Motor function, paratonia and glycation cross-linked in older people

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Chapter 6

Psychometric Properties of the MyotonPRO in Dementia Patients with Paratonia

Hans Drenth, Sytse U. Zuidema, Wim P. Krijnen, Ivan Bautmans, Cees van der Schans, Hans Hobbelen

*Gerontology 2017, Dec 22.*
ABSTRACT

**Background**: Paratonia is a distinctive form of hypertonia, causing loss of functional mobility in early stages of dementia to severe high muscle tone and pain in the late stages. For assessing and evaluating therapeutic interventions, objective instruments are required. Objective: Determine the psychometric properties of the MyotonPRO, a portable device that objectively measures muscle properties, in dementia patients with paratonia.

**Methods**: Muscle properties were assessed with the MyotonPRO by 2 assessors within one session and repeated by the main researcher after 30 min and again after 6 months. Receiver operating characteristic curves were constructed for all MyotonPRO outcomes to discriminate between participants with \((n=70)\) and without paratonia \((n=82)\). In the participants with paratonia, correlation coefficients were established between the MyotonPRO outcomes and the Modified Ashworth Scale for paratonia (MAS-P) and muscle palpation. In participants with paratonia, reliability (intraclass correlation coefficient) and agreement values (standard error of measurement and minimal detectable change) were established. Longitudinal outcome from participants with paratonia throughout the study \((n=48)\) was used to establish the sensitivity for change (correlation coefficient) and responsiveness (minimal clinical important difference).

**Results**: Included were 152 participants with dementia (mean [standard deviation] age of 83.5 [98.2]). The area under the curve ranged from 0.60 to 0.67 indicating the MyotonPRO is able to differentiate between participants with and without paratonia. The MyotonPRO explained 10 - 18% of the MAS-P score and 8 - 14% of the palpation score. Interclass correlation coefficients for interrater reliability ranged from 0.57 to 0.75 and from 0.54 to 0.71 for intrarater. The best agreement values were found for tone, elasticity, and stiffness. The change between baseline and 6 months in the MyotonPRO outcomes explained 8 - 13% of the change in the MAS-P scores. The minimal clinically important difference values were all smaller than the measurement error.

**Conclusion**: The MyotonPRO is potentially applicable for cross-sectional studies between groups of paratonia patients and appears less suitable to measure intraindividual changes in paratonia. Because of the inherent variability in movement resistance in paratonia, the outcomes from the MyotonPRO should be interpreted with care; therefore, future research should focus on additional guidelines to increase the clinical interpretation and improving reproducibility.
INTRODUCTION

Paratonia is a well-defined characteristic movement disorder in patients experiencing dementia. Paratonia is defined as a form of hypertonia (high muscle tone with movement stiffness) with an involuntary variable resistance during passive movement. It has an estimated prevalence of 10% in the early/mild stages and up to 90–100% in later/severe stages of dementia. Paratonia progresses from active assistance during passive movement in the early stages of dementia towards strong active resistance in the later stages. Notably, the degree of resistance varies depending on the speed of movement (e.g., low resistance to slow movement and high resistance to fast movement). Furthermore, the resistance to passive movement is in any direction, and there is no clasp-knife phenomenon. This definition enables differentiation between paratonia, Parkinsonian rigidity, and spasticity after stroke.

Due to paratonia, daily care (e.g., washing and dressing) becomes uncomfortable and painful. Severe paratonia, therefore, results in a substantial increase of the caretaker’s burden and decreases the quality of life for those in the advanced stages of dementia. However, even in early stage dementia, paratonia already has a negative and significant impact on functional mobility.

The contractile component (hypertonia) in paratonia brings on worse muscle recovery and quicker muscle fatigue resulting in higher tone, stiffness and elasticity, and lower viscoelastic properties. Noncontractile components are also suggested to contribute to the movement resistance due to biomechanical and viscoelastic changes of connective tissue.

The Paratonia Assessment Instrument (PAI) is a valid and reliable instrument for assessing the presence of paratonia. The severity of paratonia is usually scored by using a Modified Ashworth Scale for paratonia (MAS-P). In clinical settings, this scale is the worldwide standard as a rating scale to measure abnormality in tone or resistance to passive movements. Because the assessor must determine muscle tone by the perceived resistance during passive movement, extensive clinical experience is necessary for the (M)AS to be reliable. In addition, it remains ambiguous which of the muscle properties such as tone, biomechanical, or viscoelastic properties are perceived by the assessor.

Valid, reliable, objective and responsive instruments for measuring muscle properties are necessary for assessing and evaluating therapeutic interventions. To measure muscle properties such as tone, elasticity, stiffness, creep, and mechanical stress relaxation (MSR) time, the Myoton device is available. A Myoton measurement is an objective, quickly applicable, painless, and noninvasive method which has been validated and proved to be reliable for patients with stroke (mean age ranging from 54.7 to 67.5 years), upper
motor neuron disorders (mean age ranging from 47.5 to 54.7 years)\textsuperscript{10,13}, Parkinson disease (mean age ranging from 61.3 to 77.3 years)\textsuperscript{15,16}, and in healthy subjects (mean age ranging from 24.5 to 71.7 years)\textsuperscript{17–21}. Recently, the MyotonPRO has been studied in a small group ($n = 16$, age ranging from 70 to 98 years) of patients with paratonia and demonstrated low to high interrater reliability, moderate to high between series intrarater reliability, and poor to moderate between day intrarater reliability and agreement\textsuperscript{22}.

Because the MyotonPRO objectively measures 5 different muscle properties on a continuous scale, we hypothesize that this tool provides a measurement of muscle tone/stiffness and is a more comprehensive and accurate alternative to the MAS-P. Therefore, if the MyotonPRO is a proven valid and reliable tool for assessing paratonia severity, it may accelerate future research in this area. The aim of this study is to determine the psychometric properties of the MyotonPRO including construct validity with the PAI, the concurrent validity against MAS-P and muscle palpation, and reproducibility and sensitivity/responsiveness to change in dementia patients with paratonia.

**METHODS**

**Design and Study Population**

The study was designed as a multicenter, prospective study with 2 assessments within one session and repeated assessments after 30 min and after 6 months. A convenient sample of 14 nursing homes in the Netherlands was selected as recruitment facilities. Participants were considered to be eligible for inclusion when they were community-dwelling (visiting day-care center) and/or institutionalized dementia patients with an established diagnosis according to the DSM-IV criteria. Written informed consent was obtained from participants or their legal representatives. Because the prevalence and severity of paratonia increases with the progression of dementia, we included people with dementia equally distributed over 3 dementia stages; (1) early-stage dementia (Global Deterioration Scale [GDS]\textsuperscript{23} score of 2, 3, or 4); (2) moderate-stage dementia (GDS score of 5); and (3) severe-stage dementia (GDS score of 6 or 7). This study was conducted to determine the psychometric properties of the MyotonPRO in people with paratonia. To diagnose paratonia, all 5 criteria of the PAI must be met. If for a specific participant not all criteria are met, there may be no or another tone disorder (spasticity or rigidity), and these participants were assigned to the nonparatonia group. Furthermore, participants were excluded from the study if their health was unstable. The medical ethical committee of the University Medical Centre Groningen approved the study (NL54144.042.15).
Assessment Instruments

Myoton device
The MyotonPRO (Myoton AS, Estonia) is a small, portable, handheld device for measuring mechanical muscle properties. Measurement consists of 3 main components: (1) exertion of mechanical impulse, (2) registration of co-oscillation, and (3) computation of parameters.

The tip of the 3-mm diameter probe is applied perpendicular to the skin surface above the muscle that is being measured. A constant pre-pressure (0.18 N) is applied, whereby the subcutaneous superficial tissues are slightly compressed. A brief (15 ms), low-force (0.4 N) mechanical impulse is then transmitted to the underlying muscle. The subsequent dampened oscillation of the muscle is recorded by an accelerometer and simultaneously quantifies and displays the following muscle properties:

- **Tone**: Indicates the intrinsic tension state (oscillation frequency, Hz) of the muscle at rest. The higher the oscillation frequency, the greater the muscle tension, which increases by contraction.

- **Biomechanical properties**: Elasticity (logarithmic decrement of the dampened oscillation), the muscle’s ability to recover its shape after being deformed. The smaller the value for decrement (expressed in arbitrary units), the smaller the dissipation of mechanical energy and the higher the elasticity of a tissue. Stiffness (expressed in N/m), the ability to resist an external force that is attempting to modify its shape. The higher the N/m value, the stiffer the muscle.

- **Viscoelastic properties**: MSR time (ms), the time for a muscle to restore its shape from deformation after an external force is removed. Creep (scored in a so-called Deborah number) is the gradual elongation of a muscle over time when placed under a constant tensile stress. It is estimated by the MyotonPRO as the ratio of the relaxation and the deformation time of the muscle. High values indicate high viscoelasticity.

PAI and MAS-P
The PAI is conducted with a short movement examination in which the limbs of the participant are being moved (first slowly and then accelerated) in flexion and extension, with the participant in a comfortably seated position or, when bedridden, in a supine position. The PAI diagnoses the presence of paratonia when the following 5 criteria are all satisfied: (1) an involuntary variable resistance; (2) a degree of resistance that varies depending on the speed of the movement (e.g., a low resistance to slow movement and a
high resistance to fast movement); (3) resistance to passive movement in any direction; (4) no clasp-knife phenomenon; and (5) resistance in two movement directions in the same limb or two different limbs.  

With the MAS-P, muscle tone is judged by the perceived resistance during passive movement and rated on a 5-point scale ranging from 0 to 4, in which 0 = no resistance to passive movement, 1 = slight resistance during passive movement, 2 = more marked resistance to passive movement, 3 = considerable resistance to passive movement, and 4 = severe resistance, such that passive movement is impossible. A score of 0.5 was assigned in the event of active assistance.

Manual muscle tone palpation
Manual muscle palpation is conducted to assess the muscle tone/stiffness at rest and is graded as normal, hypotonia, or hypertonia.

Clinical Global Impression
A change in perceived muscle tone/movement stiffness is assessed with the Clinical Global Impression (CGI). The CGI overall comparison of the participant’s baseline condition with the current state of general movement stiffness is rated as 1 = very much improved, 2 = much improved, 3 = minimally improved, 4 = no change, 5 = minimally worse, 6 = much worse, or 7 = very much worse.

Study Procedures
For assessing muscle properties, the m. biceps brachii was used as this is an important muscle when assessing paratonia in an upper limb. An upper limb is also affected earlier by paratonia than a lower limb. Because of the importance in upper arm functionality, the m. biceps brachii was also used in other Myoton studies.

In all nursing homes, the participants were assessed in their own or in a separate room in order to reduce external stimuli. Assessment began with the PAI and MAS-P assessment by the main researcher who has extensive clinical experience in these measurements. Then, the main researcher assessed muscle properties with the MyotonPRO. To ensure maximum relaxation during these measurements, the participants were seated in a comfortable position with both arms resting on their lap with the elbow in 90-degree flexion supported by a standard pillow (Fig. 1) or, when in a supine position, with their elbows in 90-degree flexion resting comfortably on their stomach. In these positions, it was ensured that the device could be used within the recommended 0 - 100 degrees to the gravity vector with
the probe perpendicular to the skin, and the muscle was not hanging \(^{25}\). The MyotonPRO was placed respectively on the left and right m. biceps brachii in the middle of the muscle belly which was detected by visual inspection and palpation (at approximately 1/3 of the distance between the cubital fossa and the lateral tip of the acromion) and marked with a skin marker. The multiscan mode consisting of 10 single measurements with a 1-s interval was used, resulting in a mean and coefficient of variation (CV) for the 10 measurements (i.e., one measurement set) \(^{17,19–21}\). In order to register satisfactory measurements, the CV of the parameters should be less than 3\% \(^{25}\). If this was not the case, then the measurement was repeated after corrective actions with a maximum of 3 re-measurements. If a high CV remained, the MyotonPRO manual suggests that this variability may also be caused by the participant’s neurological condition, reflecting the current condition of the muscle \(^{25}\). The set with the lowest CV was then used for the analysis.

Immediately after and blinded from the main researcher, one of the local physiotherapists (\(n = 17\)) performed the MyotonPRO measurement (interrater reliability). Prior to the study, all participating physiotherapists were instructed and trained by the main researcher on the use of the MyotonPRO device and the testing protocol. In the same session, the local physiotherapist graded the perceived tone/stiffness during palpation of the m. biceps brachii.

![Illustration of measurement of the MyotonPRO](image)
For assessing intrarater reliability and agreement, the MyotonPRO measurement was repeated by the main researcher with the same procedure after 30 min, thereby creating a sufficient time interval to minimalize clinical change\textsuperscript{12}. After 6 months, the assessments with the PAI, MAS-P, and MyotonPRO were repeated by the main researcher with the same procedure. Simultaneously, the CGI was assessed by the participant’s professional caretaker because cognitive decline in dementia could hamper the validity of self-reporting clinical change.

**Statistical Analyses**

For the sample size calculation, we established a desired validity correlation coefficient of 0.7 with 95% confidence interval (CI) between 0.57 and 0.81, which resulted in a sample size of 50 for each subgroup (early-, moderate-, and severe-stage dementia). Taking into account a withdrawal percentage of 10%, a total of 165 participants are usually required to achieve the sample size.

Descriptive statistics were used to summarize the means and standard deviations (SD). Since visual inspection of Q-Q plots did not reveal any violations of normality, independent \( t \) tests were performed for continuous data and \( \chi^2 \) tests for frequency data in order to analyze differences in characteristics between participants with and without paratonia. Since the severity of paratonia is only determined if it is diagnosed, except for the analyses for construct validity, all other analyses were conducted for participants with paratonia throughout the study. Paratonia is usually generalized throughout the body; therefore, in order to analyze whether data of only one arm could be used, we compared differences between left and right MyotonPRO outcomes with paired \( t \) tests. Data were analyzed using SPSS version 22 and taking a \( P \) value <0.05 as statistically significant.

**Construct Validity**

For construct validity, we validated the MyotonPRO with the PAI. Receiver operating characteristic (ROC) curves were constructed by plotting the sensitivity and 1 – specificity for all possible cut-off points of MyotonPRO outcomes in order to discriminate between participants with and without paratonia. We expect that the outcomes from the MyotonPRO on tone and stiffness are higher, and elasticity and viscoelastic properties are lower in participants with paratonia as the result of hypertonia (e.g., muscle in contracted state)\textsuperscript{5}. The area under the ROC curve (AUC) reflects the ability of the MyotonPRO scores to differentiate between participants with and without paratonia. The area under the ROC curve ranged from 0.5 to 1; a higher score indicates better discrimination\textsuperscript{28}. Sensitivity and
specificity proportions were estimated by applying Youden’s index in which we selected the optimal cut-off point of the ROC curve, where the calculated sensitivity + specificity is maximal 29, and 95% CI were calculated.

**Concurrent Validity**

Concurrent validity of the muscle properties measured with the MyotonPRO was determined using the Spearman correlation (\(\rho\)) test to establish correlation with the MAS-P scores and to establish correlation with muscle palpation of the m. biceps brachii. Correlation coefficients were interpreted as negligible (0 - 0.3), low (0.3 - 0.5), moderate (0.5 - 0.7), high (0.7 - 0.9), or very high (0.9 - 1.0) 30. For the analysis, we used the MAS-P score of the elbow extension as this represents the resistance of passive movement in the m. biceps brachii.

**Reproducibility**

Reproducibility concerns the degree to which repeated measurements with the MyotonPRO provide similar answers and can be divided into reliability and agreement. Measures of agreement refer to the absolute measurement error, i.e. how close the scores on repeated measures are presented in the units of measurement of the corresponding MyotonPRO outcomes. Measures of reliability refer to the relative measurement error, i.e. the variation between subjects in relationship to the total variance of the measurements 31. Interrater and intrarater (test-retest after 30 min) reliabilities were analyzed through the intraclass correlation coefficient (ICC) using a 2-way mixed model with absolute agreement and single measures where ICC >0.75 is evaluated as being excellent, between 0.40 and 0.75 as being fair to good, and less than 0.40 as being poor 32. For agreement estimation, we used the standard error of measurement (SEM) and the minimal detectable change (MDC). The SEM provides the range within which a participant’s genuine score may fall. The SEM was estimated as \(\text{SEM} = \text{SD} \times \sqrt{1 - \text{ICC}}\), where the SD is the pooled SD of the corresponding MyotonPRO outcome from test and retest 33. The SEM% indicates the relative amount of measurement error and was defined as \(\text{SEM}\% = (\text{SEM}/\text{mean}) \times 100\), where the mean is that for the corresponding measurements from test-retest. The SEM% of <10% is suggested as being small 34. The MDC represents the magnitude of change necessary to exceed the measurement error of 2 repeated measures at a 95% CI and was calculated as \(\text{MDC}_{95} = \text{SEM} \times \sqrt{2} \times 1.96\) 35. \(\text{MDC}_{95}\%\) was defined as \(\text{MDC}_{95}\% = (\text{MDC}/\text{mean}) \times 100\), where an \(\text{MDC}_{95}\%\) smaller than 10% is suggested to be excellent and an \(\text{MDC}_{95}\%\) smaller than 30% to be acceptable 12,36.
Sensitivity to Change and Responsiveness

Two concepts are applied in the assessment of evaluative instruments. We endorse the recommendation that a distinction should be made between sensitivity and responsiveness. Sensitivity to change refers to the capacity of instruments to statistically measure change. Responsiveness addresses the detection of clinically relevant or important change. For sensitivity to change, the changes in the MyotonPRO and MAS-P measurements between baseline and 6 months were examined by the Pearson coefficient ($r$) between score changes. Responsiveness was determined by the minimal clinical important difference (MCID). The MCID was established with an anchor-based method in which longitudinal change after 6 months in the MyotonPRO outcomes was related to an external criterion for important change (the “anchor”), being the CGI for change scale. The CGI “anchor” scores were used to categorize participants into 3 subgroups (CGI scores): “improved” (1 - 3), “no change” (4), and “worse” (5 - 7). To estimate the MCID, the mean change scores on the 5 MyotonPRO outcomes were calculated by subtracting each participant’s 6-month score from the baseline score. The mean change scores of the subgroup reported as being “worse” were used to determine the MCID. We tested for significance score changes between the anchor subgroups using one-way ANOVA.

RESULTS

From the 168 eligible participants, 16 were unable to participate due to various reasons (11 had to be excluded because they were restless, became agitated, or were too ill for assessment, and 5 died). At baseline, 152 participants (101 [66.4%] female and 51 [33.6%] male with a mean age [SD] of 83.5 [8.2]) were assessed, of which 70 (46.1%) were diagnosed with and 82 (53.9%) without paratonia by using the PAI. After 6 months, 41 participants (27%) were lost to follow-up (11 were excluded because of restlessness, agitation, or were too ill to be reassessed, 5 were transferred to unknown addresses, and 26 died). From the 111 remaining participants, 55 (49.5%) were diagnosed with and 56 (50.5%) without paratonia. From the original 70 participants with paratonia at baseline, 48 (68.6%) remained and were included for longitudinal assessments. Figure 2 illustrates the flow and number of participants through the study. Baseline characteristics are summarized in Table 1.

Paired t test analysis between the left and right arm indicated no significant differences in MyotonPRO outcomes. We used the left m. biceps brachii for analysis because the left arm was mostly the non-dominant arm in studies with healthy subjects. By using the data of the non-dominant arm, the influence of preceding physical activity was suggested to be reduced.
Construct Validity

The ROC analyses revealed that all MyotonPRO outcomes had sufficient ability to differentiate between participants with and without paratonia. In participants with paratonia tone, elasticity and stiffness were higher and viscoelasticity was lower. The AUC determined for tone was 0.66, $P = 0.001$; elasticity 0.61, $P = 0.017$; stiffness 0.60, $P = 0.028$; creep 0.67, $P < 0.001$; and MSR time 0.65, $P = 0.001$. Sensitivity and specificity estimated for tone was 70% (95% CI: 63 - 77%) and 54% (95% CI: 46 - 62%), respectively; elasticity 66% (95% CI: 58 - 74%) and 56% (95% CI: 48 - 64%), respectively; stiffness 60% (95% CI: 52 - 68%) and 59% (95% CI: 51 - 67%), respectively; creep 63% (95% CI: 55 - 71%) and 61% (95% CI: 53 - 69%), respectively; and MSR time 60% (95% CI: 52 - 68%) and 59% (95% CI: 51 - 67%), respectively.

Concurrent Validity

Table 2 shows that a statistically significant correlation was ascertained between the MAS-P score and tone ($\rho = 0.42$, $P < 0.001$), stiffness ($\rho = 0.31$, $P = 0.009$), creep ($\rho = -0.39$, $P = 0.001$), and MSR time ($\rho = -0.38$, $P = 0.001$), but not for elasticity ($\rho = -0.23$, $P = 0.051$). A statistically significant correlation was also found between manual biceps palpation and tone ($\rho = 0.37$, $P = 0.002$), stiffness ($\rho = 0.28$, $P = 0.019$), creep ($\rho = -0.31$, $P = 0.009$), and MSR time ($\rho = -0.33$, $P = 0.005$), but not for elasticity ($\rho = -0.13$, $P = 0.279$).

**Figure 2.** Flow and number of participants throughout the study
### Table 1. Baseline characteristics of participants without and with paratonia

<table>
<thead>
<tr>
<th></th>
<th>No Paratonia</th>
<th>Paratonia</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 82 (53.9%)</td>
<td>n = 70 (46.1%)</td>
<td></td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>56 (68.3)</td>
<td>45 (64.3)</td>
<td>ns</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>26 (31.7)</td>
<td>25 (35.7)</td>
<td>ns</td>
</tr>
<tr>
<td>Age, years</td>
<td>83.5 (8.7)</td>
<td>83.5 (7.7)</td>
<td>ns</td>
</tr>
<tr>
<td>Early dementia (GDS 0-4), n (%)</td>
<td>37 (45.1)</td>
<td>14 (20)</td>
<td>0.001</td>
</tr>
<tr>
<td>Moderate dementia (GDS 5), n (%)</td>
<td>26 (31.7)</td>
<td>22 (31.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Severe dementia (GDS 6-7), n (%)</td>
<td>19 (23.2)</td>
<td>34 (48.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Alzheimer’s Disease, n (%)</td>
<td>40 (48.8)</td>
<td>32 (45.7)</td>
<td>ns</td>
</tr>
<tr>
<td>Vascular dementia, n (%)</td>
<td>14 (17.1)</td>
<td>16 (22.9)</td>
<td>ns</td>
</tr>
<tr>
<td>Mixed AD/VaD, n (%)</td>
<td>9 (11.0)</td>
<td>11 (15.7)</td>
<td>ns</td>
</tr>
<tr>
<td>Fronto-temporal, n (%)</td>
<td>5 (6.1)</td>
<td>2 (2.9)</td>
<td>ns</td>
</tr>
<tr>
<td>Parkinson/Lewy body, n (%)</td>
<td>1 (1.2)</td>
<td>2 (2.9)</td>
<td>ns</td>
</tr>
<tr>
<td>Otherwise specified, n (%)</td>
<td>13 (15.8)</td>
<td>7 (10.0)</td>
<td>ns</td>
</tr>
<tr>
<td>Dementia duration, months</td>
<td>50.8 (44.0)</td>
<td>61.3 (40.4)</td>
<td>ns</td>
</tr>
<tr>
<td>Co-morbidities, n</td>
<td>1.6 (1.1)</td>
<td>1.5 (1.1)</td>
<td>ns</td>
</tr>
<tr>
<td>CVD, n (%)</td>
<td>34 (41.5)</td>
<td>18 (25.7)</td>
<td>0.022</td>
</tr>
<tr>
<td>CeVD (CVA, TIA), n (%)</td>
<td>23 (28.0)</td>
<td>19 (27.1)</td>
<td>ns</td>
</tr>
<tr>
<td>DM, n (%)</td>
<td>16 (19.5)</td>
<td>16 (22.9)</td>
<td>ns</td>
</tr>
<tr>
<td>Internal, n (%)</td>
<td>15 (18.3)</td>
<td>7 (10.0)</td>
<td>ns</td>
</tr>
<tr>
<td>Cancer, n (%)</td>
<td>8 (9.8)</td>
<td>12 (17.1)</td>
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<td>COPD, n (%)</td>
<td>9 (11.0)</td>
<td>5 (7.1)</td>
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<tr>
<td>Systemic, n (%)</td>
<td>5 (6.1)</td>
<td>8 (11.4)</td>
<td>ns</td>
</tr>
<tr>
<td>Digestive tract, n (%)</td>
<td>3 (3.7)</td>
<td>4 (5.7)</td>
<td>ns</td>
</tr>
<tr>
<td>Musculoskeletal, n (%)</td>
<td>2 (2.4)</td>
<td>3 (4.3)</td>
<td>ns</td>
</tr>
<tr>
<td>Parkinson’s disease, n (%)</td>
<td>-</td>
<td>2 (2.9)</td>
<td>ns</td>
</tr>
<tr>
<td>Depression, n (%)</td>
<td>1 (1.2)</td>
<td>1 (1.4)</td>
<td>ns</td>
</tr>
<tr>
<td>Epilepsy, n (%)</td>
<td>-</td>
<td>1 (1.4)</td>
<td>ns</td>
</tr>
<tr>
<td>Polypharmacy (≥ 5 meds), n (%)</td>
<td>53 (64.6)</td>
<td>47 (67.1)</td>
<td>ns</td>
</tr>
<tr>
<td>Psychotropics, n (%)</td>
<td>8 (9.8)</td>
<td>14 (20.0)</td>
<td>0.068</td>
</tr>
<tr>
<td>MAS-P*</td>
<td>0.4 (0.5)</td>
<td>1.9 (1.1)</td>
<td>&lt;0.001</td>
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<tr>
<td>Muscle palpation*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hypotonia, n (%)</td>
<td>10 (12.3)</td>
<td>9 (12.9)</td>
<td>ns</td>
</tr>
<tr>
<td>normal, n (%)</td>
<td>65 (80.2)</td>
<td>47 (67.1)</td>
<td>ns</td>
</tr>
<tr>
<td>hypertonia, n (%)</td>
<td>6 (7.4)</td>
<td>14 (20)</td>
<td>0.023</td>
</tr>
<tr>
<td>Tone (Hz)*</td>
<td>12.14 (1.34)</td>
<td>13.18 (1.92)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Elasticity (log decrement)*</td>
<td>1.81 (0.36)</td>
<td>1.67 (0.36)</td>
<td>0.017</td>
</tr>
<tr>
<td>Stiffness (N/m)*</td>
<td>234.30 (25.44)</td>
<td>244.70 (36.03)</td>
<td>0.046</td>
</tr>
<tr>
<td>Creep (Deborah number)*</td>
<td>1.71 (0.24)</td>
<td>1.54 (0.29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MSR time (ms)*</td>
<td>27.51 (3.92)</td>
<td>25.05 (4.58)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

AD = Alzheimer disease; CeVD = cerebral vascular disease; COPD = chronic obstructive pulmonary disease; CVA = cerebral vascular accident; CVD = cardio vascular disease; DM = diabetes mellitus; GDS = Global Deterioration Scale; MSR = mechanical stress relaxation; ns = not statistically significant; TIA = transient ischemic attack; VaD = vascular dementia.

Data represent mean values (SD) unless indicated otherwise.

*: Data from the left arm.
Reproducibility

Table 3 shows that the inter- and intrarater reliabilities were fair to good across the MyotonPRO outcomes (ICC: 0.57 - 0.75 and ICC: 0.54 - 0.71, respectively). Intrarater agreement, expressed as the SEM in the units of measurement of the MyotonPRO for tone was 1.17 (Hz), elasticity 0.18 (log decrement), stiffness 21.60 (N/m), creep 0.20 (Deborah number), and MSR time 3.00 (ms). The SEM% for tone was 8.9%, elasticity 11%, stiffness 8.9%, creep 12.6%, and MSR time 11.8%. The MDC_{95} for tone was 3.24 (HZ), elasticity 0.50 (log decrement), stiffness 59.87 (N/m), creep 0.54 (Deborah number), and MSR time 8.29 (ms). The MDC_{95}% for tone was 24.6%, elasticity 29.9%, stiffness 24.7%, creep 34.6%, and MSR time 32.8%.

Sensitivity to Change

A statistically significant correlation was found between baseline and increase in MAS-P scores and increase in tone ($r = 0.29, P = 0.043$) and decrease in elasticity ($r = -0.36, P = 0.011$), creep ($r = -0.35, P = 0.014$), and MRS time ($r = -0.34, P = 0.017$), but not for increase in stiffness ($r = 0.02, P = 0.878$) after 6 months (Fig. 3).

Responsiveness

Per subgroup based on the CGI anchors, 29 participants with paratonia were reported with having no change, 19 were reported as worsening, and none of the participants improved. Table 4 shows that the MCID in the units of measurement of the MyotonPRO (SD) for tone was 0.56 (1.86), elasticity 0.11 (0.45), stiffness 1.79 (39.02), creep 0.12 (0.31), and MSR time 1.69 (4.37). One-way ANOVA revealed significant differences in the changes in the MyotonPRO outcomes for tone ($P = 0.005$), elasticity ($P = 0.032$), creep ($P = 0.001$), and MSR time ($P = 0.005$) among participants who were reported to have worsened, suggesting sufficiently discriminative change categories. There was no statistically significant difference in MAS-P change ($P = 0.173$) among the change categories.
### Table 3. Reproducibility: inter- and intrarater reliability and agreement

<table>
<thead>
<tr>
<th>MyotonPRO</th>
<th>T0 rater 1 (SD)</th>
<th>T0 rater 2 (SD)</th>
<th>Intrarater reliability ICC (95% CI)</th>
<th>T1 rater 1 (SD)</th>
<th>Intrarater reliability ICC (95% CI)</th>
<th>SEM (%)</th>
<th>MDCᵥ₉₅ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tone (Hz)</td>
<td>13.18 (1.92)</td>
<td>13.00 (1.86)</td>
<td>0.70 (0.55 – 0.80)</td>
<td>13.12 (1.77)</td>
<td>0.60 (0.43 – 0.74)</td>
<td>1.17 (8.9)</td>
<td>3.24 (24.6)</td>
</tr>
<tr>
<td>Elasticity (log decrement)</td>
<td>1.67 (0.36)</td>
<td>1.71 (0.41)</td>
<td>0.64 (0.48 – 0.76)</td>
<td>1.68 (0.32)</td>
<td>0.71 (0.57 – 0.80)</td>
<td>0.18 (11.0)</td>
<td>0.50 (29.9)</td>
</tr>
<tr>
<td>Stiffness (N/m)</td>
<td>244.70 (36.03)</td>
<td>240.49 (34.78)</td>
<td>0.75 (0.63 – 0.84)</td>
<td>239.13 (31.27)</td>
<td>0.59 (0.41 – 0.70)</td>
<td>21.60 (8.9)</td>
<td>59.87 (24.7)</td>
</tr>
<tr>
<td>Creep (Deborah number)</td>
<td>1.54 (0.29)</td>
<td>1.60 (0.28)</td>
<td>0.57 (0.39 – 0.71)</td>
<td>1.58 (0.29)</td>
<td>0.54 (0.35 – 0.68)</td>
<td>0.20 (12.6)</td>
<td>0.54 (34.6)</td>
</tr>
<tr>
<td>MSR time (ms)</td>
<td>25.05 (4.58)</td>
<td>25.74 (4.30)</td>
<td>0.62 (0.45 – 0.74)</td>
<td>25.56 (4.53)</td>
<td>0.57 (0.38 – 0.70)</td>
<td>3.00 (11.8)</td>
<td>8.29 (32.8)</td>
</tr>
</tbody>
</table>

*ICC = intra class correlation; MDC = minimal detectable change; MSR = mechanical stress relaxation; SD = standard deviation; SEM = standard error of measurement. T0 = baseline; T1 = retest after 30 minutes.*
Table 4. *Mean change scores categorized by CGI Anchor*

<table>
<thead>
<tr>
<th>CGI Anchor</th>
<th>Improved</th>
<th>No change</th>
<th>Worse</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>0</td>
<td>29</td>
<td>19</td>
</tr>
<tr>
<td><strong>MyotonPRO</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tone (Hz)</td>
<td>-</td>
<td>0.95 (1.67)</td>
<td>-0.56 (1.86)*</td>
</tr>
<tr>
<td>Elasticity (log decrement)</td>
<td>-</td>
<td>-0.21 (0.51)</td>
<td>0.11 (0.45)*</td>
</tr>
<tr>
<td>Stiffness (N/m)</td>
<td>-</td>
<td>7.93 (39.99)</td>
<td>1.79 (39.02)</td>
</tr>
<tr>
<td>Creep (Deborah number)</td>
<td>-</td>
<td>-0.21 (0.34)</td>
<td>0.12 (0.31)*</td>
</tr>
<tr>
<td>MSR time (ms)</td>
<td>-</td>
<td>-2.81 (5.53)</td>
<td>1.69 (4.37)*</td>
</tr>
<tr>
<td>MAS-P</td>
<td>-</td>
<td>0.28 (0.89)</td>
<td>-0.05 (0.64)</td>
</tr>
</tbody>
</table>

MSR = mechanical stress relaxation; MAS-P = modified Ashworth scale for paratonia
* P <0.05, statistically significant.

**Figure 3. Scatterplots. Correlation between change in MAS-P and change in MyotonPRO outcomes after 6 months**
DISCUSSION

This study was conducted to assess the psychometric properties of MyotonPRO in order to investigate if this device is an objective and more accurate alternative to the MAS-P in patients with paratonia. With the MAS-P, muscle tone is measured by the perceived resistance during passive movement. The MyotonPRO exerts a local passive movement of the muscle and is able to measure a construct of 5 different parameters of tone and stiffness. We regard the MyotonPRO a feasible tool. Measurement time takes approximately 10 s to about 1 min if it needs to be repeated up to 3 times because of unsatisfactory CV values. The participating physiotherapist found the MyotoPRO easy to use after some practicing. We assessed the validity, reproducibility, sensitivity to change, and responsiveness of the MyotonPRO in a cohort of dementia patients.

Validity

We found evidence that the MyotonPRO is able to differentiate between people with and without paratonia. Muscle tone, elasticity (lower decrement), and stiffness were significantly higher, and viscoelasticity (creep and MSR time) was significantly lower in people with paratonia which is to be expected when a muscle is not relaxed or it contracts. Paratonia is an active resistance to passive movement caused by the inability to relax or unintentionally contracted muscles. In view of the sensitivity and specificity values found in this study, the MyotonPRO cannot yet be recommended to diagnose paratonia. Although significant, the correlation coefficients indicate a small correlation between the MyotonPRO outcomes and the MAS-P, which are similar between the MyotonPRO outcomes and manual muscle palpation. The indication of muscle tone by manual palpation proved challenging in our cohort as many participants had low biceps muscle mass, which makes the results questionable. Revealed correlations with the MAS-P are in concordance with the validity study using MAS measurements in stroke survivors. Leonard et al. found higher correlation coefficients with the MAS in their study with people with spasticity but with the notification that variables were reduced by clustering MAS scores into fewer categories. Possible explanations for the low correlation with the MAS-P can be given from the fact that MAS measurements have the tendency to cluster scores in the lower range, limiting its ability to discriminate between patients. In addition, while the main researcher has experience in using the MAS-P, some subjectivity cannot be ruled out. Notwithstanding that a MAS measurement is the criterion for clinical muscle tone assessment, one could contend that it is not a suitable “golden” standard and hypothesize that the MyotonPRO is more accurate than the MAS-P.
Reproducibility

In the current study, inter- and intrareliability for the MyotonPRO was evaluated as fair to good. The best agreement was found for tone, elasticity, and stiffness with small SEM% and acceptable MDC\(_{95}\)%. A person exhibits genuine change when the change between repeated measurements is larger than the MDC\(_{95}\) \(^{31}\). Viscoelastic properties exceed the SEM% and MDC\(_{95}\) % and, therefore, require large values to detect real change and are not sensitive for detecting small relevant changes. In the study by van Deun et al. \(^{22}\), the reliability coefficients were higher in people with paratonia, but these were within session reliability values. On the other hand, their between-days reliability coefficients were lower. Resistance in paratonia is known to be variable. In particular, in the early stages of dementia, paratonia can fluctuate between no resistance, actively assisting, and active resistance against passive movement \(^{2,3}\). We also found that, especially in people with advanced dementia, keeping the participants from moving during the tests was challenging, and the measurements were often repeated because of unsatisfactory CV values. Bias induced by this variability cannot be completely ruled out but is an undeniable and essential clinical presentation of dementia patients with paratonia. Although it is suggested that a series of 10 taps is sufficient for Myoton measurement \(^{21}\), van Deun et al. \(^{22}\) found that adding a second series of taps improved reproducibility in patients with paratonia. Future research on diurnal variation is necessary to establish whether paratonia (and thus MyotonPRO measurements) vary over time. This is important for increasing the clinical interpretation and improving reproducibility.

Sensitivity to Change and Responsiveness

The MyotonPRO is able to record change over time in patients with paratonia. Monitoring change over time is important for studying intervention effects, and the MDC and MCID can be used for the interpretation of the MyotonPRO outcome to determine whether the observed change is real or meaningful. To be able to distinguish meaningful or important change from the measurement error, the MCID should be at least as large as the MDC \(^{38}\). In this study, all of the MyotonPRO outcomes exceeded this threshold, meaning that, if a person has a change score as large as the MCID, it cannot be certain that this change is not due to a measurement error.

Peripheral biomechanical changes through cross-linking processes by advanced glycation end-products (AGEs) are suggested as contributing to the perceived resistance in paratonia \(^6\). Cross-linking of intramuscular collagen tissue is associated with increased muscle stiffness and reduced viscoelastic properties \(^{40}\), which were detected by the MyotonPRO. On the other hand, the MyotonPRO measured higher elasticity in the paratonia group which is not to be expected if there was AGE-induced biomechanical stiffness and elasticity loss. As
mentioned previously, the MyotonPRO registers higher tone, elasticity and stiffness, and lower viscoelasticity in contracted versus relaxed muscles. This could indicate that the peripheral biomechanical changes were less prominent and overruled by the inability to relax or hypertonia in this cohort. It might also be hypothesized that AGE induced effects on collagen tissue results in a mechanism to maintain some elastic properties in low quality muscles. Couppé et al. found in their study that collagen concentration was reduced in tendon tissue, whereas cross-linking AGEs concentration was elevated in older aged men versus younger aged men but found no difference in biomechanical properties. Further research is necessary to study this more in depth.

Strengths and Limitations

This is the first study to assess all MyotonPRO properties and study sensitivity to change and responsiveness after 6 months in dementia patients with paratonia. This study also has a number of limitations. First, we were not able to use a true objective standard for determining criterion validity. Laboratory techniques for objectively assessing muscle properties, such as magnetic resonance elastography or ultrasound imaging, are not clinically feasible and often too stressful in this patient group. Second, we experienced difficulties in assessing muscle tone by manual palpation due to the low muscle mass of the m. biceps brachii. Due to this, it was often difficult to determine the exact location of the muscle belly. Validating the MyotonPRO against the MAS and muscle palpation, therefore, might have caused an underestimation of our results. Third, we did not control for variables that could influence muscle properties such as body weight/BMI, room and body temperature, blood flow, alcohol consumption, and the degree of preceding physical activity, which could have influenced the results.

Clinical Implications

Accurate and objective measurement of paratonia severity proves challenging. Because the MDC values surpass the MCID, the responsiveness of detecting small relevant changes in this population is complicated. Hence, at this moment, we cannot recommend the MyotonPRO to be used to evaluate paratonia progress over time. The MyotonPRO is more precise and objective than MAS-P measurements and is potentially suitable to evaluate therapeutic interventions, cross-sectional between groups, but because of the inherent characteristics of paratonia (e.g., variability in movement resistance), the outcomes from the MyotonPRO should be interpreted with care. Multiple measurements during a period of time might adjust for the diurnal variation of paratonia.
CONCLUSION

The MyotonPRO is potentially applicable to quantify paratonia severity in cross-sectional and controlled intervention studies between groups of people with paratonia. Nevertheless, it appears less suitable to measure clinically relevant intra-individual changes in paratonia. Because of the inherent variability in movement resistance in paratonia, the outcomes from the MyotonPRO should be interpreted with care. Therefore, future research should focus on additional guidelines for MyotonPRO measurements for increasing the clinical interpretation and improving reproducibility in dementia patients with paratonia.
REFERENCES


