this objective, the concept of unidimensionality will play a key role on the scale development. Indeed, if the unidimensionality is respected, the measure obtained on the developed scale will be not influenced by factors external to the variable itself such as the type of NMD or the age of the patient. Consequently, the questionnaire development study will insist on the unidimensionality of the scale but the other psychometric qualities will be also verified.
**Measurement of activity limitations**

The measurement of activity limitations in patients with NMD can be considered as a priority since most patients report difficulties in daily life (McDonald, 2002) and since the measurement of motor impairments cannot precisely predict their functional abilities (Merkies et al., 2003, Arnould et al., 2007). Systematic evaluation could optimize health care of patients with NMD. First, it could quantify the residual abilities of the patient at the beginning of his/her follow-up, define the treatment objectives and follow the evolution of the patient’s condition. Second, the evaluation provides information to clinicians about the treatment effectiveness in order to adjust and optimize the patient’s rehabilitation and to compare different treatments.

Activity limitations are rarely assessed directly, in the manner of physical variables (e.g., height or weight), but are instead measured indirectly by how they manifest (Hobart et al., 2007). Such a characteristic is referred to as a “latent” variable in the same sense as pain, quality of life, or depression (Thurstone, 1959, Rasch, 1980, Tesio et al., 2007a). Typically, activity limitations are measured by item questionnaires which are usually accepted to measure the behaviors (also named items) expected to be representative of the property itself or the variable to be assessed (Merbitz et al, 1989). These questionnaires could assessed different aspects of activity limitations such as qualitative observations on the patient’s performance, the time required to perform a daily activity, the level of dependence to these activities or the perceived difficulty in performing daily activities reported by the patient himself/herself (self-reported questionnaire) or reported by a proxy (proxy-reported questionnaire). Each of these administration methods of activity limitations presents advantages and drawbacks (Kivinen et al., 1998, Ferrer et al., 1999, Owens et al., 2002). In the present study, the perceived difficulty self-reported by the patients was preferred to the other ways of measurement because it offers the benefit of being inexpensive and easy to administer, and it informs clinicians on how well patients manage in their home environments (Owens et al, 2002). Moreover, self-report is the perception of the patient himself/herself of his/her own abilities in his/her daily across a period of time and is not influenced by the emotional state or the general state of form at the time of the evaluation, which could be the case in
Activity limitations in patients with neuromuscular disorder observational methods (Ferrer et al., 1999). However, to validate the use of a self-reported questionnaire to assess activity limitations in patients with NMD, the patients’ self-perceptions of their difficulties will be compared with external examiners’ observations of the patients’ performances. This study will constitute a second objective of the present work.

Activity limitations are often evaluated by different numbers of items and response categories, according to the questionnaire used (Coster et al., 2004). Nevertheless, whatever the response format used, a numerical value is assigned to each response so that a higher number represents a higher level of the variable (e.g., in the dichotomous response format: 0 = impossible, 1 = possible; in the polytomous response format: 0 = impossible, 1 = with much difficulty, 2 = difficult, 3 = with few difficulties, 4 = easy). Typically, the scores for each item are summed, generating a total score that quantifies the variables of an individual (Thurstone, 1959, Hobart et al., 2007, Tesio et al., 2007a). Using such total scores to compute mathematical or statistical operations have some limitations and could lead to a misinterpretation of the results (Merbitz et al., 1989, Wright & Linacre, 1989, Wright & Young, 1997). First, the numbers assigned to response categories of polytomous items represent an ordinal scale because two successive categories are separated by unknown distances (Merbitz et al., 1989, Wright & Linacre, 1989, Stevens, 1946). For instance, consider a questionnaire measuring activity limitations on a five-level response scale: impossible (0), with much difficulty (1), difficult (2), with few difficulties (3) and easy (4). Is the distance between impossible (0) and with much difficulty (1) identical to the distance between with few difficulties (3) and easy (4) while in terms of number, the distance is equal to one point in both cases? The distance between impossible (0) and difficult (2) is greater than between difficult (2) and with few difficulties (3), but does it represent twice as much distance? The scores can therefore be compared as “higher than” or “lower than,” but no information can be given on “how much higher” or “how much lower.” Second, there is no reason why an individual having the same score for different items should represent the same “amount” of the latent variable (Bond & Fox, 2001, Penta et al., 2005, Tesio et al., 2007a). For example, a patient with a score of “easy” for “walking upstairs” has intuitively fewer activity limitations than a patient responding “easy” for “washing one’s hands.” Finally, some questionnaires measure more than one variable. Indeed,
it often appears that a multidimensional questionnaire reports information about different aspects of the patient without omitting important characteristics (Tesio, 2007b). Therefore, clinicians using multidimensional questionnaires may feel that an overall view of the patients’ functional status has been assessed (Wolfe, 2002). The most representative example is the Functional Independence Measure (Hamilton et al., 1994). This questionnaire comprises 18 items divided in two dimensions assessed on a 7-level scale. The motor sub-scale includes 13 items, while the cognitive sub-scale includes five items. Problems with such questionnaires lie in the fact that the total score refers to more than one attribute of the subject. For instance, a total score of 108 out of 126 could have different interpretations: the subject could present moderate motor independence (73/91) with high cognitive independence (35/35) or high motor independence (91/91) with moderate cognitive independence (17/35). The limitations of the questionnaires concerning the raw scores and the multiple assessed variables are related to the psychometric qualities defined as linearity and unidimensionality, and none of the instruments assessing activity limitations in patients with NMD possesses both these qualities.

Scales measuring activity limitations in patients with NMD are often disease-specific ([no author], 1996, Steffensen et al., 2001, Merkies et al., 2002, Lue et al., 2006) or evaluate patient limb function on a single grade (e.g., Vignos or Brooke grades (Brooke et al., 1981)). Moreover, no scale has been developed to follow the patients’ evolution from childhood to adulthood. It was therefore deemed necessary to develop a new scale with good psychometric qualities to quantify activity limitations in adults and children with NMD. Reliability, validity and responsiveness are rather easy to test, whereas linearity and unidimensionality require other methodological considerations. The Rasch model, however, provides a solution to transform ordinal scores into linear measures and to verify unidimensionality of the items (Rasch, 1980).

**The Rasch model**

The Rasch model belongs to the family of “Item Response Theory” (IRT) models which were developed to overcome the limitations of ordinal scales described above (Hambleton et al., 1991, Bertrand & Blais, 2004, Hobart et al.,
2007). They are based on the assumption that patients with a higher level of activity should have a higher probability, relative to patients with a lower activity level, to successfully achieve any item. The Rasch model is a probabilistic approach developed by the Danish mathematician George Rasch in the 1960’s and is now successfully and widely used in health and human sciences (Conrad & Smith, 2004). The model states that the probability to pass a given item only depends on the item difficulty and the subject ability, and it estimates the item difficulty and subject ability from the proportion of responses to each item on a common linear scale (Rasch, 1980). The latent variable activity limitations can actually be conceptualized as a continuum representing infinite activity levels from “less active” to “most active.” Measuring a patient’s activity limitations involves determining the patient location along this continuum. The items of a questionnaire are the graduations of the scale, and therefore, they must cover the whole range of activity limitations assessed in the studied population.

Figure 2: Activity continuum. Arrows represent patient (upper arrows) and item (lower arrows) location on the activity continuum.

Figure 2 represents the activity continuum along which the patients are located from less active to most active and the items from easiest to most difficult. An item is considered easy if many patients pass the item, while an item is considered difficult when few patients pass the item. Similarly, a patient has a high level of activity if he/she passes many items, and a patient has a low level of activity if he/she fails many items. As illustrated in Figure 2, Patient A has a low activity

Activity limitations in patients with neuromuscular disorders
level since his/her activity level is high enough just to pass the first item; Patient B has a moderate level of activity and is expected to successfully perform the two easiest items; and Patient C has a high activity level and can likely succeed in all items except the most difficult one. As this figure principally applies to a dichotomous response format (i.e., able/unable to achieve the daily activity), other Rasch models have been developed for polytomous response formats also called “rating scales” (e.g., impossible/difficult/easy) (Andrich, 1978a, Andrich, 1978b, Masters, 1982). These models state that the probability of giving any response category to an item only depends on the patient’s ability, item difficulty, and threshold difficulties. Thresholds ($\tau$), located between two adjacent response categories, correspond to the activity levels needed for the patient to have a higher probability of selecting a particular response category rather than the next lower one.

In a polytomous response format (Figure 3) where activities can be answered on a three-level scale (impossible/difficult/easy), the thresholds between successive response categories are the graduations of the scale. Therefore, patients located beneath the first threshold are most likely to be unable to accomplish the activity; patients with an activity level located between the two thresholds are expected to perform the activity with difficulty; and patients located after the second threshold are most likely to complete the activity easily.

![Figure 3: Polytomous response format. The graduations of the activity continuum are represented by the item thresholds (lower arrows). The first threshold ($\tau_1$) corresponds to the activity level required to respond “difficult” rather than “impossible,” while the second threshold ($\tau_2$) is located at the activity level required to respond “easy” rather than “difficult.” Item difficulty (tick; $\delta$) is simply the average value of its thresholds.](image-url)
If three response categories give the scale two graduations per item, it is tempting to construct questionnaires with numerous response categories for each item. Indeed, if the continuum is divided into more parts, the measurement precision, sensitivity to change, and reliability would be expected to be improved (Tesio, 2003, Cano et al., 2006, Decruynaere, 2007, Hobart et al., 2007). Nevertheless, too many response categories could cause confusion in the respondents’ minds, thereby decreasing measurement precision instead of improving it. The Rasch model also offers the ability to verify the category functioning or, in other words, to determine how well all response categories are discriminated by the patients. Successive response categories for each item should represent increasing levels of activity. For instance, a patient performing an activity with difficulty should respond with a lower level of activity than a patient performing the same activity easily. The Rasch model investigates the category functioning by verifying whether thresholds between adjacent categories are located at increasing levels of activity (Andrich, 1996). Different studies have already demonstrated that patients can hardly discriminate among more than three response categories for assessing ability to perform daily activities (Penta et al., 2001, Arnould et al., 2004).

Rasch analysis can be also used to verify how the items contribute to the definition of the unidimensional activity construct (Bond & Fox, 2001). Unidimensionality of an instrument is met when it measures only one variable without being influenced by other factors (e.g., gender, language community or type of NMD) (Wright & Linacre, 1989, Bond & Fox, 2001). In the case of latent variables, the theoretical concept of unidimensionality is never totally met in practice, since the separation of one trait from the others is extremely difficult (Andrich, 1988). However, approximating this ideal in the observed data is required if subjects must be quantitatively compared on the same attribute (e.g., activity limitations) (Wright & Linacre, 1989). The unidimensionality is tested by comparing the observed responses to an item with the expected responses predicted by the model. The degree of similitude between both responses is computed through the fit statistic reported by the different softwares proposed for Rasch analysis (Wright & Stone, 1979, Wright & Masters, 1982, Bond & Fox, 2001). Statistics determine how closely the items define the underlying construct and detect items that do not contribute to the definition of the unidimensional variable.
A part of the unidimensionality can also be verified by the invariance of scale among different subgroups of patients (Smith, 1992). No sample characteristic such as gender, type of NMD, or language community for instance should systematically influence responses to any item. The lack of invariance is called “item bias” or “differential item functioning” (DIF) (Smith, 1992). A DIF may induce a systematic misfit to a common scale calibrated for all subjects, and therefore constitute a threat to the invariant use of the same scale for all subjects. The use of the Rasch model allows a common scale for all patients with NMD to be developed by verifying the DIF among diagnosis group and by indentifying items presenting such bias.

As for linearity, the Rasch model uses a logistic relation to transform the ordinal total score into linear measures of latent variables (e.g., activity limitations). The linear measures are expressed in logits (i.e., log-odds units), a measurement unit defined as the natural logarithm of the odds of successful achievement by a patient for any item. This unit is constant along the measurement scale in such a way that the measures of different patients can therefore be quantitatively compared and treated as a continuous variable.

In the present work, the Rasch model will be used for: (1) scale development, by investigating response-category functioning, item unidimensionality, and item invariance across several person-related factors; (2) for transforming ordinal total scores into linear measures in studies using the developed scale as outcome measure, and (3) for verifying if the patients’ measure of new studied samples fit the model. However, the Rasch model has other measurement applications in health and human sciences. It can be useful for adjusting or optimizing existing scales in terms of category functioning or item unidimensionality, for validating scales across different cultures, and for developing item-banking or computer-adaptive testing.

**Specific purposes of the study**

Assessment in patients with NMD consists principally of measures of motor impairment (Brooke et al., 1981, Haigh et al., 2001), since they are well
known by clinicians and their measures do not require much equipment. The conventional treatments in patients with NMD are above-all focused on the diminution of motor impairments by maintaining or improving joint mobility, muscle strength and endurance (Hornyak & Pangilinan, 2007). Nevertheless, a reduction of motor impairments does not directly lead to a higher ability in performing daily activities (Merkies et al., 2003, Arnould et al., 2007). Therefore, activity limitations should be measured specifically. A new scale of activity limitations was first developed in children and adults with NMD. The use of the Rasch model provided a scale to assess the fundamental psychometric qualities. Secondly, relationships between motor impairments and activity limitations were investigated to verify the assumption that reduced motor impairments do not necessarily lead to higher activity levels. Finally, to complete the investigation of psychometric qualities, a longitudinal study of the developed questionnaire was carried out to evaluate its sensitivity to change.

Chapter 1 presents the development of ACTIVLIM, a Rasch-built measure of activity limitations and its validation in children and adults with NMD. ACTIVLIM is a self-reported questionnaire that assesses the difficulties adult patients and parents of affected children perceive when they or their children perform daily activities. This questionnaire originally included 126 daily activities and was submitted to 369 patients. The Rasch model selected 22 daily activities to define a linear and unidimensional measure of activity limitations in patients with NMD. The validity and the reproducibility of the results were also studied. The development and the validation of ACTIVLIM are presented as published in Neuromuscular Disorders. A second section of Chapter 1 demonstrates why the measure of activity limitations in children with NMD as assessed using the ACTIVLIM questionnaire is based upon the perception of their parents. A third section of Chapter 1 compares the difficulties self-perceived by the patients with the difficulties observed by external examiners. The agreement between both measures is very good, indicating that the use of ACTIVLIM as a self-reporting questionnaire is a valid method to assess activity limitations in patients with NMD. This section is presented as accepted for publication in Archives of Physical Medicine and Rehabilitation.
Chapter 2 investigates the relationships between motor impairments and activity limitations as measured with the ACTIVLIM questionnaire. As the anatomical basis and pathophysiology are different from one NMD to another, the relationships between impairments and activity limitations were investigated in six main diagnostic groups and in the whole sample without diagnostic distinction. Gait speed and muscle weakness in proximal and flexor muscle groups were significantly but moderately correlated to the activity limitations, indicating that the latter cannot simply be inferred from motor impairments but should be independently measured and treated. These results are presented as a modified version of the article submitted for publication to the Journal of Neurology, Neurosurgery and Psychiatry.

Chapter 3 investigates the sensitivity to change of the ACTIVLIM questionnaire. As NMD are progressive disorders, it is important that the ACTIVLIM questionnaire be able to assess the change over time in the activity level of patients with NMD in order to characterize the disease course and to quantify the effects of new treatments on activity limitations in these patients. This chapter is presented as a modified version of the article submitted for publication in Neuromuscular Disorders.

Finally, the last section discusses the results of the different chapters and presents perspectives for future research.
Chapter 1

ACTIVLIM: A Rasch-built measure of activity limitations in children and adults with neuromuscular disorders

1.1. DEVELOPMENT AND VALIDATION OF THE ACTIVLIM QUESTIONNAIRE

Abstract
A common measure of activity limitations for both children and adults with neuromuscular disorders was developed using the Rasch model. A self-reported questionnaire containing daily activities was submitted to 245 adult patients and to the parents of 124 affected children from the two major Belgian communities. They were asked to provide their perceived difficulty in performing daily activities on a three-level scale. The 22 items of the final scale define a unidimensional and linear measure of activity limitations and show a continuous progression in their difficulty. The item difficulty hierarchy is invariant with regard to the diagnosis, community, gender and age. The scale exhibits a good precision, since the 22 items are well targeted on our sample (r=0.96); furthermore, it is reproducible over time (ICC=0.93). The patients’ measures are related to the Functional Independence Measure motor score (ρ=0.85), to the Brooke (ρ=0.63) grade and to the Vignos (ρ=0.83) grade.

Published as:
1.1.1. **Introduction**

Most neuromuscular disorders (NMD) have a progressive clinical course that is characterized by a decrease of muscle strength (Piccininni et al., 2004) leading to an impaired motor function. Some consequences are fatigue, problems with locomotion and loss of functionality in activities of daily living. The International Classification of Functioning, Disability and Health (ICF) describes an individual’s functioning in three domains taking into account his health condition (WHO, 2001). These domains are (1) body functions and anatomical structures, (2) activity, and (3) participation. Problems in each domain are, respectively, impairments, activity limitations, and participation restrictions. In NMD patients, impairments such as muscle weakness are frequently assessed using quantitative or manual testing (Brooke et al., 1981, Haigh et al., 2001). However, the evaluation of the functional abilities of patients can be also considered as a priority. These could be assessed from the level of *activity limitations* defined as the difficulties a patient may have in executing daily activities (WHO, 2001). The achievement of daily activities depends on the muscle strength, but the relationship between the two is not straightforward (Merkies et al., 2003). It is a combination of motor function, compensatory behaviour of the patient, and personal (e.g. age, lifestyle, motivation) and environmental (e.g. architectural characteristics, ground type) factors. For these reasons, the activity level should be evaluated separately and not simply inferred from the patients’ impairments.

Instruments specifically applicable to the population being studied are essential for clinical evaluation (Wade, 1992), and a common scale for both children and adults makes it possible to follow patient status across time. The existing scales measure the functional status of NMD patients, either in a restrictive and general way, with a description of patients’ limb function on a single grade (e.g., Vignos or Brooke grades (Brooke et al., 1981) or they don’t measure the activity limitations themselves. The Functional Independence Measure (Linacre et al., 1994) takes into account technical or human assistance and gives a measure of the patients’ autonomy. A motor function measure was recently developed and validated for NMD paediatric and adult patients (Berard et al., 2005). This scale proposes a motor measure focused on the observation of analytical tasks achieved by the patients. The
time wasted for observation could be reduced by self-reported measures, especially since observed functional abilities are not psychometrically superior or easier to administer than reported measures (Myers et al., 1993). Self-reported measures in adult patients are usually considered the gold standard (Sprangers & Aaronson, 1992). In child functional assessment, parents are valid proxies since they report a finer perception of their children’s abilities than the children themselves do (Chambers & Johnston, 2002, Arnould et al., 2004). The purpose of the study is to develop ACTIVLIM, a self-reported questionnaire of activity limitations in children and adults with any NMD by submitting it to the adult patients and to the parents of the affected children.

1.1.2. Patients and Methods

1.1.2.1. Patients

This multicentric study was approved by the medical ethics committees of the Université catholique de Louvain and of the Katholieke Universiteit Leuven. The patients were recruited through the neuromuscular reference centres of two university hospitals, each in a different Belgian language community (Dutch and French). Moreover, 10 percent of the children came from three centres specializing in NMD. Adult patients and parents of affected children gave written informed consent before the evaluation.

Age, gender, language community, type of NMD, Functional Independence Measure motor score (Linacre et al., 1994), and Vignos & Brooke Grades (Brooke et al., 1981) were included as independent demographic and clinical indices in the validation analysis. Three hundred and sixty-nine patients (124 children and 245 adults) with a diagnosis of neuromuscular disorder were assessed by the same examiner. Sample description is given in table 1.
Table 1: Patient sample description (n=369)

<table>
<thead>
<tr>
<th></th>
<th>Adults (n=245)</th>
<th>Children (n=124)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male, %</td>
<td>56</td>
<td>68</td>
</tr>
<tr>
<td>female, %</td>
<td>44</td>
<td>32</td>
</tr>
<tr>
<td><strong>Age, years: mean (range)</strong></td>
<td>47 (16-80)</td>
<td>10 (6-16)</td>
</tr>
<tr>
<td><strong>Spoken language</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dutch, %</td>
<td>42</td>
<td>64</td>
</tr>
<tr>
<td>French, %</td>
<td>58</td>
<td>36</td>
</tr>
<tr>
<td><strong>Diagnosis</strong>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DMD/BMD* or LGMD, %</td>
<td>15</td>
<td>38</td>
</tr>
<tr>
<td>HN, %</td>
<td>16</td>
<td>28</td>
</tr>
<tr>
<td>MD, %</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>ALS, %</td>
<td>9.5</td>
<td></td>
</tr>
<tr>
<td>SMA, %</td>
<td>5.5</td>
<td>11</td>
</tr>
<tr>
<td>FSHD, %</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Others (e.g. CM, CMD, PPS,...), %</td>
<td>32</td>
<td>23</td>
</tr>
<tr>
<td><strong>Mobility level</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking, %</td>
<td>70</td>
<td>66</td>
</tr>
<tr>
<td>Wheelchair, %</td>
<td>30</td>
<td>34</td>
</tr>
<tr>
<td><strong>FIM</strong>**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor score, median (range)</td>
<td>80 (25-91)</td>
<td>81 (31-91)</td>
</tr>
<tr>
<td><strong>Physical therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No, %</td>
<td>34</td>
<td>11</td>
</tr>
<tr>
<td>Yes, %</td>
<td>64</td>
<td>89</td>
</tr>
</tbody>
</table>


** FIM = Functional Independence Measure

1.1.2.2. Questionnaire development

The ACTIVLIM questionnaire was designed to cover the widest range of daily activities and it included activities for children and for adults. The preliminary questionnaire included 138 items selected from various existing scales: ABILHAND (Penta et al., 1998, Penta et al., 2001), ABILHAND-Kids (Arnould et al., 2004), Physical Functioning Subscale of SF-36 (Ware & Sherbourne, 1992), Sickness Impact Profile (Bergner et al., 1981), Amyotrophic Lateral Sclerosis Functional Rating Scale (1996), ADL Self-Report (Ahlstrom & Gunnarsson, 1996), Paediatric Quality of Life Inventory (Varni et al., 1999), Lower Extremity Functional Scale (Binkley et al., 1999), EK Scale (Steffensen et al., 2001), and Level of
Rehabilitation Scale III (Velozo et al., 1995). These items were submitted to 32 experts on patients with NMD (neurologists, physicians, physical therapists, occupational therapists, nurses and a psychologist) and to 23 NMD adult patients. The experts were asked to determine the relevance of the activities for a NMD child and for a NMD adult. The adult patients were asked to evaluate the perceived difficulty in performing each activity. Both experts and adult patients were asked to propose other relevant items not included in the original item set.

The questionnaire for adult patients was achieved by removing 52 items, either because experts considered them irrelevant (44 items), or because the analysis of the 23 adults’ responses through the Rasch model showed that they did not contribute to the definition of a unidimensional variable (8 items) (Wright & Linacre, 1989). Five items were added to the set following experts’ and patients’ suggestions. The adult patients were therefore assessed with a 91-item experimental questionnaire.

The experimental questionnaire for children included 99 items, since 39 items from the original set of 138 items were eliminated because experts considered them to be irrelevant.

1.1.2.3. Instrument

The ACTIVLIM questionnaire explored difficulties of performing daily activities that required the use of upper limbs or/and the use of lower limbs. The adult patients and the parents of affected children filled in either the adult form or the child form of the questionnaire. They were asked to provide their perceived difficulty in performing each activity using a three-level scale: impossible (0), difficult (1), easy (2). Each activity must be completed without technical or human assistance. Activities unfamiliar to individual patients were recorded as missing responses (2.2 % of the data).
1.1.2.4. Procedure

A French or a Dutch version of the questionnaire was presented to patients. The questionnaires were self-completed by the adults or by the parents of the affected children either during their multidisciplinary consultation at the Neuromuscular Centres or in the specialized centres for NMD children. The items were randomly presented to avoid an effect caused by the item order. Two hundred and twenty-seven patients were assessed a second time three weeks after the first evaluation in order to investigate the test-retest reliability of the scale.

1.1.2.5. Data Analysis

To calibrate a common scale for both children and adults with NMD, responses of the parents and those of adult patients should form a single matrix. From the 91-item questionnaire for adult patients and from the 99-item questionnaire for children, 64 items were identical in both questionnaires. The remaining 27 items specifically designed for adults (91 items – 64 items) were recorded as a missing response in the data of the parents of the affected children. Similarly, the 35 specific items for children (99 items – 64 items) were recorded as a missing response in the data of the adult patients. The final data matrix therefore included 126 items (64 common, 35 children specific and 27 adult specific items) that were analysed with the Rasch Unidimensional Measurement Models computer program (RUMM2020, RUMM Laboratory Pty Ltd, Perth, Western Australia).

Since the number of adults involved in the study was twice as large as the number of children, the responses of the adult patients could have a significant effect on the scale calibration. To remedy this problem, the adult sample was divided into two equal stratified samples. Responses of the first adult sample were analysed with the responses of the parents in order to calibrate the ACTIVLIM scale (sample-1).

Stratified adult samples (sample-1 and sample-2) were formed in such a way that they include the same proportions of patients as the total adult sample according to their principal characteristics (gender, language community, diagnosis and age) (see Table 1). Both samples are therefore equivalent to the original sample in terms of proportion men/women, Dutch/French speakers and types of NMDs and in terms of mean age. This strategy allows the calibration of sample-2 to be compared to the calibration of sample-1 since bias due to the composition of the samples should be avoided.
Analysis of responses of the second adult sample with those of the parents was useful for validating the scale (sample-2).

1.1.2.6. The Rasch model

The Rasch model estimates the item difficulty and the patient activity level on a common linear scale (Merbitz et al., 1989, Wright & Linacre, 1989) from the responses given to each item within a probabilistic framework (Rasch, 1980). This model is used to investigate response category functioning, scale unidimensionality, patient targeting and scale reliability (Smith et al., 2002). The category functioning is studied by verifying that successive response categories for each item represent increasing levels of activity and that thresholds between adjacent categories are located in the expected order. The thresholds correspond to the activity levels required to have a higher probability to select a category rather than the previous one. The Rasch model also makes it possible to verify that all items contribute to the definition of the unidimensional activity construct (Bond & Fox, 2001). To test unidimensionality, the sample is divided along the variable into level groups called class intervals. For each item, the degree of similitude between the observed responses in each class interval and the expected responses predicted by the model is computed through a standardized residual and a Chi-square fit statistic reported by the software (Wright & Masters, 1982). The standardized residual of an item corresponds to the sum of the differences between the observed and the expected scores over each class interval, divided by the standard deviation of the differences. It is sensitive to item discrimination. Positive values represent an under-discrimination of the item; whereas negative values represent an over-discrimination of the item. The Chi-square fit statistic represents the deviations from the model expectations. The targeting is checked by comparing the mean patient location to the mean item difficulty. The software also reports the reliability that indicates the level of measurement precision attained.
1.1.2.7. Item selection

Starting from the 126 experimental items, indices reported from successive analyses were used to select the items that constituted the final ACTIVLIM scale. If an item did not present the following criteria, it was removed from the experimental set.

a) An ordered rating scale

Adults and parents were asked to provide their perceived difficulty on a three-level response scale: impossible (0), difficult (1) or easy (2). The thresholds between adjacent categories should be located in an increasing order, indicating that categories were well discriminated. When the thresholds were reversed, the rating scale did not function as expected. Any item presenting disordered thresholds was deleted.

b) The response categories have the same discrimination across all items

To apply a rating scale model to the data and thus to make the clinical interpretation of the scores easier, each response category must be discriminated in the same way through all items (Wright, 1999, Linacre, 2000). Items presenting discrimination significantly different from the average (Z-test) were removed. Moreover, the discrimination of the categories was compared between the adults and the parents of the affected children using a t-test.

c) All items fit a unidimensional scale

Fit statistics (standardized residual and Chi-square statistic) were used to detect items that did not contribute to the definition of a unidimensional variable. Items were deleted when they presented values below -2.5 or above 2.5 for the standardized residuals (Andrich & Sheridan, 2005) or when their p-value of the Chi-square statistic was below 0.05.
d) No item presents a differential item functioning (DIF)

The invariance of item difficulty hierarchy was checked with regard to 4 dichotomous patient-related factors: gender (male or female), patient category (child or adult), language community (Dutch or French speaker) and type of NMD (proximal or distal NMD). A DIF can be detected by a two-way analysis of variance for each item by comparing scores across each level of patient-related factor and across levels of the activity construct, i.e. the class intervals (Pallant & Tennant, 2007). A significant main effect for the patient-related factor shows the presence of a uniform DIF; whereas a non-uniform DIF corresponds to a significant interaction effect (patient-related factor x class interval). Items that present a uniform or/and a non-uniform DIF were removed.

e) No redundancy in item location

Since each response category is discriminated in the same way through the items, the two thresholds of the items are equidistant. The thresholds of two items with the same difficulty will therefore have the same location along the variable without increasing the scale reliability. When items were redundant, one of them was deleted, preferably keeping items common to adults and children.

1.1.2.8. Scale validity

A Rasch analysis with sample-2 responses on the selected activities made it possible to validate item difficulty hierarchy and scale psychometric properties. A comparison of item hierarchy between sample-1 and sample-2 was carried out using a DIF test (Wright & Stone, 1979). Secondly, the construct validity was tested by examining the degree of association between the ACTIVLIM measures of patients and the widely used scales (Merkies et al., 2002): Functional Independence Measure motor score, Vignos and Brooke grades. Moreover, relationships between measures of patients and demographic (age, gender, community) and clinical (type of NMD) indices were studied to examine consistency with plausible hypotheses (Engelberg et al., 1996). A correlation coefficient was computed for continuous indices and a one-
way analysis of variance for groups of nominal indices. Analyses were performed with the SigmaStat© software.

1.1.2.9. Scale reliability

A reliability index was determined as the proportion of observed measure variance attributable to the true measure variance (Traub & Rowley, 1991). Moreover, the test-retest reliability of the adults’ and the parents’ responses was determined by the intraclass correlation coefficient (Shrout & Fleiss, 1979). A DIF test was carried out to verify the invariance of item difficulty hierarchy across the first and the second assessment.

1.1.3. Results

1.1.3.1. Refinements of the ACTIVLIM scale for NMD children and adults

The successive analyses through the Rasch model selected 22 items from the original 126-item set. Seven items presented reversed thresholds, 14 items had a different discrimination of the response categories, 49 items did not contribute to the definition of the unidimensional construct, 22 items showed a uniform or a non-uniform DIF (2 items with regard to the gender patient-related factor, 9 for the patient category, 4 for the language community and 7 items for the type of NMD) and 12 items were redundant. Moreover, the discrimination of the categories was not significantly different in adults and children’s parents \((t = 0.179, p = 0.86)\). The final ACTIVLIM scale contains 14 common activities, 4 specific activities for children, and 4 specific activities for adults (table 2).

1.1.3.2. Psychometric properties of the ACTIVLIM scale in NMD children and adults

The calibration of the final 22-item ACTIVLIM scale is presented in table 2. The items are classed in decreasing difficulty order from top to bottom (range: 3.57 to -3.33 logits), with higher logit values representing more difficult items. The
activity measure is expressed in logits (i.e. log-odds units), a linear unit defined as the natural logarithm of the odds of successful achievement by a patient for any item. This unit is constant along the measurement scale and the zero of the scale is set by convention at the average difficulty of the whole selected item set. The table also shows the standard error (SE) of the item difficulty estimates (mean: 0.17, range: 0.13 to 0.26), the standard residual (mean: -0.57, range: -1.86 to 0.54), the fit statistic computed as a chi-square and the associated p-value. All 22 items define a unidimensional scale of activity limitations in NMD patients since p-values do not show a significant difference between observed and expected scores. The reliability index of the final scale is equal to 0.96, indicating that 7 groups of activity levels can be statistically distinguished within the patient sample (Fisher, 1992).

Table 2: Activity scale calibration for adults and children with neuromuscular disorders

<table>
<thead>
<tr>
<th>Items*</th>
<th>Difficulty (logits)</th>
<th>SE (logits)</th>
<th>Residual (z)</th>
<th>Fit ($\chi^2$)</th>
<th>degrees of freedom**</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Hopping on one foot</td>
<td>C</td>
<td>3.57</td>
<td>0.23</td>
<td>0.96</td>
<td>6.20</td>
<td>4</td>
</tr>
<tr>
<td>b. Carrying a heavy load</td>
<td>A</td>
<td>3.03</td>
<td>0.20</td>
<td>-0.43</td>
<td>1.79</td>
<td>4</td>
</tr>
<tr>
<td>c. Running</td>
<td>C</td>
<td>2.78</td>
<td>0.21</td>
<td>-0.56</td>
<td>0.52</td>
<td>4</td>
</tr>
<tr>
<td>d. Walking more than 1 KM</td>
<td>A</td>
<td>2.29</td>
<td>0.18</td>
<td>-0.61</td>
<td>4.17</td>
<td>4</td>
</tr>
<tr>
<td>e. Walking upstairs</td>
<td>B</td>
<td>1.47</td>
<td>0.13</td>
<td>-1.86</td>
<td>10.11</td>
<td>9</td>
</tr>
<tr>
<td>f. Standing for a long time</td>
<td>A</td>
<td>1.30</td>
<td>0.18</td>
<td>0.41</td>
<td>0.72</td>
<td>4</td>
</tr>
<tr>
<td>g. Stepping out of a bath tub</td>
<td>B</td>
<td>1.18</td>
<td>0.14</td>
<td>-0.61</td>
<td>9.01</td>
<td>9</td>
</tr>
<tr>
<td>h. Walking downstairs</td>
<td>B</td>
<td>1.03</td>
<td>0.13</td>
<td>-1.50</td>
<td>3.07</td>
<td>9</td>
</tr>
<tr>
<td>i. Taking a bath</td>
<td>B</td>
<td>0.27</td>
<td>0.14</td>
<td>-1.02</td>
<td>10.39</td>
<td>9</td>
</tr>
<tr>
<td>j. Putting on a backpack</td>
<td>C</td>
<td>0.04</td>
<td>0.21</td>
<td>-0.92</td>
<td>5.12</td>
<td>4</td>
</tr>
<tr>
<td>k. Dressing one's lower body</td>
<td>B</td>
<td>-0.23</td>
<td>0.14</td>
<td>-1.19</td>
<td>7.47</td>
<td>9</td>
</tr>
<tr>
<td>l. Walking outdoors on level ground</td>
<td>B</td>
<td>-0.26</td>
<td>0.14</td>
<td>-1.10</td>
<td>10.45</td>
<td>9</td>
</tr>
<tr>
<td>m. Getting into a car</td>
<td>A</td>
<td>-0.33</td>
<td>0.19</td>
<td>-1.13</td>
<td>5.23</td>
<td>4</td>
</tr>
<tr>
<td>n. Taking a shower</td>
<td>B</td>
<td>-0.45</td>
<td>0.15</td>
<td>-1.10</td>
<td>10.84</td>
<td>9</td>
</tr>
<tr>
<td>o. Wiping one's upper body</td>
<td>B</td>
<td>-0.86</td>
<td>0.15</td>
<td>0.77</td>
<td>8.53</td>
<td>9</td>
</tr>
<tr>
<td>p. Putting on a T-shirt</td>
<td>B</td>
<td>-1.19</td>
<td>0.16</td>
<td>-0.12</td>
<td>7.10</td>
<td>9</td>
</tr>
<tr>
<td>q. Hanging a jacket on a hatstand</td>
<td>B</td>
<td>-1.28</td>
<td>0.16</td>
<td>-0.48</td>
<td>3.62</td>
<td>9</td>
</tr>
<tr>
<td>r. Sitting on the toilet</td>
<td>B</td>
<td>-1.49</td>
<td>0.16</td>
<td>-1.01</td>
<td>10.97</td>
<td>9</td>
</tr>
<tr>
<td>s. Washing one's upper body</td>
<td>B</td>
<td>-1.64</td>
<td>0.17</td>
<td>-0.45</td>
<td>14.59</td>
<td>9</td>
</tr>
<tr>
<td>t. Opening a door</td>
<td>B</td>
<td>-2.73</td>
<td>0.19</td>
<td>0.37</td>
<td>14.22</td>
<td>9</td>
</tr>
<tr>
<td>u. Closing a door</td>
<td>C</td>
<td>-3.16</td>
<td>0.26</td>
<td>-0.54</td>
<td>2.38</td>
<td>4</td>
</tr>
<tr>
<td>v. Washing one's face</td>
<td>B</td>
<td>-3.33</td>
<td>0.21</td>
<td>0.54</td>
<td>9.57</td>
<td>9</td>
</tr>
</tbody>
</table>

* A, B or C corresponds respectively to an adult, to a common or to a child activity.
** degrees of freedom are the number of class interval (CI) - 1; the specific items were composed of 5 CI while the common items were composed of 10 CI in order to balance the number of subjects per CI (+/- 23 subjects)
1.1.3.3. Item and psychometric properties validity

The Rasch analysis of the 22 final items on sample-2 responses gives identical psychometric properties: item difficulty range from 3.57 to -3.5 logits, mean SE of item difficulty estimates is equal to 0.17, all the items present a non-significant p-value for fit statistics, and the reliability index is equal to 0.96\(^2\). Moreover, the differential item functioning plot presented in Figure 1 compares the item difficulty hierarchy as estimated by the sample-1 and the sample-2. The 22 items lie within the 95% confidence interval of the identity line, indicating that the items were consistently estimated by both samples.

![Figure 1: Item difficulty hierarchy estimated by sample-1 and sample-2. Most difficult items are plotted in the upper right part of the figure. Control lines (solid lines) indicate the 95% confidence intervals of the ideal invariance. All items (dots) lie within the control line, indicating that both samples estimated the item difficulty consistently.](image)

\(^2\) The person fits statistics were also investigated in order to verify the adequacy of the patients’ responses to the model. The summary person fit statistics of sample-1 and sample-2 are close to a standardized normal distribution (mean ± SD: -0.326 ± 0.838 for sample-1 and -0.325 ± 0.822 for sample-2) indicating that the responses of patients in sample-1 and sample-2 fit the Rasch model for the 22 selected items. Moreover, the mean location and standard deviation of the sample-2 measures equivalent to 0.81 ± 2.78 logits is close to the mean location of the sample-1 measures (0.76 ± 2.70 logits) indicating that the overall activity level of both samples was comparable as the sample characteristics were.
1.1.3.4. Description of the ACTIVLIM scale

Figure 2 shows the structure and the targeting of the final linear ACTIVLIM scale in NMD patients. The overall mean patient location is equal to 0.7 logits, indicating that the selected items are well targeted to the NMD sample. Moreover, the range of measurement represented by the thresholds distribution fits the distribution of the patients’ abilities. According to the distribution of patients’ measures, adult patients with a measure above 1.83 logits and children with a measure above 2.36 logits should achieve all activities easily or with some difficulty.

1.1.3.5. Construct validity

No significant differences in ACTIVLIM measures were observed with regard to age (R = -0.04, p = 0.428), language community (F = 0.294, p = 0.588), gender (F = 0.004, p = 0.95), and patient category (F = 0.31, p = 0.654). A difference in ACTIVLIM measures was found with regard to the type of NMD (F = 15.92, p < 0.001). A post-hoc analysis indicates that the patients with proximal NMD have a lower activity level than do patients with other types of NMD. The ACTIVLIM measures were correlated with the Functional Independence Measure motor score (ρ = 0.85), the Vignos (ρ = -0.83), and the Brooke (ρ = -0.63) grades (Figure 3).
Activity limitations in patients with neuromuscular disorders

Figure 2: Top panel: Distribution of activity measures of the 369 NMD patients, the children’s measures as perceived by their parents are in white and the self-perceived adults’ measures are in grey. Nine children (C) and 20 adults (A) with extreme scores cannot be assessed by the activity scale because all activities were either impossible (2 C + 12 A) or easy (7 C + 8 A). Upper middle panel: A patient’s expected response for each item as a function of the activity measure. Zero is, by convention, set at the average item difficulty. For example, being able to easily put on a T-shirt requires a measure of at least 0.03 logits; whereas any patient with a measure below -2.39 would be unable to fully accomplish this activity. Conversely, a patient with a measure of 0 logits would be expected to perform the six easiest activities without difficulty, to perform the average activities with some difficulties, and would be unable to perform the six most difficult activities. Lower middle panel: Ogival relationship that makes it possible to convert the ordinal total score into a linear activity measure. Total score ranges from 0 to 44 because 22 items scored from 0 to 2. The activity measure in logits is an infinite measure. Although this relationship is quasi-linear in its central part, a unitary increment in total score encompasses larger differences of activity measure at both ends of the scale. Bottom panel: Scale graduations represented by the 44 thresholds (2 thresholds by item). The first graduation corresponds to the activity level required to endorse “difficult” rather than “impossible” for the item “washing one’s face” and the last one represents the activity level required to select “easy” rather than “difficult” for the item “hopping on one foot.”
1.1.3.6. Test-retest reliability

The test-retest reliability (delay: 24 ± 9 days) of the patient measures is shown in Figure 4 (right panel). Most of the measures lie within the 95 % CI of the identity line, indicating that adults and parents tend to consistently estimate their own or their child’s activity level. Moreover, the ICC for the patient measures is equal to 0.93. The left panel shows the DIF plot of the item difficulty hierarchy between the first and the second assessment. Two items identified by their labels lie outside the 95 % CI of the identity line. The ICC of the item estimates is equal to 0.98, indicating a good reproducibility of the item hierarchy.
Activity limitations in patients with neuromuscular disorders

1.1.4. DISCUSSION

The purpose of this study was to develop a common measure of activity limitations using the Rasch model and to validate it in both adults and children with NMD. The ACTIVLIM questionnaire was constructed from the adults’ and the parents’ perception of the difficulty in performing activities of daily living. The 22 items selected for the final version of the ACTIVLIM scale share the same ordered rating scale structure, fit a unidimensional scale and present no differential item functioning across age, gender, speech community and type of NMD.

The few items removed because of reversed thresholds indicate that both adults and the parents of affected children correctly discriminate the three proposed response categories (Andrich, 1996). Moreover, a common rating scale model for children and adults could be applied since the response categories were equally
discriminated by the adults and the parents of the affected children (Wright, 1999). The perception of the parents was indeed preferred to that of the children’s because children have a more dichotomous perception of their abilities (Chambers & Johnston, 2002). They perceived the activities either as “impossible” or “easy” with rare intermediate responses (Arnould et al., 2004). Therefore, the use of the children’s responses could lead to a narrower range of measurement, with more patients with extreme measures, leading to a less appropriate scale for the NMD sample.

Despite the temptation to construct a scale measuring different facets of NMD patient (e.g. activity limitations, fine hand motor skills, cognition,…), ACTIVLIM is a unidimensional scale that only measures activity limitations without other characteristics potentially leading to biased results of the evaluation (Wright & Linacre, 1989). The large number of items that did not contribute to the definition of the unidimensional variable may indicate that the experimental questionnaire measures more than one variable (Bond & Fox, 2001). Seventy percent of such deleted items mainly require hand and finger strength in order to be achieved (e.g., cutting meat, fastening the snaps of a jacket, unscrewing a bottle cap) and they appear to assess the manual ability of the patients. The reasons for the unsuitability of these items to the model can be explained after data examination (Andrich, 1999). The patients with a distal NMD have more difficulties in performing the manual activities than do patients with a proximal NMD; whereas the former have a higher level of activity. For this reason, the scores observed for the manual items do not correspond to the scores predicted by the model. The final ACTIVLIM scale does not include exclusively digital and manual activities, but it is suitable for all types of NMD and is reliable enough to be clinically useful. A scale of manual ability is however being developed for NMD patients.

The differential item functioning tests allowed to select items with no significantly different hierarchy between the compared person-related factors. For example, the hierarchy of the 22 selected items is invariant if the item difficulty is estimated by patients with a proximal NMD or by patients with a distal NMD. The same invariance was also observed between males and females and between Dutch and French speakers for the 22 final items, and between adults and children for the 14 common items.

Chapter 1: The ACTIVLIM questionnaire
The hierarchy of the 22 items retained for the scale is consistent with the psychomotor qualities and with the energy expenditure necessary to perform the activities. The activities requiring more balance, force or endurance, and therefore higher energy expenditure (Ainsworth et al., 2000), tend to be more difficult for NMD patients. The easiest activities can be often managed in a sitting position, using adaptive strategies. The most difficult activities usually involve lower limbs, and wheelchair-bound patients would answer “impossible” for these activities. As “impossible” correspond to “0”, total raw score of wheelchair-bound patients will be lower than the one of walking patients, as well as their activity level expressed in logits (Figure 2, third panel). In addition, the hierarchy of the 22 selected items was consistently estimated by both samples of patients (Figure 1) and the psychometric properties of the sample-2 scale are equivalent to the calibration of sample-1. This indicates that the selected items correspond to pertinent and appropriate activities to assess activity limitations in any NMD patients.

Among the 22 final items, 4 items specifically evaluate children with NMD and 4 specifically evaluate adults with NMD. Following experts’ advices, the 4 specific items for adults (items b, d, f and m) were not relevant for a child evaluation while 3 specific items for children (item a, c, and j) were not relevant for an adult evaluation. The fourth child item (item u) did not fit the unidimensional construct of activity limitations in the first Rasch analysis based upon the responses of 23 adult patients.

The standard errors associated with the item difficulty estimates (mean: 0.17 logits) conform to the expectation for most variables and are low enough to make the measurement precision high (Linacre, 1994). The ACTIVLIM scale presents good reliability since the 44 graduations are well targeted on our sample, representing a wide range of functional states (R = 0.96). Only 4% of the patients were unable to perform at least one activity. Most of these patients had a proximal NMD and all of them were wheelchair-bound (Vignos grade of 9) with an extremely affected upper limb function (Brooke grades of 5 or 6). Likewise, 4% of the patients were able to easily complete all the activities. Most of these patients had a distal NMD or myotonic dystrophy. All of them were able to raise their arms above their heads without flexing the elbows (Brooke grade of 1) and were able to walk and to go upstairs without assistance or using a railing (Vignos grades of 1 or 2). This low
percentage of patients located at the ends of the scale indicates that the scale has no significant ceiling or floor effect (McHorney et al., 1994). The wide range of scale graduations and the 22 items are sufficient to measure activity limitations in patients with any diagnosis of NMD.

The difficulty of two items (“closing a door” and “putting on a T-shirt”) slightly differs between the first and the second assessment (Figure 4). However, the differential item functioning of the two items is not high enough to compromise the test-retest reliability of the questionnaire. The high intraclass correlation coefficient found for the item hierarchy (ICC = 0.98) after a delay of 1 month indicates that the questionnaire is reproducible over time. Moreover, the adult patients and the parents of the affected children respectively evaluate themselves and their children consistently after about 1 month.

The analyses of the relationships between the patients’ measures with other widely used scales, such as the Vignos and Brooke grades and the motor score of the FIM, highlighted the good construct validity of the scale, with correlation coefficients of -0.83, -0.63 and 0.85, respectively. A higher activity level relates to lower Vignos and Brooke grades and to a higher level of independence. The Vignos and the Brooke grades respectively class the function of the lower and the upper limbs into a single category. Nevertheless, each category represents a rather wide range of ACTIVLIM measures in logits (Figure 3). ACTIVLIM is therefore more complete and precise than both of these grades since it allows to differentiate groups of patients within a same category of Vignos and Brooke grades. Concerning the FIM, few studies have validated it in a NMD population (Uchikawa et al., 2004, Jensen et al., 2005); although it is one of the most commonly used questionnaires in the evaluation of NMD patients (Haigh et al., 2001). Moreover, the motor score of the FIM seems not to be precise enough to distinguish groups of patients in the high levels of the motor score (Figure 3). Indeed, half of patients have a motor score above 80, indicating a high level of independence; while their activity measures range from -0.55 to 5.9 logits, representing a wide range of activity levels. These results confirm the observations in patients with poliomyelitis sequelae (Thoren-Jonsson & Grimby, 2001), among which a large number were independent in the activities of daily living, even if they reported difficulties in these activities. However, the FIM motor score and ACTIVLIM measure different aspects of the...
Activity limitations in patients with neuromuscular disorders

ACTIVLIM evaluates activity limitations in terms of difficulties in performing daily activities without technical or human assistance, and the FIM measures the independence of the patient taking into account the environmental factors (WHO, 2001). For example, patients who can propel their wheelchair themselves are considered independent for the locomotion item “walk/wheelchair” (item L); yet following the ACTIVLIM questionnaire, it is “impossible” for them to walk more than one kilometre (item d), since a wheelchair is considered to be a form of technical assistance. ACTIVLIM could however determine the technical assistance necessary to achieve some items. Furthermore, this scale is more precise and detailed than the FIM and it can remedy to the lack of sensitivity of the FIM.

The relationships between the patients’ measures and demographic and clinical indices appear as clinical information. The significant relationship between the patients’ measures and the type of NMD confirms previous reports (Thoren-Jonsson & Grimby, 2001, Berard et al., 2005) that patients with distal NMD and with myotonic dystrophy are less disabled in their functional status than are patients with proximal NMD and in particular those with Duchenne muscular dystrophy. The measures of the patients were not related to age, gender or speech community.

The Rasch model was used to construct and validate the ACTIVLIM scale. This particular methodology provided a measurement scale with fundamental psychometric qualities known as linearity and unidimensionality. This questionnaire has also good reliability, precision, construct validity and reproducibility. Moreover, ACTIVLIM can be used for evaluation of both adults and children with NMD making possible to follow the disease course from childhood to adulthood using a single scale. The hierarchy of the items is invariant across age, gender, language community or type of NMD indicating that ACTIVLIM can be used for any patients with NMD. Finally, the questionnaire is extremely easy to administer, since it can be completed in 5 minutes in the waiting room by the patient himself or a child’s parent. Nevertheless, ACTIVLIM does not claim to replace clinical evaluation methods that principally measure the impairments (manual muscle testing, range of motion, timed tasks test etc.) (WHO, 2001); it is rather complementary to these.
Further applications of the ACTIVLIM scale include the study of its responsiveness. The high precision of the scale ensures to statistically predict a good sensitivity to change in activity limitations induced, for instance, by the progressive course of the disease or by treatment. Nevertheless it must be clinically verified. Moreover, its relationships with impairment measures and its similarity between the self-reported version and the achievement of daily activities observed by a therapist will also be investigated.
1.2. **ACTIVLIM in Children with NMD: Why a Questionnaire Completed by the Child’s Parents?**

**Abstract**

During the development of the ACTIVLIM questionnaire, we assumed from previously published studies that the parents of the affected children report a more accurate perception of their children’s abilities than the children themselves do. The parents’ responses were therefore used to calibrate the ACTIVLIM scale using the Rasch model. This complementary study was conducted to verify this assumption by separately analyzing the children’s and parents’ responses. The use of the children’s responses provided a narrower range of measurement (9.3 logits versus 10.8 logits) due to the dichotomous perception of their abilities, leading to a lower reliability ($r=0.94$ versus $r=0.96$). From these results, the children’s activity limitations are better evaluated by their parents, confirming our hypothesis.

*This study is a supplement to the paper “ACTIVLIM: a Rasch-built measure of activity limitation in children and adults with neuromuscular disorders.”*
1.2.1. **Introduction**

The ACTIVLIM questionnaire is a measure of activity limitations developed in 124 children and 245 adults with neuromuscular disorders (NMD) using the Rasch model (Vandervelde et al., 2007). This questionnaire is a self-reported measure focused on the difficulties that the adult patients or the parents of the affected children perceived when they or their children, respectively, perform daily activities. The perception of these difficulties was evaluated on a three-level scale (0=impossible, 1=difficult, 2=easy). The parents’ perception was preferred to the children’s because previous studies have demonstrated that the children tended to unsuitably discriminate the three response categories, assessing the daily activities either as “impossible” or “easy” with rare intermediate responses (Chambers & Johnston, 2002, Arnould et al., 2004). The aims of this complementary study were (1) to verify this hypothesis in children with NMD by analyzing separately the children’s and their parents’ responses, and (2) to compare the ACTIVLIM calibration from the 124 children’s responses with the one from their parents’ responses. Moreover, test-retest reliability was investigated in children’s responses to confirm or refute the results. Indeed, children may have answered the questionnaire randomly because, for instance, they did not clearly understand the instructions.

1.2.2. **The Response Category Functioning in Children with NMD and their Parents**

The functioning of response categories is studied when the response scale includes more than two levels of responses. We examined whether the different categories are used by the studied population in accordance with the underlying variable (Andrich, 1996). In the case of ACTIVLIM, each number assigned to response category should represent a higher level of activity (Linacre, 1999). The Rasch methodology provides a helpful framework for verifying whether successive response categories for each item represent increasing level of activity and whether thresholds between adjacent categories are located in the expected order (Andrich,
A threshold corresponds to the location along the variable for which two adjacent categories have an equal probability of being observed. If the thresholds are located in an increasing order, the response categories are well discriminated by the sample since each category in turn is the most probable category to be observed (Figure 1 left panel). On the other hand, reversed thresholds indicate that the rating scale does not function as expected (Figure 1 right panel). In this figure, the second threshold is located before the first one, indicating that category 1 did not emerge, i.e., will never be the most likely to be observed.

Moreover, the distance between two ordered thresholds gives information on how the middle category is discriminated; the wider the distance between adjacent thresholds, the more clearly the middle category is distinguished (Linacre, 1999). When successive thresholds are more than five logits apart, the category they define is too wide, leading to a loss of measurement precision (Linacre, 2002).
The responses of the 124 children with NMD and their parents were analyzed separately with the RUMM2020© software (see section 1.1. for sample description). The experimental version of the questionnaire contained 99 items to measure activity limitations in children with NMD. The children correctly distinguished each of the three response categories for 65 items because 34 items presented reversed thresholds. Their parents’ responses, on the contrary, provided only 4 items with reversed thresholds. Moreover, the average distance between the two thresholds was compared in the children’s and their parents’ responses on just the set of 65 items that presented ordered thresholds in both data sets. The increase of activity level required for selecting “easy” rather than “impossible” was equal to 2.35 logits for the parents (Figure 2, left panel) and 1.25 logits for the children (Figure 2, right panel).

Figure 2: Category probability curves averaged across the 65 items with ordered thresholds retained after the children’s response analysis. The left panel shows the categories as rated by the parents, while the right panel shows the categories as rated by the children. Each curve represents the probability of the category being observed as a function of the patient’s activity level (0=impossible, 1=difficult and 2 =easy).

The number of items presenting reversed thresholds and the narrower distance between the two thresholds for the remaining items suggests that the
children with NMD have a more dichotomous perception of their activity level, as assumed during the questionnaire development. They tended to answer to the items either with the category “impossible” (“you cannot achieve the activity alone; you need help to achieve the activity”) or with the category “easy” (“you can achieve the activity without help; there is really no problem with achieving it alone”). The definition of the category “difficult” (“you can do the activity alone, without any technical or human help, but with some difficulties”) was therefore less obvious for the children than for their parents.

1.2.3. **Impact of the children’s responses on the calibration of the ACTIVLIM questionnaire**

Despite the fact that children have a more dichotomous perception of their abilities, their responses could be adequate to define a precise and reliable activity scale. Table 1 summarizes the number of items deleted from each selection criterion described in the methods of section 1.1 and the main results of both ACTIVLIM calibrations: (1) the calibration obtained from the adult patients’ responses coupled with those of the children’s parents presented in section 1.1 and (2) the calibration obtained from the adult patients’ responses coupled with those of the children themselves.

From the analysis taking into account the children’s and adults’ responses, more items were deleted because they had disordered thresholds (19 versus 7 in the original analysis for the ACTIVLIM calibration). The version of ACTIVLIM obtained from the children’s and adult’s responses contained 11 common activities, three specific activities for children and three specific activities for adults. However, the discrimination of the categories was significantly different in adult patients and in children ($t=-6.883$, $p < 0.001$), the rating scale model was divided into three subsets of items: (1) a subset for the 11 activities evaluated by both the children and the adult patients, (2) a subset for the three specific activities for children and (3) a subset for the three specific activities for adult patients. The post-hoc analysis showed that the three child activities had a narrower distance between both thresholds (1.3 logits) than the two other subsets of items (1.98 and 2.08 logits for the adult and common activities, respectively).
The children’s locations estimated by both calibrations of the ACTIVLIM questionnaire are presented in Figure 3. The children’s own responses are consistent with their parents’ responses since 90% of the activity measures lie within the 95% of confidence interval. Nevertheless, the scale based upon the parents’ responses covers a wider range of the variable than the children’s one (10.8 logits and 9.3 logits, respectively) and the parents’ scale could discriminate children with extreme scores represented by the dots at the end of the children’s measurement range (Y-axis). This narrower measurement range and the higher number of extreme children lead to a less precise measurement scale, as reported by a lower reliability index (r=0.94) in the children’s scale than in the parents’ one (r=0.96).

Consequently, the original calibration of the ACTIVLIM questionnaire based upon the parents’ perception is more adequate for assessing the patients with NMD since it provides a wider range of measurement, leading to greater precision of this measurement and fewer patients with extreme scores. In other words, the activity limitations were more accurately perceived by the children’s parents as compared to the children themselves.
1.2.4. Test-retest reliability of children responses

Test-retest reliability was investigated to verify whether children are consistent in their dichotomous responses. The questionnaire was submitted to the children twice with a delay of 24 ± 9 days. The item hierarchy and the category functioning of the items selected from the ACTIVLIM calibration with the children’s and adult patients’ responses were compared between both evaluations. Figure 4 shows the item hierarchy estimated by the children at the first and the second evaluation. All the items are lying within the 95% CI of the identity line, indicating that the children consistently estimated the item difficulty hierarchy after 24 ± 9 days. The intraclass correlation coefficient of the item estimates is equal to 0.95, also indicating a good reproducibility of the item hierarchy. Therefore, children with NMD were consistent in their responses on the questionnaire.
Figure 4: Differential item functioning plot of the item difficulty perceived by the children at the first and the second assessment, and the 95% of confidence interval (solid line) of the ideal invariance. Most difficult items are plotted in the top/right part of the figure.

Figure 5 shows the category probability curves averaged across the items estimated by the children during the first and the second evaluation. The increase of activity level required for selecting “easy” rather than “impossible” is equal to 0.98 logits for the first evaluation (Figure 5, left panel) and 1.24 logits for the second evaluation (Figure 5, right panel). The paired t-test showed no difference in the category discrimination between the two evaluations (t=0.968, p-value=0.351), indicating that the children consistently perceived the response categories at the first and second evaluations. In conclusion, these results strengthen the notion that children have a more dichotomous perception of their abilities than their parents and that they did not randomly answer the ACTIVLIM questionnaire.
First assessment

Second assessment

Figure 5: Category probability curves averaged across the items estimated by the children during the first and the second assessment and selected from the ACTIVLIM calibration with the children’s and the adults’ responses. The left panel shows the categories as rated during the first evaluation, while the right panel shows the categories as rated during the second evaluation. Each curve represents the probability of the category to be observed as a function of the patient’s activity level (0=impossible, 1=difficult and 2=easy).

1.2.5. Conclusions

This study showed that the children with NMD had a more dichotomous perception of their difficulties in performing daily activities than their parents had, as was suggested during the ACTIVLIM questionnaire development. This fact was confirmed by good reproducibility of the item hierarchy and category functioning estimated by the children. This lack of discrimination of response categories led to narrower range of measurement and a lower reliability of the scale. For these reasons, the activity limitations in children with NMD were more suitably evaluated by their parents, as all items of the original ACTIVLIM calibration could share the same structure of the response scale.
1.3. **COMPARISON BETWEEN SELF-REPORTED AND OBSERVED ACTIVITY LIMITATIONS IN ADULTS WITH NMD**

**Abstract**

*Objectives:* To investigate the agreement between the self-reported and examiner-reported difficulties of patients with neuromuscular disorders (NMD) in performing daily activities at home. *Design:* Comparison between two methods of administering a measurement instrument. *Setting:* Neuromuscular reference center in a university hospital. *Participants:* Fifty-seven adult patients with diagnosed neuromuscular disorders living at home. *Intervention:* Not applicable. *Main Outcome Measure:* The ACTIVLIM questionnaire. *Results:* The intra-class correlation coefficient (ICC\(_{2,1}\)) between the measures was very good, (ICC\(_{2,1}= 0.87\)), indicating a good agreement between self-perceived and observed measures. *Conclusion:* The use of ACTIVLIM as a self-reporting questionnaire is a valid method for assessing activity limitations in patients with NMD.

*Published as*

1.3.1. **INTRODUCTION**

Neuromuscular disorders (NMD) are hereditary or acquired diseases of the motor unit (Mangione-Smith et al., 2002), and sometimes involve parts of the central nervous system. Most of these diseases have a progressive clinical course characterized by decreased muscle strength leading to impaired motor function (Piccininni et al., 2004). Consequences of these diseases include fatigue, problems with locomotion and loss of functionality in activities of daily living. Difficulties in performing daily activities are defined by the World Health Organization as activity limitations (WHO, 2001). Activity limitations in patients with NMD can be measured with a new scale, the ACTIVLIM questionnaire, which was developed and validated using the Rasch model (Vandervelde et al., 2007). It presents very good psychometric qualities including reliability, construct validity, reproducibility, linearity and unidimensionality. Moreover, it offers the benefits of being inexpensive and easy to administer. This questionnaire is comprised of self-reported measures focused on the patients’ perceptions of their activity limitations and informs clinicians on how well patients manage in their home environments (Owens et al., 2002). Nevertheless, self-reported measures are subjective evaluations, which could be influenced by factors such as culture, level of education or emotional state (Kivinen et al., 1998). For these reasons, performance-based measures have been developed because they are considered to be more objective and standardized for the assessment of the functional status of patients (Ferrer et al., 1999, Owens et al., 2002). The relationships between self-reported and performance-based measures have been studied in various pathologies, (Cress et al., 1995, Reuben et al., 1995, van den Ende et al., 1995, Kempen et al., 1996, Hoeymans et al., 1996, Wijlhuizen & Ooijendijk, 1999, Itzkovich et al., 2003, Mannerkorpi et al., 2006) but different items and scoring procedures were used for both measures. Indeed, most of the self-reported items correspond to usual daily activities assessed with rating scales determining the degree of difficulty or assistance required to complete these activities, whereas the performance-based items are often timed, and correspond to standardized tasks (Coman & Richardson, 2006). Scoring the performance by direct observation with rating scales is also used as method of functional assessment (Salter et al., 2005). Nevertheless, comparing scores observed on rating scales by
The ACTIVLIM questionnaire clinicians with self-reported scores was never carried out in patients with NMD and certainly not with the aim of validating the use of a self-reporting questionnaire. The purpose of this study was to compare self-reported and observed measures using the ACTIVLIM questionnaire in order to endorse or question the use of a self-reported questionnaire in future clinical and research settings to assess activity limitations in patients with NMD.

1.3.2. **Methods**

1.3.2.1. Patients

This study was approved by the medical ethics committee of the Université catholique de Louvain. The patients were recruited through the Neuromuscular Reference Center of the Cliniques universitaires Saint-Luc in Brussels. The patients gave written informed consent before the evaluation. Fifty-seven adult patients with a diagnosed neuromuscular disorder were assessed by four physical therapists. Patient descriptions are given in table 1.

1.3.2.2. Self-reported and observed measures

Both self-reported and observed measures were obtained with the ACTIVLIM questionnaire so that they were standardized in item and scoring procedure. This questionnaire consists of 22 daily activities presented in the questionnaire development study (Vandervelde et al., 2007) and was originally developed using the Rasch model, which allows the conversion of ordinal scores into linear measures located on a unidimensional scale (Rasch, 1980). These linear measures are expressed in logits (i.e., log-odd units), the constant measurement unit of activity scale; the higher the value in logits, the higher the activity level of the patient.
The self-reported measures were obtained by asking patients to provide their perceived difficulty in performing each activity on the ACTIVLIM questionnaire, without using technical or human help, on a three-level ordinal scale (0 = impossible, 1 = difficult or 2 = easy). The patients were observed at their homes so that they could be in their usual environment when performing the activities to be assessed (Rogers et al., 2003). The physical therapists observed the patients performing the activities and assessed the difficulty experienced by the patients in completing these activities. The scoring procedure of the observed measures was identical to the self-reported measures (0 = impossible, the patient is unable to achieve the activity without using technical or human help, 1 = difficult, the patient is able to achieve the activity without any help but experiences some difficulty, and 2 = easy, the patient is able to achieve the activity without any help and experiences no difficulty).
1.3.2.3. Procedure

The evaluation comprised three stages. The first self-reported measure (SR-1) was collected by mail about two weeks before a home visit by the physical therapists. The patients’ responses were not disclosed to the therapists to prevent influencing their observations. Secondly, the patients performed each activity of the ACTIVLIM questionnaire within the limits of their abilities during the evaluation at home. The physical therapists observed the patients performing the activities and rated each of them on the ACTIVLIM ordinal scale (O1). For ethical reasons, some activities such as “taking a bath,” “taking a shower” or “washing one’s upper body” were mimicked, and the patients explained how they usually performed them. Finally, a second self-reported measure (SR-2) was collected about one month after the home visit. In each questionnaire, the activities were randomly presented in order to avoid any effects caused by the item order. Moreover, the objective of the study was not revealed to the patients to prevent any influence on their responses.

The 57 patients were evaluated by four examiners (E1, E2, E3 and E4). First, 26 patients were simultaneously assessed by E1 and E2 with an excellent inter-rater reliability (intra-class correlation coefficient (ICC) = 0.98). Second, five patients were assessed by E1, E3 and E4 with also an excellent inter-rater reliability (ICC = 0.99). Hence, the last 26 patients were evaluated by one examiner (E3 or E4). One observed measure was retained for the 31 patients evaluated by two or three examiners, and these measures were put together with the 26 measures observed by E3 or E4. As a result, each patient had only one observed measure for further data analyses.

1.3.2.4. Statistical analysis

The self-reported and observed responses were first fitted to the Rasch model using the Rasch Unidimensional Measurement Models computer program (RUMM2020, RUMM Laboratory Pty Ltd, Perth, Western Australia). This software reported overall fit statistics which were close to standardized normal distribution for item and person fit residuals (mean ± SD: -0.036 ± 0.4 and -0.266 ± 0.937, respectively for SR-1, -0.322 ± 0.863 and -0.177 ± 0.660, respectively for O1 and -0.031 ± 0.566 and -0.144 ± 0.946, respectively for SR-2) and were not significant.
for the chi-square item-trait interaction (p=0.56, 0.28, 0.42 for SR-1, O1 and SR-2, respectively). As a result, the ordinal total scores obtained from the self-reported and observed ACTIVLIM questionnaires could be transformed into interval-level measures of activity limitations. Three linear measures of the patients’ activity level (S-R1, O1 and S-R2) were reported in such a way that they could be quantitatively compared and treated as a continuous variable.

The invariance of item hierarchy across the three evaluations was checked using differential item functioning test (DIF). A DIF can be detected by a two-way analysis of variance for each item by comparing scores across each level of patient-related factor (SR-1, O-1 and SR-2 in this case) and across levels of the activity construct, i.e. the class intervals (Pallant & Tennant, 2007). A significant main effect for the patient-related factor shows the presence of a uniform DIF; whereas a non-uniform DIF corresponds to a significant interaction effect (patient-related factor x class interval).

The agreement between the self-reported and observed measures was calculated using the intra-class correlation coefficient (ICC_{2,1}) (Shrout & Fleiss, 1979). The ICC_{2,1} was computed as a two-way ANOVA where the “targets” (i.e., the patients) were one source of variability and the “raters or measures” (the self-perceived and observed activity levels) were the second source of variability (McGraw & Wong, 1996). This coefficient is preferred to the Pearson correlation coefficient because it takes into account the extent of the relative discrepancies between the evaluations, while the Pearson coefficient measures the degree of linearity between two measures (Hamilton et al., 1994, McGraw & Wong, 1996).

The Kappa coefficient was used to quantify item-by-item agreement between both administration methods of the ACTIVLIM questionnaire (Cohen, 1960).

1.3.3. Results

No significant DIF, uniform or non-uniform, was found across the three evaluations (p≥ 0.1) indicating that the item hierarchy is invariant if the item difficulty is evaluated by the patients or by the external examiners.
The ICC between S-R1 and O1 and between S-R1 and S-R2 were equal to 0.87 and 0.93, respectively, indicating good agreement between the measures. Figure 1 shows the relationships between the different measures obtained by self-reporting or observation in relation to the line $x = y$. For example, the score of patient “a” lies on this identity line, indicating a perfect agreement between his activity level obtained by the self-reported questionnaire and the one obtained by observation. For patient “b,” the self-reported score was lower than the score obtained by observation.

Most of the items showed Kappa coefficients between 0.44 and 0.99 for their response agreement between SR-1 and O-1. Only the item “carrying a heavy load” had a Kappa coefficient of 0.25.

1.3.4. Discussion

The self-perceived difficulty of 57 adult patients with NMD in performing daily activities was compared to the difficulty in performing the same activities as

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*Chapter 1: The ACTIVLIM questionnaire*
Activity limitations in patients with neuromuscular disorders observed by 4 physical therapists. Both perceived and observed measures were obtained using the ACTIVLIM questionnaire, allowing the use of the same items and the same scoring procedure for each measure. The high intraclass correlation coefficient between self-perceived and observed activity limitations (ICC = 0.87) indicates a good agreement between these measures in patients with NMD. Therefore, the use of self-reported questionnaire is a valid method for assessing activity limitations in patients with NMD. Additionally, self-reporting presents considerable advantages over observation. The self-reported questionnaire is low in cost and extremely easy to administer, since it can be completed in 5 minutes in the waiting room by the patient himself, while the observation of daily activities at home took about 45 minutes. The self-reported ACTIVLIM questionnaire could be therefore integrated in any research protocols to evaluate activity limitations in patients with NMD. Moreover, such questionnaire is really easy to use for clinicians who want to assess and characterize evolution of these patients in neuromuscular clinics for example.

The values of the Kappa coefficients showed moderate to excellent agreement between the first self-reported and observed responses of each item except for the item “carrying a heavy load”. Indeed, many patients evaluated this task as “impossible” while the examiners evaluated it as “difficult”. This is probably due to the fact that during the observation, the load was standardized for all patients and was smaller or lighter than what some of them imagined when they filled in the questionnaire.

The patients’ perceptions were stable and reproducible after a delay of approximately 45 days, as shown by the ICC of 0.93 between the SR-1 and the SR-2 measures, despite the fact that after the delay, the patients better understood some items of the questionnaire. Indeed, performing daily activities in front of physical therapists could influence the patients’ perceptions of the difficulty of these activities and therefore the second self-reported measures (SR-2). The reproducibility of the patients’ measures was previously studied during the development of the ACTIVLIM questionnaire, and the 369 patients with NMD evaluated their activity levels consistently over a period of about one month (ICC = 0.93) (Vandervelde et al., 2007). The present study confirms this previous result and
shows that receiving further information about these activities has no effect on the patients’ perceptions of their activity levels.

Some differences could be observed between self-perceived and observed activity limitations, especially for patients with an activity level higher than 2 logits (Figure 1, upper panel). The observed activity levels of these patients are higher than the self-reported ones, indicating that either the external examiners overestimated the patients’ activity levels, or the patients underestimated them. On the one hand, this could be due to the fact, as previously suggested, that patients with lack of self-confidence tend to report a lower level of functioning as compared to their performance-based functioning (Smith & Williams, 1992, Kempen et al., 1996). On the other hand, some patients show motivation that could have improved their performance during observation, possibly because they were conscious of being part of an experimental study (Campbell et al., 1995) or because they were aware of the presence of the examiners (Karamehmetoglu et al., 1997). However, personality, motivation and affective functioning were not evaluated in this study, and therefore, their influence on SR-1 and O1 cannot be determined. Nevertheless, these slight divergences did not affect the good concordance between the self-reported and observed activity levels expressed by the ICC of 0.87. The present results apply to adult patients with NMD. Self-reported measures could be, indeed, overestimated or underestimated in other pathologies such as those with cognitive impact. Further researches are, however, required to verify this assumption.

1.3.5. Conclusion

The ICC between the two measures shows very good agreement between self-reported and observed measures, which indicates that the questionnaire is a valid method for assessing activity limitations in patients with NMD. Moreover, the patients’ perceptions were reproducible after a delay of 45 days, even though they had performed the activities in front of physical therapists.
Chapter 2: 
Motor impairments and their relationships with activity limitations in patients with NMD

Abstract
Motor impairment and their relationships with activity limitations assessed by the ACTIVLIM questionnaire were investigated in 245 patients with neuromuscular disorders. Measures of motor impairments consisted of (1) a grip strength test using a Jamar dynamometer, (2) a manual muscle testing bilaterally performed in eighteen muscle groups and (3) a gait speed spontaneously adopted by the patients using the 10-meter timed walking test. Activity limitations were poorly correlated with grip strength in both hands (r=0.3 and 0.36) and moderately correlated with gait speed (r=0.53). The Spearman’s coefficients of correlation between the manual muscle testing and activity limitations were moderate to very poor (p=0.5 to 0.17). The relationships between motor impairments and activity limitations are not so straightforward in patients with neuromuscular disorders, indicating that the activity limitations should be separately assessed and cannot be simply inferred from motor impairment measures.

This chapter is a modified version of the paper submitted as:
2.1. **Introduction**

The International Classification of Functioning, Disability, and Health (ICF) proposed by the World Health Organization gives a framework to describe an individual’s functioning taking into account his health condition in three separate components (WHO, 2001): (1) body functions and anatomical structures, (2) activity defined as the achievement of daily activities, and (3) participation defined as involvement of the subject in a life situation. Problems or difficulties that a subject may have in each component are impairments, activity limitations and participation restrictions, respectively. Although these components are separately defined, they are related but not necessarily in a straightforward relationship (Merkies et al., 2003, Arnould et al., 2007). Indeed, two individuals with the same level of impairments will not necessarily have the same level of activity or participation. The nature and the strength of the relationships between impairments and activity limitations have been only studied in patients with polyneuropathies (Merkies et al., 2003) among patients with neuromuscular disorders (NMD).

The principal impairments of patients with NMD consist in a deterioration of the motor function characterized by a progressive decrease of muscle strength (Mangione-Smith et al., 2002). The location and severity of motor impairments in patients with NMD widely vary according to the etiology of the disease since the origin of the muscle weakness, its physiopathology, and the related symptoms depend on the type of NMD (Hogrel et al., 2006). The activity limitations in patients with NMD were recently studied by developing and validating a new scale of activity limitations, the ACTIVLIM questionnaire (Vandervelde et al., 2007).

The first objective of this study was to draw up the prevalence of motor impairments in patients with NMD. Secondly, the relationships between motor impairments and activity limitations in patients with NMD were assessed to verify the clinical assumption that a reduction of the motor impairments by the conventional treatments will result in a higher ability in performing daily activities (WHO, 2001). Indeed, conventional treatments such as physical therapy or orthopedic devices tend to maintain or improve joint mobility, muscle strength and endurance but are focused to a lesser extent on the management of daily activities.
(Hornyak & Pangilinan, 2007). The relationships between motor impairments and activity limitations were investigated first in different diagnosis groups of NMD and, secondly in a wider sample of NMD without diagnosis distinction. This approach could therefore interest clinicians who take care of patients with a specific NMD but also the ones who follow large groups of patients in neuromuscular clinics.

2.2. Patients and Methods

2.2.1. Patients

This multicentric study was approved by the medical ethics committees of the Université catholique de Louvain and of the Katholieke Universiteit Leuven. The patients were recruited through the Neuromuscular Reference Centers of two university hospitals. Moreover, 10 percent of the children came from three other centers specializing in NMD. Adult patients and parents of affected children gave written informed consent before the evaluation. Two hundred and forty-five patients (46 children from 6 to 16 years and 199 adults from 16 to 80 years) with a diagnosed neuromuscular disorder were assessed by two experienced examiners (n=127 for examiner 1 and n=118 for examiner 2). Six main diagnosis groups could be sorted out from the sample, each of them including more than 5% of the sample: (1) Duchenne, Becker and limb-girdle muscular dystrophy (DMD/BMD/LGMD) (n=45, 6-72 years), (2) hereditary neuropathy (HN) (n=44, 8-80 years), (3) myotonic dystrophy (MD) (n=37, 16-72 years), (4) facio-scapulo-humeral dystrophy (FSHD) (n=12, 12-67 years), (5) spinal muscular atrophy (SMA) (n=14, 9-61 years) and (6) amyotrophic lateral sclerosis (ALS) (n=18, 46-80 years). Patients not belonging to one of these groups made up the group “others” (n=76, 6-80 years) including the rest of neuromuscular disorders such as post-polio syndrome, congenital muscular dystrophy or metabolic myopathy for instance. A description of the sample is given in table 1.
Activity limitations in patients with neuromuscular disorders

Table 1: Patient sample description (n=245)

<table>
<thead>
<tr>
<th>Gender</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>male, %</td>
<td>58</td>
</tr>
<tr>
<td>female, %</td>
<td>42</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>DMD/BMD or LGMD, %</td>
<td>18</td>
</tr>
<tr>
<td>HN, %</td>
<td>18</td>
</tr>
<tr>
<td>MD, %</td>
<td>15</td>
</tr>
<tr>
<td>ALS, %</td>
<td>7</td>
</tr>
<tr>
<td>SMA, %</td>
<td>6</td>
</tr>
<tr>
<td>FSHD, %</td>
<td>5</td>
</tr>
<tr>
<td>Others (e.g., CM, CMD, PPS, …), %</td>
<td>31</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mobility level</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking, %</td>
<td>69</td>
</tr>
<tr>
<td>Wheelchair-bound, %</td>
<td>31</td>
</tr>
</tbody>
</table>


2.2.2. Motor impairment assessment

The patients were assessed individually in a quiet room during their multidisciplinary consultation at the Neuromuscular Centers or in the specialized centers for children with NMD. The tests were clearly explained to the patients and included strength measures and a measure of spontaneously adopted gait speed.

Strength measures comprised grip strength and manual muscle tests. The measure of grip strength has been reported as providing information about activity limitations (Spiegel et al., 1987, Thyberg et al., 2005) and even predicting functional limitations in elderly (Giampaoli et al., 1999, Rantanen et al., 1999). The grip strength was measured with a Jamar dynamometer (Therapeutic Equipment Corporation, Clifton, New Jersey, USA) according to the procedure described by Mathiowetz et al. (Mathiowetz et al., 1985). The average of the maximal force
exerted on the dynamometer across three trials gave the measure of grip strength expressed in Newton. Grip strength was recorded for both hands.

Manual Muscle Testing (MMT) is a usually used non-instrumented method for measuring muscle strength in patients with NMD (Haigh et al., 2001). Nine muscle groups of the upper limb (shoulder abductors and flexors, elbow flexors and extensors, wrist flexor and extensors, digits flexors, extensors and interossei muscles) and nine muscle groups of the lower limb (hip flexors, extensors and abductors, knee flexors and extensors, ankle dorsiflexors and plantar flexors, toe flexors and extensors) were bilaterally tested according to the 6-grade Medical Research Council scale (0 = no movement; 1 = flicker of movement; 2 = movement of the joint when the effect of gravity is eliminated; 3 = movement through full range of the joint, against gravity; 4 = movement of the joint, against gravity and against added resistance; 5 = full strength) (Medical Research Council, 1976). Positions of the patient and the examiners were standardized according to the procedure described by Kendall et al. (Kendall et al., 1993).

The gait speed spontaneously adopted by the patient was reported to be a reliable index of locomotor impairment in patients with various pathologies of the lower limbs (hemiparetic, paraparetic, tetraparetic, orthopedic and paraplegic patients) (Bernardi et al., 1999). The spontaneous gait speed in our patients with NMD was obtained using the 10-meter timed walking test. The 10-m test was considered as a reliable and valid measure in patients with amyotrophic lateral sclerosis (Goldfarb & Simon, 1984), in immune mediated polyneuropathies (Merkies et al., 2003), and in patients with Charot-Marie-Tooth neuropathy (Solari et al, 2008). The patient was asked to walk a distance of 10 meters at his own preferred and comfortable speed. The time taken to complete the task was recorded and the gait speed was expressed in meters per second. Any help necessary to walk the 10 meters was allowed. Fourteen percent of the patients used one or two crutches, 15 percent used an ankle-foot orthosis or orthopedic shoes and 2 percent needed personal support for balance for example. No data were recorded for wheelchair-bound patients.
2.2.3. Activity limitations assessment

Activity limitations were assessed with the ACTIVLIM questionnaire (Vandervelde et al., 2007). This questionnaire assesses the difficulties a patient may have in executing daily activities (WHO, 2001). It contains 22 daily activities designed for both children and adults with NMD. The children’s parents and the adult patients were asked to provide the difficulty they perceived in performing each activity on a three-level ordinal scale (0 = impossible, 1 = difficult or 2 = easy). Participants were instructed that the activities should be completed without technical or human help. The ordinal total score obtained on the ACTIVLIM questionnaire was subsequently transformed into an interval-level measure of activity limitations according to the Rasch model (Rasch, 1980). The activity limitations scale has a constant measurement unit, called logit, and its origin is conventionally fixed at the average item difficulty; the higher the value in logits, the higher the activity level of the patient. As the measures are linear, they can be treated as continuous variables and the activity level of patients with NMD can be quantitatively compared.

2.2.4. Statistical analysis

The scores of grip strength and gait speed were transformed into standardized z-scores according to normative data available in the literature (Mathiowetz et al., 1985, Mathiowetz et al., 1986, Wheelwright et al., 1993, Bohannon, 1997). This procedure determines the extent to which a NMD patient deviates from normal given his/her gender and age for grip strength and given his/her gender, age and height for gait speed. Grip strength and gait speed in walking patients were considered as significantly impaired when the z-score was lower than −2.

The grades of the MMT represent ordinal scores and are separated by unknown distances. Therefore, mathematical and statistical operations on such scores can lead to an incorrect interpretation of results (Merbitz et al., 1989). For these reasons, the scores of the MMT were individually analyzed and when the score
of the MMT was less than 5 on the MRC scale, patients were considered to have strength impairment of this specific muscle group.

The relationships between motor impairment and activity limitations were studied in each of the six main diagnosis groups and in the whole sample without diagnosis distinction. A Pearson’s correlation coefficient was used to determine the strength of the linear relationship between the z-scores of grip strength and of gait speed and the ACTIVLIM measures while a Spearman’s correlation coefficient was used for the relationship between MMT and the ACTIVLIM measures. Analyses were performed with the SigmaStat© software.

2.3. RESULTS

2.3.1. Motor impairments

The extent of each motor impairment in the six diagnosis groups and in the total sample is represented on Table 2 by the proportion of patients that obtained a z-score lower than -2 to the grip strength test, a z-score lower than -2 to the gait speed test, and a score lower than 5 to the MMT.

All diagnostic groups present a high proportion of patients with impaired gait speed in walking patients (range: 45% in ALS group to 75% in FSHD group). The proportion of patients presenting grip strength impairment ranges from 18% for left grip strength in FSHD group till 87% for right grip strength in MD group. Considering the total sample, 60% of the 169 walking patients present gait speed impairment. Sixty percent of the patients present grip strength impairment in right hand, 53% of them present grip strength impairment in the left hand, and 47% present grip strength impairment in both hands.

The scores of MMT show no significant difference between right and left sides for all muscle groups (Wilcoxon Signed Rank test, p>0.1) in such a way that the values of the right side were arbitrarily chosen for further analyses. In patients with DMD/BMD/LGMD, muscle weakness is principally located in the proximal muscles of the upper and the lower limbs (range: 56 to 96%). In patients with HN, the distal muscles of lower limbs and the interossei muscles are mainly affected.
(range: 72 to 41 %). Patients with MD present weakness in the finger flexors and interossei muscles while all patients with FSDH present reduced muscle strength in the shoulder muscle groups. Finally, weakness is mostly located in the proximal muscle of the upper and the lower limbs in patients with SMA (range: 63% to 92%), and is mostly located in the distal muscles of lower limbs and in the finger muscle for patients with ALS (range: 40% to 55%).

As for the total sample, the muscle strength of the lower limbs is more impaired than the muscle strength of the upper limbs. According to the muscle groups, 39% to 55% of the patients present weakness in lower limb muscles whereas 24% to 49% of them present weakness in upper limb muscles. Finally, only 8% of the patients obtain a grade of 5 on the MRC-scale in all their muscle groups.

### Table 2: Prevalence of motor impairments according to type of NMD

<table>
<thead>
<tr>
<th></th>
<th>DMD/BM DLGMD</th>
<th>HN*</th>
<th>MD*</th>
<th>FSHD*</th>
<th>SMA*</th>
<th>ALS*</th>
<th>Others</th>
<th>Total sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grip strength (R)</td>
<td>73</td>
<td>48</td>
<td>87</td>
<td>55</td>
<td>77</td>
<td>67</td>
<td>46</td>
<td>66</td>
</tr>
<tr>
<td>Grip strength (L)</td>
<td>78</td>
<td>40</td>
<td>81</td>
<td>18</td>
<td>77</td>
<td>61</td>
<td>35</td>
<td>53</td>
</tr>
<tr>
<td>Gait speed in walking patients</td>
<td>69</td>
<td>63</td>
<td>52</td>
<td>75</td>
<td>50</td>
<td>45</td>
<td>65</td>
<td>60</td>
</tr>
</tbody>
</table>

**Upper limb proximal muscles**

- Shoulder flexion: 78 %
- Shoulder abduction: 76 %
- Elbow flexion: 72 %
- Elbow extension: 56 %

**Upper limb distal muscles**

- Wrist flexion: 48 %
- Wrist extension: 51 %
- Finger flexion: 42 %
- Finger extension: 48 %
- Interossei: 42 %

**Lower limb proximal muscles**

- Hip extension: 96 %
- Hip abduction: 96 %
- Hip flexion: 90 %
- Knee extension: 87 %
- Knee flexion: 77 %

**Lower limb distal muscles**

- Ankle dorsiflexion: 48 %
- Ankle plantar flexion: 26 %
- Toe extension: 47 %
- Toe flexion: 38 %

* DMD = Duchenne Muscular Dystrophy, BMD = Becker Muscular Dystrophy, LGMD = Limb-Girdle Muscular Dystrophy, MD = Myotonic Dystrophy, HN = hereditary neuropathy, SMA = Spinal Muscular Atrophy, FSHD = Facio-Scapulo-Humeral Dystrophy, ALS = Amyotrophic Lateral Sclerosis.
2.3.2. Activity limitations

The activity limitations measures of patients with NMD are concisely presented here because they were already described in a previous study (Vandervelde et al., 2007). The ACTIVLIM measures are significantly different with regard to type of NMD (F = 10.55, p < 0.001). The post-hoc analysis indicates that the patients with proximal NMD (mean ± SD: -1.1 ± 3.07 logits in DMD/BMD/LGMD group and -0.46 ± 3.43 logits in SMA group) have a lower activity level than the group with other NMD (mean ± SD: 0.66 ± 2.35 logits), the FSHD group (mean ± SD: 1.56 ± 1.99 logits), the HN group (mean ± SD: 1.97 ± 2.1 logits) and the MD group (mean ± SD: 2.71 ± 2.1 logits). The MD group has also a significantly higher activity level than the ALS group (mean ± SD: 0.39 ± 2.31 logits) and the group with other NMD.

2.3.3. Relationships between motor impairments and activity limitations

Figure 1 shows the relationships between gait speed (panel a), grip strength (panel b) and activity limitations for each of the six main diagnosis groups. Activity limitations are significantly correlated with the gait speed for the DMD/BMD/LGMD, HN, MD and ALS groups (r=0.61, 0.63, 0.71 and 0.69, respectively). No relationship between activity limitations and gait speed is found in SMA and FSHD groups. Activity limitations are significantly correlated with the grip strength only in the proximal NMD with a higher correlation in the SMA group (r=0.86 and 0.82) than in the DMD/BMD/LGMD group (r=0.53 and 0.59). No relationship between activity limitations and grip strength is found in the HN, MD, FSHD and ALS groups.
Figure 1a: Relationships between activity limitations measured by the ACTIVLIM questionnaire and gait speed, for the six main diagnosis groups (Duchenne, Becker and limb-girdle muscular dystrophy (DMD/BMD/LGMD), hereditary neuropathy (HN), myotonic dystrophy (MD), Facio-scapulo-humeral muscular dystrophy (FSHD), spinal muscular atrophy (SMA) and amyotrophic lateral sclerosis (ALS)). The Pearson correlation coefficients between activity limitations and gait speed are reported in the lower right corner of each figure. Significance level of the correlation coefficients are also indicated (* for p-value < 0.05 and ** for a p-value < 0.001). Wheelchair-bound patients are not represented in this figure. The dotted lines show a z-score of 2 and a z-score of -2, the limits between which a patient obtained a z-score not significantly different from normal values.
Figure 2b: Relationships between activity limitations measured by the ACTIVLIM questionnaire and grip strength in the right hand (▼) and grip strength in the left hand (▲) for the six main diagnosis groups (Duchenne, Becker and limb-girdle muscular dystrophy (DMD/BMD/LGMD), hereditary neuropathy (HN), myotonic dystrophy (MD), Facio-scapulo-humeral muscular dystrophy (FSHD), spinal muscular atrophy (SMA) and amyotrophic lateral sclerosis (ALS)). The Pearson correlation coefficients between activity limitations and grip strength in right hand (rGSr) and grip strength in left hand (rGSl) are reported in the lower right corner of each figure. Significance level of the correlation coefficients are also indicated (* for p-value < 0.05 and ** for a p-value < 0.001). The dotted lines show a z-score of 2 and a z-score of -2, the limits between which a patient obtained a z-score not significantly different from normal values.

Figure 2 shows the relationship between gait speed, grip strength and activity limitations in the total sample of patients with NMD. Activity limitations are significantly but poorly correlated with the grip strength in both hands (r = 0.3 and 0.36) and moderately correlated with gait speed (r = 0.56). Patients with an activity level lower than -2 logits have no z-score for gait speed (Figure 2 upper panel) because these patients are wheelchair-bound.
Figure 2: Relationships between activity limitations measured by the ACTIVLIM questionnaire and gait speed (upper panel), grip strength in the right hand (middle panel) and grip strength in the left hand (lower panel) for all patients of the sample. Correlation coefficients are all significant with a p-value < 0.001. The dotted lines show a z-score of 2 and a z-score of -2, the limits between which a patient obtained a z-score not significantly different from normal values.
Chapter 2: Motor impairments and their relationships with activity limitations

The relationships between the MMT and activity limitations are reported in Table 3. The MMT of all muscles groups are strongly correlated with the activity limitations in patients with DMD/BMD/LGMD while in patients with HN, the MMT and the activity limitations are poorly correlated. In patients with MD, the MMT of the distal muscles of the upper and the lower limbs are more correlated with activity limitations than the proximal muscles groups. In patients with SMA, the MMT of the distal muscles of the upper limbs are strongly correlated with activity limitations. As for patients with ALS and FSDH, the highest correlations between MMT and activity limitations are located in the distal muscles of the lower limbs.

In the total sample, the flexor and the proximal muscle groups tend to have a stronger relationship with the activity limitations (range: $p = 0.50$ to $0.44$) than the extensor and the distal muscle groups.

### Table 3: Spearman’s coefficients of correlation between activity limitations and MMT

<table>
<thead>
<tr>
<th></th>
<th>DMD/BMD</th>
<th>HN°</th>
<th>MD°</th>
<th>FSHD°</th>
<th>SMA°</th>
<th>ALS°</th>
<th>Total sample</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>n = 45</td>
<td>n = 44</td>
<td>n = 37</td>
<td>n = 11</td>
<td>n = 14</td>
<td>n = 18</td>
<td>n = 245</td>
</tr>
<tr>
<td><strong>Upper limb proximal muscles</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shoulder flexion</td>
<td>0.73**</td>
<td>0.27</td>
<td>0.23</td>
<td>0.59</td>
<td>0.45</td>
<td>0.51*</td>
<td>0.47**</td>
</tr>
<tr>
<td>Shoulder abduction</td>
<td>0.61**</td>
<td>0.20</td>
<td>0.30</td>
<td>0.66*</td>
<td>0.25</td>
<td>0.38</td>
<td>0.43**</td>
</tr>
<tr>
<td>Elbow flexion</td>
<td>0.75**</td>
<td>0.25</td>
<td>0.24</td>
<td>0.53</td>
<td>0.56*</td>
<td>0.10</td>
<td>0.48**</td>
</tr>
<tr>
<td>Elbow extension</td>
<td>0.68**</td>
<td>0.26</td>
<td>0.39*</td>
<td>0.40</td>
<td>0.29</td>
<td>0.05</td>
<td>0.40**</td>
</tr>
<tr>
<td><strong>Upper limb distal muscles</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist flexion</td>
<td>0.43*</td>
<td>-0.16</td>
<td>0.42**</td>
<td>0.01</td>
<td>0.88**</td>
<td>0.18</td>
<td>0.27**</td>
</tr>
<tr>
<td>Wrist extension</td>
<td>0.45*</td>
<td>-0.02</td>
<td>0.34*</td>
<td>0.10</td>
<td>0.88**</td>
<td>0.06</td>
<td>0.34**</td>
</tr>
<tr>
<td>Finger flexion</td>
<td>0.62**</td>
<td>0.03</td>
<td>0.35*</td>
<td>0.01</td>
<td>0.93**</td>
<td>-0.02</td>
<td>0.17**</td>
</tr>
<tr>
<td>Finger extension</td>
<td>0.73**</td>
<td>-0.07</td>
<td>0.53**</td>
<td>0.35</td>
<td>0.94**</td>
<td>0.10</td>
<td>0.31**</td>
</tr>
<tr>
<td>Interossei</td>
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<td>0.21</td>
<td>0.46**</td>
<td>-0.50</td>
<td>0.95**</td>
<td>0.20</td>
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<td><strong>Lower limb proximal muscles</strong></td>
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<tr>
<td>Hip flexion</td>
<td>0.59**</td>
<td>0.04</td>
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<td>0.50</td>
<td>0.73*</td>
<td>0.37</td>
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<td>Hip flexion</td>
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<td>-0.03</td>
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<td>0.47</td>
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<td>0.02</td>
<td>0.35*</td>
<td>0.69*</td>
<td>0.58</td>
<td>0.42</td>
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<td>Knee extension</td>
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<td>0.18</td>
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<td>0.73*</td>
<td>0.66*</td>
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<tr>
<td>Toe extension</td>
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<td>-0.03</td>
<td>0.99*</td>
<td>0.35**</td>
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<tr>
<td>Toe flexion</td>
<td>0.83**</td>
<td>0.36</td>
<td>0.14</td>
<td>0.01</td>
<td>0.32</td>
<td>0.89**</td>
<td>0.48**</td>
</tr>
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</table>

° DMD = Duchenne Muscular Dystrophy, BMD = Becker Muscular Dystrophy, LGMD = Limb-Girdle Muscular Dystrophy, HN = Hereditary Neuropathy, MD = Myotonic Dystrophy, ALS = Amyotrophic Lateral Sclerosis, SMA = Spinal Muscular Atrophy, FSHD = Facio-Scapulo-Humeral Dystrophy.

* 0.05<p<0.01, ** p<0.01
2.4. Discussion

Motor impairments and their relationships with activity limitations as assessed by the ACTIVLIM questionnaire were investigated in six main diagnosis groups of NMD and in 245 patients all diagnoses taken together. Sixty percent of the walking patients presented gait speed impairment, 47 percent presented grip strength impairment in both hands and 92 percent of the patients presented weakness of at least one muscle group. Gait speed was significantly correlated to activity limitations in DMD/BMD/LGMD, HN, MD and ALS groups while the grip strength was significantly correlated to them in DMD/BMD/LGMD and SMA groups. The correlations between MMT and activity limitations largely varied according to muscle groups and to diagnosis groups (range: $\rho = -0.5$ to 0.95). In the whole sample, activity limitations were moderately correlated with gait speed ($r=0.56$) and poorly correlated with grip strength in both hands ($r=0.3$ and 0.36). The Spearman’s coefficients of correlation between the MMT and activity limitations were moderate to very poor ($\rho=0.5$ to 0.17).

2.4.1. Motor impairments

The prevalence of motor impairment according to the type of NMD found in our sample (Table 2) corresponded to the pattern described in the literature for each diagnosis group.

The principal motor impairment in the DMD/BMD/LGMD are located in the proximal muscles of the upper and the lower limbs, which is consistent with others studies (Kilmer et al., 1993, McDonald et al., 1995a, McDonald et al., 1995b, Mc Donald et al., 1995c). These authors found that the proximal muscle groups were weaker than the distal muscle groups. Moreover, they highlighted the fact that the muscles of the lower limbs are weaker than the muscles of the upper limbs for the patients with DMD and BMD (Mc Donald et al., 1995 a and 1995b). In the present study, the proportion of patients presenting impaired lower and proximal MMT (77% to 96%) are higher than the proportion of patients presenting impaired upper and proximal muscles MMT (56% to 78%).
In patients with HN, the distal muscles of the lower limbs and the interossei muscles were principally impaired. These results confirmed those of others studies (Carter et al., 1995b) who found that the distal muscle groups were weaker than the proximal ones. Moreover, the shoulder muscles were nearly not affected in their sample such as in our sample. Other authors found similar proportions of patients with impaired ankle dorsiflexors, ankle plantar flexors and toe extensors than in our sample (Teunissen et al., 2003). Nevertheless, only 30% of their patients presented an MMT of the interossei muscles below the grade of 5 while 64% of the patients presented this motor impairment in our sample.

The grip strength in both hands is the principal motor impairment of patients with MD in our sample (87% and 81% for right and left hand, respectively). Others authors found that their 36 patients with MD were significantly weaker in grip strength than normal population (Nitz et al., 1999). The mean and standard deviation of grip strength, also assessed with the Jamar dynamometer, was of $103 \pm 66$ N, which is very similar of the values found in our sample of 37 patients ($\text{mean} \pm \text{SD}: 117 \pm 75$ N). In the present study, the distal muscles of the upper and the lower limbs were the most impaired muscles, what confirmed previous observations of (Nitz et al., 1999). However, another study highlighted that weakness were generalized in all muscle groups (Johnson et al., 1995) but the authors did not assessed the finger and toe muscles.

All patients with FSHD presented an impaired MMT of the shoulder muscle groups and the proximal muscles of the lower limbs are more impaired than the distal ones. Kilmer et al. (Kilmer et al., 1995) found similar results with a greater involvement of the proximal muscle groups; they also noticed that the ankle dorsiflexors were weaker than the ankle plantar flexors just like the results in our sample. The principal motor impairments in patients with SMA were located in the proximal muscle groups with a higher proportion of patients with impaired proximal muscles in the lower limbs (70% to 91%). Our results confirmed those of others studies (Carter et al., 1995a, Kroksmark et al., 2001). The motor impairments in
patients with ALS were principally located in the distal muscle groups, which is consistent with the results of another study (Jette et al., 1999).

The gait speed was the main motor impairment found in the 245 patients with NMDs. Indeed, 31% of the 245 patients were wheelchair-bound and 60% of the 169 walking patients presented gait speed impairment. Reduced walking speed could be attributable to muscle weakness of the lower limbs (Lohmann Siegel et al., 2004). In our data, muscle strength of the lower limbs was more impaired than the muscle strength of the upper limbs according to the proportion of patients presenting an impaired MMT (Table 2). Previous study suggested that walking speed is weakly associated with the strength of a single muscle of the lower limbs and that each muscle group has a relatively equal influence on walking speed (Willén et al., 2004). When the MMT of the lower limbs was correlated with walking speed in our data, the values of the Spearman’s coefficients of correlation ranged from 0.23 to 0.34 confirming the suggestions of this previous study (Willén et al., 2004). Moreover, as proximal and/or distal weakness in the lower limbs could lead to impaired gait speed, these observations are totally consistent with the heterogeneity of our sample. Indeed, the present sample consisted of pathologies with predominant weakness in proximal muscles of lower limbs such as DMD, BMD, LGMD, SMA and FSHD and pathologies with predominant weakness in distal muscles such as HN, MD and ALS.

Forty-seven percent of the patients presented grip strength impairment that can be partly attributable to hand muscle weakness (Kozin et al., 1999). Indeed, in our data, the MMT scores of the fingers flexors, fingers extensors and interossei are related to grip strength with correlation coefficients of 0.6, 0.47 and 0.43, respectively. Nevertheless, more patients show grip strength impairment (60 % for the right hand and 53 % for the left hand) than patients presenting weakness in the hand muscles (33% for fingers flexors, 44% for fingers extensors and 49% for interossei muscles). This difference can be explained by the fact that other intrinsic hand muscles not tested with the MMT in our study could also influence the grip strength (Kozin et al., 1999). Moreover, the Jamar dynamometer is an objective and linear measure that is more sensitive to small strength decrease than the ordinal scores of MMT (Schwartz et al., 1992).
2.4.2. Relationships between motor impairments and activity limitations

The measure of the gait speed spontaneously adopted by the patients showed the highest correlation with the ACTIVLIM measures (figure 2, upper panel) among all motor impairments. The spontaneous gait speed was considered as a measure of locomotor impairment (Bernardi et al., 1999) and calculated from the 10-m walking test. However, this test is in some way on the border between the components “body function and structure” and “activity” of the ICF since it can also reflect the difficulties in performing an activity such as walking (WHO, 2001). This link between the measure of gait speed and the activity limitations measured by ACTIVLIM could explain their good correlation. Moreover, the walking activity is largely represented in the ACTIVLIM measures since five items out of the 22 ones included in the questionnaire are directly related to the walking ability of the patient. Nevertheless, despite this best correlation between gait speed and activity limitations as measured by the ACTIVLIM questionnaire, the measure of gait speed could only explain just over 30% of the ACTIVLIM measure variance (i.e. r²=0.31). Lastly, the gait speed can just give a measure for walking patients while the ACTIVLIM measures can also distinguish the activity level of wheelchair-bound patients.

The gait speed was moderately correlated with activity limitations in patients with DMD/BMD/LGMD, HN, MD and ALS (r= 0.61 to 0.71 on figure 1a). These correlations could partially be explained by the weakness in the proximal muscles of lower limbs in patients with DMD/BMD/LGMD and by the weakness in the distal muscles of the lower limbs in patients with HN and ALS. Proportions of patients with MD presenting muscle weakness in the lower limbs (Table 2) are, however, quite low. Reduced gait speed and its relationships with activity limitations could eventually be associated to daytime sleepiness, apathy or lack of motivation, which are clinical aspects frequently encountered in patients with MD (Rubinsztejn et al., 1998, van der Werf et al., 2003). No relationship was found in patients with FSHD and SMA, probably due to the small number of walking subjects in each of these diagnosis groups (7 and 4, respectively).
Grip strength in both hands was poorly correlated to the activity limitations as measured by the ACTIVLIM questionnaire (Figure 2, middle and lower panel). Nevertheless, grip strength seems to be an indicator of the global state of the patients with NMD. On Figure 2, patients with an activity level below -2 logits systematically presented grip strength impairment since they lie below -2 z-score on the grip strength axis, and these patients are also wheelchair-bound. Others authors already observed that wheelchair-bound patients with SMA presented significantly lower grip strength than walking patients with SMA (Merlini et al., 2004). In other words, patients with normal grip strength are probably not wheelchair-bound and therefore have a high probability to report an activity level above -2 logits.

The grip strength was moderately correlated with activity limitations in patients with DMD/BMD/LGMD (r=0.53 and 0.59) and strongly correlated with activity limitations in patients with SMA (r=0.86 and 0.82) indicating that the grip strength could be an indicator of the activity level in these patients, or it rather reflects the global state of these patients. On the other hand, no correlation was found between these both variables in patients with HN, MD, FSHD and ALS indicating that impaired grip strength does not necessarily exclude a high level of activity. The onset of HN, MD and ALS is often characterized by hand and finger muscle weakness (Pareyson, 2004, Schara & Schoser, 2006, Mitchell & Borasio, 2007) that can be detected by grip strength impairment (Kozin et al., 1999) without affecting the activity level of the patients yet.

The relationships between activity limitations and muscle strength measures are poor to moderate in the total sample indicating that high levels of activity do not necessarily require full muscle strength. Indeed, the MMT is an analytical measure while the achievement of daily activities is a combination of movements involving several muscle groups. Moreover, patients with muscle weakness can develop compensatory strategies that allow them to complete daily activities without human or technical help and to have, consequently, a higher activity measure.
The disparity of the Spearman’s correlation coefficients between MMT and activity limitations reflected the discrepancies of anatomical basis and physiopathology of the NMD. These differences are the most obvious between the DMD/BMD/LGMD, the HN and MD groups, each of them including almost the same number of patients (n=45, 44 and 37 respectively) and therefore allowing some comparisons in the values of the correlation coefficients. In patients with DMD, BMD or LGMD, each MMT is significantly correlated with the activity level with values ranging from 0.43 till 0.83, in the HN group only the MMT of the knee flexors is moderately correlated with the activity level (ρ=0.45), and in the MD group, distal limb muscle groups are poorly to moderately correlated with the activity level (ρ=0.34 to 0.53). The activity level of patients with DMD/BMD/LGMD seems to be more dependent of the muscle weakness than the one of patients with HN or with MD. Indeed, unlike DMD/BMD/LGMD group, the muscle weakness and atrophy are not the only clinical signs in these latter groups, the sensory loss and feet deformities of in HN and myotonia, daytime sleepiness or lack of motivation in MD could also influence the difficulties in performing daily activities as assessed by the ACTIVLIM questionnaire (Pareyson, 2004, Schara & Schoser, 2006, Rubinsztein et al., 1998). Very strong correlations between MMT and activity limitations were found in the wrist and hand muscle groups of patients with SMA, in ankle and toe extensors of patients with FSHD and in toe flexors in patients with ALS. Nevertheless, the small number of patients (n=14, 11 and 18 respectively) leads to be cautious in the interpretation of these results.

Despite the moderate correlations between muscle strength measures and activity limitations, the values of the correlation coefficients in the whole sample are consistent with the daily activities included in ACTIVLIM (Vandervelde et al., 2007). On the one hand, the correlations of the MMT of the flexors and proximal muscles groups with the ACTIVLIM measure emphasize the need to use these muscles to achieve the 22 daily activities of ACTIVLIM. For instance, washing one’s face and putting on a T-shirt require functional shoulder and elbow flexors to be easily performed. Similarly, when walking upstairs or stepping out of a bath tub, functional hip and knee flexors are needed to lift the legs. On the other hand, the
items of ACTIVLIM do not include activities requiring hand and finger strength with the result that grip strength measures and MMT scores of the hands and wrists have the lowest correlation with the ACTIVLIM measures.

The main limitation of this study is the lack of regression analysis allowing motor impairments to be combined in order to predict the highest proportion of the variance in measures of activity limitations. Multiple linear regression analysis cannot be performed in this study because of the ordinal non-parametric nature of the data. To get round this problem, non-parametric regression could be used but a larger sample would be necessary to obtain conclusive results. Measuring muscle strength with a quantitative technique as the quantitative muscle testing (QMT) could be another method allowing linear regression to be performed. Indeed, the QMT presents the great advantage of being a linear measure, but it is also recognized to be a more objective and sensitive measure of muscle strength than the MMT scores (Aitkens et al., 1989, Mendell & Florence, 1990). These further analyses could be interesting in the whole sample but also in the different diagnosis groups.

Although all motor impairments were significantly related to a decrease in activity level, their relationships were poor to moderate with the measure of activity limitations. It does not mean that clinical tests such as MMT, grip strength test or the 10-meter walking test are useless but they cannot precisely predict what the patients can perform as daily activities in their usual environment. For this reason, activity limitations should be measured separately. This result supports the theoretical standpoint of the ICF that motor impairments and activity level are not related in a predictable straightforward relationship (WHO, 2001). Although this relationship was rarely investigated in patients with neuromuscular disorders, our observations confirm other studies (Nair et al., 2001, Uchikawa et al., 2004, Merkies et al., 2003). In patients with immune mediated polyneuropathies, 64 % of the variance of the disabilities was explained by impairment measures (Merkies et al., 2003). In patients with DMD, correlations between strength measures and functional ability assessed
by the Functional Independence Measure or the Barthel Index ranged from 0.39 to 0.56 (Nair et al., 2001, Uchikawa et al., 2004). Therefore, the reduction of motor impairments could contribute to but not totally predict a corresponding higher activity level. Consequently, interventions focused on daily activities should continue to be the most important aim in patient rehabilitation in order to preserve the patient’s independence as long as possible (Siegel, 1981, Fowler, 1982). An ideal intervention should always endeavor to coordinate physical therapy for its key role in preventing muscle strength decrease and joint immobility and occupational therapy for its key role in the management of meaningful daily activities. Teaching patients how to optimize their motor function should be an important part of the rehabilitation since it can help the patients developing adaptive strategies to compensate their motor impairments (Kakulas, 1999).

The present study stressed the importance to treat and measure activity level independently as it is not simply the integration of motor function in daily activities. Consequently, interventions intended to reduce motor impairments are rather complementary to those intended to improve patients’ activity levels.
Chapter 3:
Responsiveness study of the ACTIVLIM questionnaire

Abstract
Recently, a self-reported scale of activity limitations, ACTIVLIM, was developed and validated in patients with neuromuscular disorders (NMD). The purpose of this study was to investigate its sensitivity to change. One hundred thirty-two patients with NMD were assessed twice, with 21 ± 4 months in between, using the ACTIVLIM questionnaire. Mean score change, effect size, standardized response mean paired t-test and an individual-level statistical approach were calculated for groups of patients according to their self-rated functional status evolution and for three diagnostic groups (Duchenne muscular dystrophy, myotonic dystrophy, Charcot-Marie-Tooth neuropathy). The responsiveness indices showed that the change in activity measures was higher in patients who reported deteriorated functional status and in patients with Duchenne muscular dystrophy. The clinical significance of change represented about 1 logit, which corresponds to about 10% of the ACTIVLIM measurement of change. The ACTIVLIM questionnaire showed a good sensitivity to change and could be useful in clinical and research settings to characterize the disease course of NMD.

This chapter is a modified version of the paper submitted as:
3.1. Introduction

Most neuromuscular disorders (NMD) have a progressive clinical course characterized by a decrease in muscle strength leading to impaired motor function (Piccininni et al., 2004). Consequences of these diseases include fatigue, problems with locomotion and loss of functionality in daily activities. Difficulties in performing daily activities are defined by the World Health Organization as activity limitations (WHO, 2001). Activity limitations in patients with NMD can be measured with a new scale, ACTIVLIM, which was recently developed and validated using the Rasch model (Vandervelde et al., 2007). This questionnaire presents excellent psychometric qualities, including reliability, construct validity, reproducibility, linearity and unidimensionality. Nevertheless, its sensitivity to change has not yet been studied. Sensitivity to change, or responsiveness, is defined as the ability of an instrument to detect important changes over time (De Bruin et al., 1997) and is a required psychometric quality for any instrument to be used in clinical trials and research designs (Wright & Young, 1997, Hsueh & Hsieh, 2002).

The purpose of this study was to investigate the responsiveness of the ACTIVLIM questionnaire in patients with NMD. The systematic use of a sensitive questionnaire dedicated to patients with NMD could help characterizing the clinical course of the disorders and quantifying the effects of new treatments on their activity limitations. As there is no consensus how best to assess the sensitivity to change of measures, responsiveness will be investigated in terms of statistical significance and in terms of clinical significance.

3.2. Patients and methods

3.2.1. Patients

This study was approved by the Medical Ethics Committees of the Université catholique de Louvain and the Katholieke Universiteit Leuven. The patients were recruited through the neuromuscular reference centers of two
university hospitals. Adult patients and the parents of affected children gave written informed consent before evaluation. Fifty-three children (41 boys and 12 girls; mean age: 10 years) and 79 adults (48 men and 31 women; mean age: 44 years) diagnosed with NMD were included in this study. Three main diagnostic groups were indentified, each of them including more than 10% of the patients: Duchenne muscular dystrophy (DMD) (n=27, i.e., 20% of total sample, 6-25 years), Charcot-Marie-Tooth neuropathy (CMT) (n=20, i.e., 15 % of total sample, 7-50 years) and myotonic dystrophy with adult onset (MD) (n=17, i.e., 13% of total sample, 16-72 years). The patients not belonging to one of these groups were affected by another NMD such as Becker or limb-girdle muscular dystrophy, spinal muscular atrophy or post-polio syndrome. The patients did not receive any particular treatment other than physical therapy or, for instance, drugs to ease pain.

3.2.2. Procedure

Patients were assessed twice, with 21 ± 4 months in between (range: 11-27 months), using the ACTIVLIM questionnaire. This questionnaire consists of 22 daily activities presented in the questionnaire development study (Vandervelde et al., 2007), and it was originally developed using the Rasch model, which allows the conversion of ordinal scores into linear measures located on a unidimensional scale (Rasch, 1980). These linear measures are expressed in logits (i.e., log-odd units), the constant measurement unit of the activity scale; for this scale, a higher value in logits corresponds to a higher activity level of the patient.

The first (t1) and second (t2) activity measures were obtained by asking the adult patients and the parents of the affected children to note the difficulty they perceived in performing each activity on the ACTIVLIM questionnaire, without using technical or human help. The questionnaire had a three-level scale: (0) impossible, (1) difficult and (2) easy. Moreover, during the second evaluation, patients were asked to provide personal perceptions of their functional status evolution since the first evaluation: (a) improvement, (b) stability or (c) deterioration.

Chapter 3: Responsiveness of the ACTIVLIM questionnaire 83
3.2.3. Data analysis

The responses of both evaluations were first fitted to the Rasch model using the Rasch Unidimensional Measurement Models computer program (RUMM2020, RUMM Laboratory Pty Ltd, Perth, Western Australia). This software reported overall fit statistics that were close to the standardized normal distribution for item and person fit residuals. The mean and standard deviation of the item fit residuals were -0.324 ± 0.684 and -0.292 ± 0.332 for t1 and t2, respectively, while the mean and standard deviation of the person fit residual were -0.318 ± 0.810 and -0.263 ± 0.706 for t1 and t2, respectively. Moreover, the chi-square item-trait interactions were not significant (p=0.13 and 0.98 for t1 and t2, respectively). As a result, the ordinal total scores obtained from the ACTIVLIM questionnaire could be transformed into interval-level measures of activity limitations. Two linear measures of the patient’s activity level (t1 and t2) were reported in such a way that they could be quantitatively compared and treated as a continuous variable. Moreover, standard errors of measurement associated with the activity level of each patient were displayed by the software.

a) Statistical method

The sensitivity to change of the ACTIVLIM questionnaire was first statistically tested according to both group-level and individual-level approaches. The group-level approach consisted of computing different responsiveness indices in groups of patients. In this study, groups of patients were constituted according to two criteria. The first criterion concerned a self-reported functional status evolution (improvement, stability or deterioration) and responsiveness indices were expected to be higher in groups of patients who reported an improved or deteriorated functional status than in patients who reported a stable functional status. The second criterion was concerned the natural evolution of patients included in the three main diagnoses in our sample (DMD, CMT and MD), constituting 48% of the total sample. The changes in activity limitations observed in patients from these three diagnosis groups were compared in order to determine whether they are supported by the natural evolution known in these patients. Because there is no agreement...
regarding how best to assess the sensitivity to change of measures, this study reported the most frequently cited indices in responsiveness studies (Middel & van Sonderen, 2002). Paired t-test, effect size and standardized response mean were calculated in each group of functional status evolution and in the three diagnostic groups. Paired t-tests were used to detect statistically significant changes in activity level between the first and the second evaluation. The null hypothesis was rejected when the p-value was below 0.05. However, paired t-tests are sensitive to sample size, and different sample sizes can lead to different decisions in terms of significance (Middel & van Sonderen, 2002). Effect size, on the other hand, enabled the comparison of responsiveness between different studies or outcome measures by standardizing the change effect in units of standard deviation without influence from the sample size (Middel & van Sonderen, 2002). Effect size (ES) is calculated according to the formula:

\[
ES = \frac{\text{mean change}}{SD_{t1}}
\]

where \(SD_{t1}\) corresponds to the standard deviation of the measures at the first evaluation. Consequently, effect size was sensitive to the distribution of the measures obtained during the first evaluation. Standardized response mean also standardized the change in the same units independent of sample size but also incorporated information about change distribution (Liang et al., 1990). Standardized response mean (SRM) is:

\[
SRM = \frac{\text{mean change}}{SD_{\text{change}}}
\]

where \(SD_{\text{change}}\) is the standard deviation of the change scores.

Higher effect sizes and standardized response means correspond to a higher magnitude of change between both evaluations.

The individual approach to testing sensitivity to change of the ACTIVLIM questionnaire consisted of taking into account the standard error of measurement associated with the patient’s activity level obtained during both evaluations. A
statistic for each patient could be computed to test the extent to which the activity measures had changed (Wright & Stone, 1979):

\[ t_{m12} = \frac{m_1 - m_2}{\sqrt{(SE_1)^2 - (SE_2)^2}} \]

where \( m_1 \) and \( m_2 \) are the activity measures at the first and the second evaluation, respectively, and \( SE_1 \) and \( SE_2 \) are their associated standard errors of measurement. Moreover, the distribution of this \( t \) statistic is approximately a standardized normal distribution (Wright & Stone, 1979). Therefore, patients with a \( t \) statistic above 1.96 or below -1.96 will show a significantly improved or deteriorated activity level, respectively.

b) Clinical significance of change

Responsiveness also implies the ability to detect clinical important change (Guyatt et al., 1987). To assess this clinical significance of change, Sloan et al. summed up two principal methods (Sloan et al., 2003). The first one estimates a minimal clinically important difference (MCID) using, among others, a patient self-report global rating of change. This estimation of MCID was based upon the definition of Juniper et al., which defined the MCID as “the smallest difference in score which patients perceived as beneficial…” (Juniper et al., 1994). The mean change in patients who reported a “small change” can therefore be considered as the MCID (Sloan et al., 2003). The second method, the empirical rule of effect size method (ERES), is a direct modification of the effect size approach. Based upon the fact that 99% of any normal distribution falls into three standard deviations (SD) of the mean and that the measurement range of any instrument theoretically transformed into a range 0 to 100 can be represented by six SD, one SD could therefore correspond to 17% (i.e. 100/6) of the measurement range (Sloan et al., 2003). The ERES method, then, defines the clinical significance of change as one half SD according to Cohen’s classification system of effect size (0.2 times the SD = small change, 0.5 times the SD = moderate change, and 0.8 times the SD = large change) (Sloan et al., 2003).
3.3. Results

The mean activity level of the 132 patients was $1.18 \pm 2.71$ logits at t1 and $0.48 \pm 2.93$ logits at t2, indicating that the overall activity level of patients with NMD significantly decreased after $21 \pm 4$ months (paired t-test, $t=6.6$, $p<0.001$). Effect size and standardized response mean were 0.25 and 0.57, respectively.

3.3.1. Group approach

a) Functional status evolution groups

Seven patients did not answer the question about their functional status evolution. Sixty-one patients reported a deteriorated functional status between both evaluations, and 60 patients reported a stable functional status. As only 4 patients reported an improved functional status, no responsiveness indices were calculated in this group of patients. Figure 1 (left panel) shows the means and the standard deviations of the activity levels at t1 and t2 in patients who reported a stable or deteriorated functional status. Table 1 reports the responsiveness indices of the ACTIVLIM questionnaire in both of these groups. The change in activity level was higher in the group of patients who reported a deteriorated functional status than in the group of patients with stable functional status ($-1.1$ logits and $-0.35$ logits, respectively). The effect size, standardized response mean and paired t-test confirmed these observations.

b) Diagnostic groups

Figure 1 (right panel) shows the means and the standard deviations of the activity levels at t1 and t2 in the three main diagnostic groups present in our sample (DMD, MD and CMT). Table 1 reports the responsiveness indices in these groups. The change in activity level was higher in the group of patients with DMD than in the groups of patients with MD or CMT ($-1.18$ logits, $-0.77$ logits and $-0.08$ logits, respectively). The responsiveness indices confirmed these observations.
Activity limitations in patients with neuromuscular disorders

**Figure 1:** Means and standard deviations of the activity levels expressed in logits at first evaluation (t1) and second evaluation (t2) in patients with stable and deteriorated functional status (left panel) and in patients with Duchenne muscular dystrophy (DMD), myotonic dystrophy (MD) and Charcot-Marie-Tooth neuropathy (CMT) (right panel).

**Table 1: Responsiveness indices based on group approach**

<table>
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<th>DMD*</th>
<th>MD*</th>
<th>CMT*</th>
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<td>Deteriorated n=61</td>
<td>DMD* n=27</td>
<td>MD* n=17</td>
</tr>
<tr>
<td>Mean change (logits)</td>
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<td>-1.1</td>
<td>-1.18</td>
</tr>
<tr>
<td>Paired t-test</td>
<td>p=0.02</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Effect size</td>
<td>0.12</td>
<td>0.46</td>
<td>0.41</td>
</tr>
<tr>
<td>Standardized response mean</td>
<td>0.3</td>
<td>0.88</td>
<td>0.81</td>
</tr>
</tbody>
</table>

*DMD = Duchenne muscular dystrophy, MD = myotonic dystrophy, CMT = Charcot-Marie-Tooth neuropathy

### 3.3.2. Individual approach

The values of the t statistic obtained by each patient could be divided into five classes, according to limits of significance: (1) $t > 1.96$, (2) $1.96 > t > 0$, (3) $t = 0$, (4) $0 > t > -1.96$ and (5) $t < -1.96$. Table 2 reports the proportions of patients in
each of these classes and according to their self-reported functional status evolution or their diagnosis. The proportion of patients with a significant deterioration was higher in patients who reported a deteriorated functional status than in patients who reported a stable functional status (36.1% and 11.7%, respectively). Similarly, this proportion was also higher in patients with DMD than in patients with MD or CMT (44.5%, 11.8% and 5%, respectively).

<table>
<thead>
<tr>
<th>Functional status evolution</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable n=60</td>
<td>Deteriorated n=61</td>
</tr>
<tr>
<td>Significant improvement, %</td>
<td>1.7</td>
</tr>
<tr>
<td>Improvement, %</td>
<td>25</td>
</tr>
<tr>
<td>No change, %</td>
<td>18.3</td>
</tr>
<tr>
<td>Deterioration, %</td>
<td>43.3</td>
</tr>
<tr>
<td>Significant deterioration, %</td>
<td>11.7</td>
</tr>
</tbody>
</table>

*DMD = Duchenne muscular dystrophy, MD = myotonic dystrophy, CMT = Charcot-Marie-Tooth neuropathy

### 3.3.3 Clinical significance of change

The MCID were assessed in patients who reported a deteriorated functional status. The mean change in this patient group is equal to 1.1 logits (Table 1).

As the range of the ACTIVLIM measures is equal to 12 logits, one theoretical SD corresponds to 2 logits (i.e. 17% of 12 logits). The ERES method therefore defines the clinically significant change as equivalent to 1 logit (i.e. a moderate change is equivalent to 0.5 times the SD).
3.4. DISCUSSION

The sensitivity to change of the ACTIVLIM questionnaire was investigated in 132 patients with NMD. The activity level of the whole sample significantly decreased after 21 ± 4 months, confirming the progressive clinical course of the NMD (Piccininni et al., 2004, Cup et al., 2007).

The responsiveness study of the ACTIVLIM questionnaire was completed by group-level and individual-level approaches. In the group-level approach, different indexes were computed in groups of patients. First, patients were classified according to their self-reported functional status evolution. The change in the activity measures, the effect size and the standardized response mean were lower in patients who reported a stable functional status than in those who reported a deteriorated functional status between the two evaluations (Table 1). On the other hand, the paired t-test showed a p-value of 0.02 in patients with self-reported stable functional status, indicating a significant decrease of their activity level. Nevertheless, despite the fact that this change was statistically significant, the patients did not consider this change as clinically meaningful confirming the assertion that a significant p-value does not necessarily provide an indication of clinical significance of change (Kazis et al., 1989, Sloan et al., 2003). In other words, the change self-reported by the patients on the 22 items of the ACTIVLIM questionnaire was more sensitive than the overall change self-reported by the same patients.

The paired t-test and standardized response mean indicated that the ACTIVLIM questionnaire also showed a good sensitivity to change taking into account the diagnosis of the patients (Table 1). The change in activity measures was higher in patients with DMD than in patients with MD or with CMT, confirming the deterioration rate of these diseases. CMT is a slowly progressive NMD (Pareyson, 2004), while the DMD progression is faster, even fatal in the third decade of life when patients are not appropriately treated (Emery, 1998). As for the clinical course of MD with adult onset, it lies somewhere between CMT and DMD since patients could become severely disabled by their fifth or sixth decade of life (Schara &
Schoser, 2006). This analysis therefore demonstrated that the ACTIVLIM questionnaire could characterize the natural evolution of the principal NMD. However, effect size was identical in the DMD and MD groups (0.41 and 0.4, respectively), whereas these values did not reflect the same change in the activity measures in both these groups (-1.18 and -0.77, respectively). This is due to the fact that effect size is sensitive to the standard deviation of the initial scores, and in the present study, the distribution of these scores is wider in patients with DMD than in patients with MD (SD at t1: 2.90 and 1.93 logits, respectively). Consequently, effect size in the DMD group did not proportionally reflect its higher change in activity measures. Effect size should therefore be carefully interpreted and is not the more relevant indicator of the ACTIVLIM responsiveness in comparing both groups. Nevertheless, these effect sizes were higher than the effect size of the CMT group (0.04), allowing the change in ACTIVLIM measure of patients with DMD or MD to be compared with the change in patients with CMT. The use of the effect size has been largely debated in the literature, and some authors have firmly recommended that its use should be completed by appropriate statistical tests and associated p-values to avoid misinterpretation of the magnitude of change (Beaton et al., 2001, Cano et al., 2006, Middel & van Sonderen, 2002). In the present study, paired t-tests and standardized response means clearly reflect the sensitivity to change of the ACTIVLIM questionnaire when comparing groups of patients.

The responsiveness of ACTIVLIM was also investigated according to an individual-level approach because a standard error of measurement was associated with the activity measure of each patient. Table 2 shows that the proportion of patients with a significant decrease of activity level was higher in patients who reported a deteriorated functional status evolution (36.1%) and in patients with DMD (44.5%), which is consistent with the results of the group-level approach. Table 2 also shows a large proportion of patients with a deterioration of their activity level in each group of patients. This decrease in the ACTIVLIM measures, even if trivial, reflects the progressive clinical course of the NMD. For instance, 50% of patients with CMT experience a deterioration of their activity level, but the t statistics of these patients range from - 0.2 to - 1.01 and are far from the limit of - 1.96, confirming an insignificant change between both evaluations. However, the individual-level approach presents a considerable advantage compared to the group-
level approach since it could report whether the activity level of a particular patient has significantly improved or decreased. Indeed, meaningful change for groups of patients may not have the same significance for individuals (Beaton et al., 2001, Cella et al., 2002). Consequently, the individual-level approach provides clinicians an alternative method of drawing conclusions from group results to individuals. Results can henceforth be interpreted patient by patient.

Finally, the clinical significance of change was estimated by two methods from the data of this study: (1) the minimal clinically important difference (MCID) and (2) the empirical rule effect size (ERES). The theoretical clinical significance of change estimated by the ERES methods (1 logits) confirms the experimental clinical significance of change found with the MCID method (1.1 logits). This clinical significance of change corresponds to less than 10% of the ACTIVLIM measurement range (range: 12 logits), which is consistent with other studies that estimated the clinical significance of change to 8% of the total measurement range (Jaeschke et al., 1989, Juniper et al., 1992, Osoba et al., 1998). Nevertheless, as the patient global rating of change was not divided into “small”, “moderate” and “large” change in this study, the estimated MCID could be lower than 1.1 logits if the patients would have the opportunity to report a “small” change. This change of about 1 logit was also found in the DMD group (Table 1), which would indicate that the change in activity limitations measured in patients with DMD after a delay of about 21 months is clinically meaningful; while the change measured in patients with MD or CMT would be too small to have a clinical significance. This present study is a first approach to define the clinical significance of change in the ACTIVLIM measures. Further studies are may help refining the current results. The ACTIVLIM questionnaire could be used for instance in clinical trials to investigate the sensitivity to change in situations of potentially more rapid change than the natural evolution of the NMDs.

In conclusion, this study shows that the ACTIVLIM questionnaire has good potential to objectively characterize the disease clinical course of patients with NMD in terms of activity limitations. It can be a useful instrument in research settings to measure, for instance, the specific benefit of neuromuscular centers in...
care and follow-up treatment of the patients. Nevertheless, the clinical significance of change should be further refined.
**Discussion and perspectives**

Daily activities are, by definition, basic and essential tasks performed everyday in human life. Impaired motor function can partly impede the ability to achieve these activities, and neuromuscular disorders (NMD) have an impact on the motor function by virtue of the degeneration of the motor unit (McDonald, 2002). Consequences of these diseases include fatigue, locomotion problems, and loss of functionality in activities of daily living. Although the principal aim of rehabilitation is to prolong or maintain patients’ functional abilities in order to preserve their independence as long as possible (Siegel, 1981, Fowler, 1982, Jensen et al., 2005), conventional treatments are still mainly focused on motor impairments (Cup et al., 2007, Hornyak & Pangilinan, 2007). For instance, interventions endeavor to maintain or increase the strength in weakened muscles, improve mobility of the restricted joints, or preserve muscle endurance to minimize the feeling of fatigue (Hornyak & Pangilinan, 2007). This traditional approach is based on the assumption that reducing motor impairments will result in fewer difficulties in performing daily activities. Nevertheless, this supposition is not firmly supported by the International Classification of Functioning, Disability and Health (ICF) proposed by the World Health Organization (WHO) (WHO, 2001). Activity limitations are indeed the result of interactions between the subject’s health condition (i.e., neuromuscular disorders) and contextual factors. They are also related to impairments, but not by a predictable relationship (WHO, 2001). Additionally, the WHO advocates not just the separate evaluation of each component but also the study of relationships among them. Motor impairments, such as muscle strength or range of motion, are the most frequently assessed in patients with NMD (Haigh et al., 2001); their distribution, location, and severity are therefore well-described according to the type of NMD (Carter et al., 1995a, 1995b, Johnson et al., 1995, Kilmer et al., 1995, McDonald et al, 1995a, 1995b, 1995c). There is, however, a lack of available instruments for objectively assessing activity limitations in patients with NMD. Consequently, such a scale was
required in patients with NMD to describe the extent of their activity limitations and then to investigate their relationships with motor impairments.

The first study was carried out using the Rasch model to develop and validate a new scale of activity limitations in children and adults with NMD. This model enables the construction of unidimensional scales and transformation of raw scores, typically reported by questionnaires, into linear measures. A questionnaire, including daily activities, was submitted to the parents of 124 children with NMD and to 245 adult patients in French and Dutch communities. They were asked to identify the difficulty they perceived in performing each daily activity on a three-level ordinal scale (0 = impossible, 1 = difficult, or 2 = easy). The 22 items were selected by the Rasch model to form the final version of the ACTIVLIM questionnaire. They share the same ordered rating scale structure, fit a unidimensional scale and present no differential item functioning across age, gender, speech community and type of NMD. This new scale showed good construct validity because the ACTIVLIM measures of the patients were correlated with the Functional Independence Measure and the Vignos and Brooke grades; it also showed good test-retest reliability because the item difficulty hierarchy and the activity level self-reported by the children’s parents and by the adult patients were consistently assessed after a delay of about one month; and the ACTIVLIM is a unidimensional and linear scale because it was developed with the Rasch model. As this scale can assess children and adults with NMD along the same continuum of activity limitations, the evolution of abilities to perform daily activities can be quantified from childhood to adulthood. Moreover, this scale is common to all patients with NMDs, allowing the use of a single scale to follow patients in neuromuscular centers for instance or allowing comparisons between diagnosis groups.

The original version of the ACTIVLIM questionnaire was developed and validated in French and Dutch so that patients from both Belgian communities could be assessed using the same scale. The 22 items were selected with the condition that their difficulty hierarchy had to be estimated without significant difference by French- and Dutch-speaking patients because linguistic equivalence of the items
does not imply metric equivalence (Tesio, 2003). A caricatural example is the activity “cycling”. French-speaking patients had many more difficulties “cycling” than the Dutch-speaking patients because French-speakers live in a much hillier Belgian region than the Dutch-speakers. The ACTIVLIM questionnaire is also available in English and could be translated into other languages according to forward and backward translations of the items. As a result, studies on activity limitations in patients with NMD could be carried out at European or international levels, and results could be compared throughout different countries. Nevertheless, the item hierarchy should be invariant across cultures to obtain a cross-cultural measure of activity limitations in patients with NMD, just as one kilogram represents the same weight throughout the world. Differential item functioning tests, one feature of the Rasch model, is a suitable solution to this cultural equivalence condition (Wright & Stone, 1979, Smith, 1992).

Conceptually, the ACTIVLIM questionnaire assesses the difficulties in performing daily activities requiring the use of lower and/or upper limbs, and it does not include exclusively digital or manual activities. However, some NMDs, such as polynuropathies, present a clinical pattern of distal muscle weakness and atrophy (Pareyson, 2004) with an impact on the ability to achieve manual activities (e.g., cutting one’s nails, buttoning up a shirt, cutting meat, etc.). This impact could be quantified by evaluating manual ability in patients with NMDs. Manual ability, defined as the capacity to use the hands and upper limbs in managing manual daily activities (Penta et al., 2001), could be assessed by the ABILHAND scale. ABILHAND was previously developed and validated using the Rasch model in chronic stroke patients, in children with cerebral palsy, and in patients with rheumatoid arthritis (Penta et al., 2001, Arnould et al., 2004, Durez et al., 2007). The purpose of this additional study would be to calibrate the ABILHAND questionnaire in patients with NMD according to the same methodology applied for the development of the ACTIVLIM questionnaire. A common linear scale should apply for both children and adults with NMD, and the selected items should define the unidimensional construct of manual ability, be invariant across diagnostic groups, gender, language community and age, and have response categories well-discriminated by all patients.
As the ACTIVLIM questionnaire is constructed as a self-reported questionnaire, it raises two additional questions: (1) Why not trust the children’s responses instead of their parents’ responses? (2) Does the patients’ self-perception reflect what we could observe when they perform the ACTIVLIM activities? To answer to the first question, we compared the children’s and their parents’ responses using the Rasch model. We could highlight that the children did not discriminate the three response categories as well as their parents, providing a more dichotomous perception of their abilities, which led to a narrower range of measurement and a lower reliability index. Consequently, the parents’ responses provided a wider range of measurement of activity limitations in children with NMD. Moreover, the use of parents’ perceptions also allowed for the measurement of activity limitations of children with cognitive impairment, even though these are not a majority among the children with NMD (Emery, 1998, Sigford & Lanham, 1998, D’Angelo & Bresolin, 2006). For the second question, we found that adult patients’ perceptions were rather close to what examiners observed, indicating that the use of a self-reporting questionnaire is a valid method for measuring activity limitations in patients with NMDs. Besides being valid, reliable, reproducible, linear, and unidimensional, the advantages of using the ACTIVLIM questionnaire over observations are considerable; the questionnaire method is very simple, cheap, and above all time-saving. Such a study could also be carried out in children with NMDs. The difficulties the children experience during the performance of the 22 activities of the ACTIVLIM questionnaire could be observed by external examiners and then compared with the parents’ self-perceptions of these difficulties. Therefore, we could also validate the use of a self-reporting questionnaire completed by the parents to assess activity limitations in children with NMD.

The development of the ACTIVLIM questionnaire resulted in an instrument with very good psychometric qualities for measuring activity limitations in patients with NMD. The relationships between motor impairments and activity limitations were therefore investigated as the ICF suggests (WHO, 2001). Chapter 2 presents these relationships in six main diagnostic groups of NMD and in a sample of 245 patients with NMD without diagnosis distinction. Motor impairments consisted of...
strength measures (i.e., grip strength and manual muscle testing of 19 bilateral muscle groups) and gait speed measures. The manual muscle testing and gait speed are typical outcome measures used in patients with NMD (Brooke et al., 1981, Goldfarb & Simon, 1984, Lord et al., 1987, Barr et al., 1991, Fowler et al., 1995, Mathieu et al., 2001, Solari et al., 2008). Grip strength, however, is systematically assessed in patients with distal problems as patients with Charcot-Marie-Tooth neuropathy or with myotonic muscular dystrophy (Svensson & Häger-Ross, 2006, Whittacker et al., 2006). Prevalence of motor impairments observed in our study reflected the pattern of each diagnosis observed in other studies (Kilmer et al., 1993, Carter et al., 1995a, 1995b, Johnson et al., 1995, Kilmer et al., 1995, McDonald et al, 1995a, 1995b, 1995c, Nitz et al., 1999, Jette et al., 1999, Kroksmark et al., 2001, Teunissen et al., 2003) Activity limitations, as assessed by the ACTIVLIM questionnaire, and motor impairments were poorly related. Gait speed presented the highest correlation with the ACTIVLIM questionnaire, although it could only predict just over30% of the variance of the activity level. The clinical tests frequently used in patients with NMDs such as MMT, grip strength or gait speed are therefore not useless but the information that they provide is not sufficient to precisely predict how much the patients can perform daily activities. Consequently, activity limitations cannot be inferred directly from motor impairments and should be evaluated independently. The results confirm the theoretical standpoint of the ICF, that each component of a subject’s functioning (i.e., body structures and functions, activity and participation) does not interact in a predictable one-to-one relationship, since other factors (personal or environmental) also interfere with these components (WHO, 2001).

The conclusions of this study have some clinical implications. The therapist cannot rely on the reduction of motor impairments to directly result in a corresponding higher activity level. Consequently, interventions focused only on muscle strengthening and on joint mobility may be of debatable value, especially as the most important aim in rehabilitation for patients with NMD is to preserve independence in daily activities as long as possible (Fowler, 1982, Jensen et al., 2005, Siegel, 1981). An ideal intervention should always endeavor to coordinate physical therapy, for its key role in preventing muscle strength decrease and joint immobility, with occupational therapy, for its key role in managing meaningful daily
activities (Kakulas, 1999). Teaching patients how to optimize their existing motor function and teaching adaptive strategies should also be an important part of rehabilitation because this can help patients learn to compensate for their motor impairments (Penta et al., 2001, Arnould et al., 2007). Developing adaptive strategies, as well as proposing assistive devices, is particularly useful for patients with NMD since there is currently no treatment allowing total recovery of their motor function (Kakulas, 1999, Foster et al., 2006, Reilly et al., 2006, Talbot, 2007). Moreover, attention should be given to potential personal factors (e.g., motivation, personality) and environmental factors (e.g., patients’ incomes, family expectations, home adaptations, financial support) that increase difficulties in achieving daily activities (Schneidert et al., 2003, Stucki et al., 2003). Further research could identify which contextual factors influence activity limitations in patients with NMD to elucidate what can be changed to facilitate the achievement of daily activities (Law, 1993, Stucki et al., 2003).

Additional study of participation restrictions in patients with NMD is another goal. Participation has not yet been described in these patients, perhaps because it is a more subjective concept and, therefore, more difficult to assess (Carter et al., 2006). Moreover, no instrument has been validated so far to measure the extent of participation restrictions in patients with NMD. SATISPART, a questionnaire measuring satisfaction in participation in chronic stroke patients and developed with the Rasch model (Bouffioulx et al., submitted), could be calibrated and validated in patients with NMDs to generate an objective scale of participation. Subsequently, relationships among impairments, activity limitations, participation restrictions and contextual factors could be examined to develop an overall view of interactions between each pair of components of the ICF and to measure the impact of the NMD on the patient’s functioning. According to the International Classification of Impairments, Disabilities and Handicaps (ICIDH), the classification adopted by the WHO before the ICF, Merkies et al. (Merkies et al., 2003) showed in immune-mediated polyneuropathies that impairments and disability measures predict 52 % and 76 % of the variance in handicap scores, respectively. As for a combination of impairments and disability measures, it accounted for 77 % of the handicap variance. This confirms that each component of the ICF should be evaluated independently since these components are not related in a straightforward
relationship. Chapter 2 stresses the importance of treating and measuring activity level independently, as activity level is not simply the integration of motor function in daily activities. This does not imply that interventions intended to reduce motor impairments are useless; rather, they complement those intended to improve a patient’s activity level. Mobilizing joints and maintaining muscle strength has a preventive role in further impairments, such as contractures or deformities (Stucki et al., 2003), or in other factors reducing activity level, such as muscle fatigue (Feasson et al., 2006).

Finally, the third chapter studied the sensitivity to change of the ACTIVLIM questionnaire, because responsiveness is one of the most important psychometric qualities required when using this instrument in clinical and research settings. One hundred and twenty-two patients were assessed once and then again after approximately 21 months, using the ACTIVLIM questionnaire both times. On the whole, the activity level of these patients decreased, reflecting the progressive disease course of the NMDs. Moreover, the change in activity level was higher in patients who reported a deteriorated functional status than in patients who reported a stable functional status between evaluations. Patients with Duchenne muscular dystrophy (DMD), one of the fastest progressing NMD, showed a greater change in their activity levels than patients with myotonic dystrophy (MD) or Charcot-Marie-Tooth neuropathy (CMT), both of which have slower rates of progression than DMD (Emery, 1998, Pareyson, 2004, Schara & Schoser, 2006).

As there is no consensus concerning how best to investigate sensitivity to change of instruments, our strategy was based on the sample division into patients who reported change and those who reported no change, to evaluate thereafter if the instrument could discriminate between these groups (Pengel et al., 2004). This strategy usually requires an external measure that already shows sensitivity to change. When no gold standard is available, however, the patient’s own perception of change is acceptable as a reliable evaluation of the occurred change (Pengel et al., 2004). Consequently, our sample was divided according to the patient’s perception of functional status evolution. Another external measure in the case of patients with NMD was the patient’s diagnosis. As each NMD does not have the same rate of
progression, the ACTIVLIM questionnaire should show a greater change in patients with quickly progressing NMDs than in patients with slowly progressing NMDs. An individual approach taking into account the standard error associated to each activity measure was also proposed in order to measure the activity change patient by patient. Indeed, meaningful change for groups of patients may not have the same significance for individuals (Beaton et al., 2001, Cella et al., 2002). This approach could therefore be useful to clinicians to interpret change in a single patient.

Finally, the clinical significance of change was also estimated from the available data. Both methods proposed in the literature (Sloan et al., 2003) provided a clinical significance of change about 1 logit, which corresponds to about 10% of the ACTIVLIM measurement of change. Other studies identified the clinical significance of change between 8 to 14% of the measurement range (Jaeschke et al., 1989, Juniper et al., 1992, Osoba et al., 1998, Ringash et al., 2007) confirming our results. Further studies using the ACTIVLIM questionnaire especially in clinical trials are needed to more precisely estimate this clinical significance of change for our questionnaire.

In conclusion, ACTIVLIM is responsive enough and possesses all required psychometric qualities to be included in further research concerning disease progression in patients with NMD. For instance, new therapeutics, including cell and gene therapies and pharmacology, are currently being designed for future testing in human clinical trials (Muntoni & Wells, 2007). The ACTIVLIM questionnaire could therefore quantify the effects of these new treatments on activity limitations of patients with NMD. Additionally, the ACTIVLIM questionnaire could be used to assess the impact of neuromuscular centers on care and follow-up of patients. Are the proposed treatments adapted to the patients? Are they effective or must they be adjusted? Which treatment is the best for this patient with this particular NMD? All these questions could be partly answered if the patients would be systematically assessed with an objective, valid, reliable, linear, unidimensional, and responsive measure, such as the ACTIVLIM questionnaire. However, clinicians might decline to use this questionnaire due to poor knowledge of and lack of information about the Rasch methodology. Indeed, scoring patients on an ordinal rating scale is less complex than acquainting oneself with a statistical method that allows the
conversion of an ordinal total score into linear measures. To help clinicians with the use of Rasch-built scales, a website has been developed that includes scoring sheets and routines that automatically provide the patient’s linear measure from his score responses (http://www.rehab-scales.org). This site also provides, after a user’s free registration, a report that includes both the patient’s measure expressed in logits and a figure (item map) that compares the expected score by the Rasch model and the patient’s observed score. The use of ACTIVLIM and the other Rasch-calibrated scales developed in our lab could, therefore, be extended into clinical practice and further into research design.

The present work provides an instrument with very good psychometric qualities to measure activity limitations in patients with NMD. It was demonstrated that these activity limitations should be independently assessed and treated, since they cannot be simply inferred from motor impairments. Therefore, to extend the use of this questionnaire in national and also international clinical practice, a website is available for clinicians.
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106  

*Activity limitations in patients with neuromuscular disorders*

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108

Activity limitations in patients with neuromuscular disorders


Activity limitations in patients with neuromuscular disorders


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APPENDICES

1. English version of the ACTIVLIM questionnaire
2. French version of the ACTIVLIM questionnaire
3. Dutch version of the ACTIVLIM questionnaire
Appendix I: English version of the ACTIVLIM questionnaire

INSTRUCTIONS FOR THE ACTIVLIM QUESTIONNAIRE

The ACTIVLIM questionnaire

The ACTIVLIM questionnaire was developed as a measure of activity limitations in children and adults with neuromuscular disorders (Vandervelde et al, Neuromuscul Disord, 2007). Activity limitations are defined as difficulties a patient may have in executing activities of daily living. The questionnaire includes 22 items that are daily activities. Among these 22 items, 4 are specifically designed for child evaluation, 4 for adult evaluation, and the remaining 14 items are common to all patients. ACTIVLIM was built either on the perception of the parents of the affected children or on the perception of the adult patients themselves. This perception concerns the difficulty in performing each activity of the questionnaire. The 22 items of ACTIVLIM defined a valid, reliable and reproducible scale. ACTIVLIM was originally developed using the Rasch measurement model. It allows to convert ordinal scores into linear measures located on a unidimensional scale.

Evaluation

For a child evaluation (between 6 and 15 years-old):
The parents fill in the questionnaire by estimating their child’s difficulty or ease in performing each activity.

For an adult evaluation (more than 16 years-old):
The patient fills in himself the questionnaire by estimating their own difficulty or ease in performing each activity.

The activities should be done:
- Without technical or human help (even if the patient actually uses help in daily life)
- Irrespective the limb(s) actually used to achieve the activity
- Whatever the strategy used (any compensation is allowed)

Three responses are presented. These assess the perception of the difficulty/ease depending on whether the activity is “impossible”, “difficult” or “easy”. Activities not attempted in the last 3 months are not scored and entered as missing responses (to tick the question mark).

So, for any activity, the four potential answers are:
- Impossible: The patient is unable to perform the activity without using any other help.
- Difficult: The patient is able to perform the activity without any help but experiences some difficulty.
- Easy: The patient is able to perform the activity without any help and experiences no difficulty.
- Question mark: The patient cannot estimate the difficulty of the activity because he has never done the activity.

Watch out!! If the activity was never attempted because it is impossible, then it must be scored “impossible” rather than “question mark”.

Activities order

The activities of the ACTIVLIM questionnaire are presented in a random order to avoid any systematic effect. Ten different random orders of presentation are used. The rater must select the next one of the 10 orders for each new assessment, no matter which patient is tested.
### ACTIVLIM - Activity Limitations Measure

**English version**

To evaluate an **adult** patient (age 16-80), please answer to the following questions.

To evaluate a **child** patient (age 6-15), please mark the following questions with the "?"

<table>
<thead>
<tr>
<th>How difficult are the following activities?</th>
<th>Impossible</th>
<th>Difficult</th>
<th>Easy</th>
<th>?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Putting on a T-shirt</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Washing one's upper body</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Dressing one's lower body</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Taking a shower</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Sitting on the toilet</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Taking a bath</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Walking downstairs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Stepping out of a bath tub</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Opening a door</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Walking outdoors on level ground</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. Washing one's face</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Hanging up a jacket on a hatstand</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Wiping one's upper body</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. Walking upstairs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Carrying a heavy load</td>
<td>A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16. Getting into a car</td>
<td>A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17. Standing for a long time (± 10 min)</td>
<td>A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18. Walking more than 1 kilometre</td>
<td>A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. Closing a door</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Hopping on one foot</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21. Putting on a backpack</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22. Running</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

To evaluate a child patient (age 6-15), please answer to the following questions.

To evaluate an adult patient (age 16-80), please mark the following questions with the "?"
Appendix II: French version of the ACTIVLIM questionnaire

Instructions pour le questionnaire ACTIVLIM

Le questionnaire ACTIVLIM a été développé afin de mesurer les limitations d’activité dans un échantillon d’enfants et d’adultes atteints de maladies neuromusculaires (Vandervelde et al, Neuromuscul Disord, 2007). Les limitations d’activité sont définies comme étant les difficultés qu’un patient peut rencontrer dans la réalisation des activités de la vie journalière. Le questionnaire est composé de 22 items correspondant à des activités de la vie de tous les jours. Parmi ces 22 items, 4 sont spécifiquement désignés pour l’évaluation des enfants, 4 pour l’évaluation des adultes et les 14 items restants sont communs à tous les patients. ACTIVLIM a été construit à partir soit de la perception des parents des enfants atteints ou soit de la propre perception des patients adultes. Cette perception concerne la difficulté à réaliser chaque item du questionnaire. Les 22 items d’ACTIVLIM définissent une échelle de limitations d’activité valide, fiable et reproductible. ACTIVLIM a été développé en utilisant le modèle de Rasch. Ce modèle permet de convertir des scores ordinaux en mesures linéaires localisées sur une échelle unidimensionnelle.

Évaluation

Pour l’évaluation d’un enfant (âgé entre 6 et 15 ans) :
Les parents remplissent le questionnaire en estimant la difficulté ou la facilité avec laquelle leur enfant exécute les activités présentées.

Pour l’évaluation d’un adulte (âgé de plus de 16 ans) :
Le patient remplit lui-même le questionnaire en estimant la difficulté ou la facilité avec laquelle il réalise les activités présentées.

Les activités doivent être réalisées :
• sans aide technique ou humaine (même si le patient a besoin d’aide dans la vie quotidienne)
• sans tenir compte du membre utilisé pour réaliser l’activité
• quelle que soit la stratégie employée.

Trois possibilités de réponses sont présentées. Celles-ci évaluent la perception de la difficulté/facilité selon que ce soit “impossible” “difficile” ou “facile”.

Les activités non réalisées depuis plus de trois mois ne sont pas évaluées et sont enregistrées comme réponses manquantes (cocher le point d’interrogation).

Donc, pour chaque activité, les quatre réponses potentielles sont :
• Impossible : Le patient est incapable de réaliser l’activité sans aide.
• Difficile : Le patient est capable de réaliser l’activité avec aide mais il éprouve certaines difficultés.
• Facile : Le patient réalise l’activité et ce, sans aucune difficulté.
• Point d’interrogation : Le patient ne peut évaluer la difficulté de l’activité car il ne l’a jamais réalisée ou pas réalisée depuis trois mois.

Attention !! Si une activité n’a jamais été réalisée parce que c’est impossible, “impossible” doit être coché plutôt que le point d’interrogation.

Ordre des activités

Les activités du questionnaire ACTIVLIM sont présentées dans un ordre aléatoire afin d’éviter un biais systématique. Il existe dix ordres de présentation aléatoires différents. L’examinateur doit sélectionner, à chaque nouvelle évaluation, l’ordre suivant le dernier utilisé et ce quel que soit le patient testé.
ACTIVLIM - Une mesure des limitations d'activité
French version

Nom:_________________________ Date:_____________________

<table>
<thead>
<tr>
<th>Quelle est la difficulté des activités suivantes?</th>
<th>Impossible</th>
<th>Difficile</th>
<th>Facile</th>
<th>?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Mettre un T-shirt</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Se laver le haut du corps</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Habiller le bas du corps</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 Prendre une douche</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 S’asseoir sur les toilettes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 Prendre un bain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 Descendre les escaliers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 Sortir de la baignoire</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 Ouvrir une porte</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 Marcher à l’extérieur sur sol plat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 Se laver la figure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 Pendre une veste à un porte-manteau</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13 S’essuyer le haut du corps</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 Monter les escaliers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pour évaluer un **adulte** (16-80 ans), veuillez répondre aux questions suivantes.
Pour évaluer un **enfant** (6-15 ans), veuillez cocher le "?” des questions suivantes.

| 15 Porter une charge lourde                       | A          |           |        |   |
| 16 Rentrer dans une voiture                       | A          |           |        |   |
| 17 Rester debout longtemps (± 10 min)             | A          |           |        |   |
| 18 Marcher plus d’1 kilomètre                     | A          |           |        |   |

Pour évaluer un **enfant** (6-15 ans), veuillez répondre aux questions suivantes.
Pour évaluer un **adulte** (16-80 ans), veuillez cocher le "?” des questions suivantes.

| 19 Fermer une porte                               | C          |           |        |   |
| 20 Sauter à cloche-pied                           | C          |           |        |   |
| 21 Mettre un sac à dos                             | C          |           |        |   |
| 22 Courir                                         | C          |           |        |   |

Ordre 1

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Appendix III: Dutch version of the ACTIVLIM questionnaire

INSTRUCTIES VOOR DE VRAGENLIJST ACTIVLIM

De vragenlijst ACTIVLIM

De vragenlijst ACTIVLIM werd ontwikkeld om de activiteitsbeperkingen van kinderen en volwassenen die aan een neuromusculaire ziekte lijden te schatten (Vandervelde et al, Neuromuscul Disord, 2007). De activiteitsbeperkingen zijn de moeilijkheden die een patiënt mag ontnemen om dagelijkse activiteiten uit te voeren. Die vragenlijst bestaat uit 22 items die dagelijkse activiteiten zijn. Tussen die activiteiten, 4 zijn kinderen gericht, 4 volwassenen gericht en 14 zijn identiek voor alle patiënten. ACTIVLIM werd gevormd vanaf, of de waarneming van de ouders van de kinderen, of de eigene waarneming van de volwassene patiënten. Die waarneming betreft de moeilijkheden om elke activiteit van de vragenlijst uit te voeren. De 22 items van ACTIVLIM vormen een valide, betrouwbare en reproduceerbare schaal van activiteitsbeperkingen. ACTIVLIM werd met het Rasch model ontwikkeld. Dit model maakt mogelijk ordinaire scores in lineaire maten om te zetten. Bovendien lokaliseert dit model de lineaire maten op een ééndimensionale schaal.

Evaluatie

Voor de evaluatie van een kind (tussen 6 en 15 jaar oud):
De ouders vullen de vragenlijst in door een schatting van de moeilijkheid of de gemakkelijkheid waarmee hun kind de voorgestelde activiteiten uitvoert.

Voor de evaluatie van een volwassene (meer dan 16 jaar oud):
De patiënt vult hijszelf de vragenlijst in door de schatting van de moeilijkheid of de gemakkelijkheid waarmee hij de voorgestelde activiteiten uitvoert.

De voorgestelde activiteiten moeten uitgevoerd worden:
- Zonder technische of menselijke hulp (zelfs als de patiënt in het dagelijkse leven wel hulp nodig heeft)
- Zonder met het gebruikte lidmaat rekening te houden om de activiteit uit te voeren
- Hoe de gebruikte strategie ook is (compensaties zijn toegelaten)

Drie categorieën worden voorgesteld. Die schatten de waarneming van de moeilijkheid/ gemakkelijkheid naar gelang die “onnodig”, “moeilijk” of “gemakkelijk” is. De activiteiten die sinds meer dan 3 maanden niet gedaan zijn, worden niet geschat en als ontbrekende antwoorden opgenomen (het vraagteken aankruisen).

Zo, voor elke activiteit zijn hieronder de vier mogelijke antwoorden:
- Onmogelijk: De patiënt kan de activiteit niet zonder hulp uitvoeren
- Moeilijk: De patiënt kan de activiteit zonder hulp uitvoeren maar heeft wel moeilijkheden.
- Gemakkelijk: De patiënt voert de activiteit zonder moeilijkheid uit.
- Vraagteken: De patiënt kan de moeilijkheid van de activiteit niet schatten omdat hij het nooit gedaan heeft.

Opgelet!! Indien een activiteit nooit gedaan werd omdat het “onnodig” is, moet “onnodig” aangekruist worden in plaats van het vraagteken.

Orde van de activiteiten

De activiteiten van de vragenlijst ACTIVLIM worden in een willekeurige orde voorgesteld om een effect door een bepaalde itemsorde te vermijden. Er bestaan 10 verschillende orden. De examinator moet voor elke nieuwe evaluatie, de orde selecteren volgend de laatste die gebruikt werd en die, wie de geteste patiënt ook is.
ACTIVLIM - Een maat van activiteitsbeperkingen

Dutch version

<table>
<thead>
<tr>
<th>Wat is de moeilijkheid van de volgende activiteiten?</th>
<th>Onmogelijk</th>
<th>Moeilijk</th>
<th>Gemakkelijk</th>
<th>?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Een T-shirt aantrekken</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Zijn bovenlichaam wassen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Onderlichaam aankleden</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 Een douche nemen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 Op het toilet gaan zitten</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 Een bad nemen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 De trap afgaan</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 Uit het bad stappen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 Een deur open doen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 Op vlak terrein buiten stappen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 Zijn gezicht wassen</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>12 Een jas op een kapstok hangen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13 Zijn bovenlichaam afdrogen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 De trap opgaan</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 Een zware last dragen</td>
<td>A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16 In een wagen stappen</td>
<td>A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17 Lang recht staan blijven (± 10 min)</td>
<td>A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 Meer dan één kilometer stappen</td>
<td>A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19 Een deur dichtdoen</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 Hinkelen</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21 Een rugzak aandoen</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22 Rennen</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Om een volwassene te schatten (16-80 jaar oud), gelieve de volgende vragen te beantwoorden.

Om een kind te schatten (6 -15 jaar oud), gelieve het "?" van de volgende vragen aan te kruisen.

<table>
<thead>
<tr>
<th>Orde 1</th>
</tr>
</thead>
</table>

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