Quantifying neural and non-neural components of wrist hyper-resistance after stroke: comparing two instrumented assessment methods
Andringa, A.; Meskers, C.; Port, I. van de; Zandvliet, S.; Scholte, L.; Groot, J. de; ...; Wegen, E. van

Citation

Version: Publisher's Version
License: Creative Commons CC BY 4.0 license
Downloaded from: https://hdl.handle.net/1887/3276413

Note: To cite this publication please use the final published version (if applicable).
Quantifying neural and non-neural components of wrist hyper-resistance after stroke: Comparing two instrumented assessment methods

Aukje Andringa a, Carel Meskers a,b,f,* , Ingrid van de Port c, Sarah Zandvliet a, Larissa Scholte a,d, Jurriaan de Groot e, Gert Kwakkel a,b,f, Erwin van Wegen a

a Department of Rehabilitation Medicine, Amsterdam Movement Sciences, Amsterdam Neuroscience, Amsterdam UMC, Vrije Universiteit Amsterdam, De Boelelaan 1117, Amsterdam, the Netherlands
b Department of Physical Therapy and Human Movement Sciences, Northwestern University, Chicago, IL, USA
c Revant Rehabilitation Centre Breda, Breda, the Netherlands
d Department of Biomechanical Engineering, Faculty of Mechanical, Maritime and Materials Engineering, Delft University of Technology, Delft, the Netherlands
e Department of Rehabilitation Medicine, Leiden University Medical Centre, Leiden, the Netherlands
f Department of Neurorehabilitation, Amsterdam Rehabilitation Research Centre, Reade, Amsterdam, the Netherlands

ARTICLE INFO

Keywords:
Stroke
Hyper-resistance
Muscle spasticity
Upper extremity
Assessment
Validity

ABSTRACT

Patients with poor upper limb motor recovery after stroke are likely to develop increased resistance to passive wrist extension, i.e., wrist hyper-resistance. Quantification of the underlying neural and non-neural elastic components is of clinical interest. This cross-sectional study compared two methods: a commercially available device (NeuroFlexor®) with an experimental EMG-based device (Wristalyzer) in 43 patients with chronic stroke. Spearman’s rank correlation coefficients (r) between components, modified Ashworth scale (MAS) and range of passive wrist extension (PRoM) were calculated with 95% confidence intervals. Neural as well as elastic components assessed by both devices were associated (r = 0.61, 95%CI: 0.38–0.77 and r = 0.53, 95%CI: 0.28–0.72, respectively). The neural component assessed by the NeuroFlexor® associated significantly with the elastic components of NeuroFlexor® (r = 0.46, 95%CI: 0.18–0.67) and Wristalyzer (r = 0.36, 95%CI: 0.06–0.59). The neural component assessed by the Wristalyzer was not associated with the elastic components of both devices. Neural and elastic components of both devices associated similarly with the MAS (r = 0.58, 95%CI: 0.34–0.75 vs. 0.49, 95%CI: 0.22–0.69 and r = 0.51, 95%CI: 0.25–0.70 vs. 0.30, 95%CI: 0.00–0.55); elastic components associated with PRoM (r = -0.44, 95%CI: -0.65–-0.16 vs. -0.74, 95%CI: -0.85–-0.57 for NeuroFlexor® and Wristalyzer respectively). Results demonstrate that both methods perform similarly regarding the quantification of neural and elastic wrist hyper-resistance components and have an added value when compared to clinical assessment with the MAS alone. The added value of EMG in the discrimination between neural and non-neural components requires further investigation.

List of abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC</td>
<td>Elastic component of wrist hyper-resistance</td>
</tr>
<tr>
<td>ECR</td>
<td>Extensor carpi radialis muscle</td>
</tr>
<tr>
<td>EMG</td>
<td>Electromyography</td>
</tr>
<tr>
<td>FCR</td>
<td>Flexor carpi radialis muscle</td>
</tr>
<tr>
<td>MAS</td>
<td>Modified Ashworth scale</td>
</tr>
<tr>
<td>NC</td>
<td>Neural component of wrist hyper-resistance</td>
</tr>
<tr>
<td>NF</td>
<td>NeuroFlexor®</td>
</tr>
<tr>
<td>PRoM</td>
<td>Range of passive wrist extension</td>
</tr>
</tbody>
</table>

* Corresponding author at: Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Rehabilitation Medicine, PO Box 7057, 1007 MB Amsterdam, The Netherlands.
E-mail address: C.Meskers@AmsterdamUMC.nl (C. Meskers).

https://doi.org/10.1016/j.medengphy.2021.10.009
Received 8 June 2021; Received in revised form 28 September 2021; Accepted 21 October 2021
Available online 24 October 2021
1350-4533/© 2021 The Author(s). Published by Elsevier Ltd on behalf of IPEM. This is an open access article under the CC BY license
to develop increased resistance to passive wrist extension, i.e., wrist hyper-resistance, in weeks to months post stroke [6,7]. This hyper-resistance of the wrist joint is hypothesized to originate from a complex interaction between impaired neuromuscular activation and altered tissue properties of the muscles spanning the joint [8,9]. Impaired neuromuscular activation includes spasticity, defined as velocity-dependent stretch hyperreflexia [10], and involuntary background activation [11]. Altered tissue properties comprise changes in elasticity, viscosity, and muscle shortening [12]. The distribution and level of aforementioned neural and non-neural tissue property-related components may change over time post stroke [13-15] and may differ between individual patients [16]. Accurate discrimination between the components is important to understand their influence on post-stroke motor recovery and may help to optimize individual treatment decisions [17]. However, this is not possible by manual assessment of joint resistance, which is the current clinical standard [18,19]. There is a need for a valid and reliable non-invasive assessment method that is easy to apply in clinical practice [19,20].

Various instrumented assessment methods have been developed that differ in setup and neuromuscular modelling [16,21–23]. The commercially available medical device NeuroFlexor® (Aggero MedTech AB, Alta, Sweden) [21] derives the neural and non-neural elastic components from resistance to a passive wrist extension movement. Construct validity [21,24,25], good to excellent test-retest reliability [25,26], and good responsiveness [27] of this device were shown. The experimental Wristalyzer [16] uses measured joint torque during an imposed perturbation of the wrist in combination with electromyography (EMG) of wrist flexor and extensor muscle activity to estimate neural and elastic components using a neuromuscular model including wrist mechanics and muscle properties. Similar instrumented assessment methods for the wrist and ankle joint have shown to be valid in patients with acute [13] and chronic [16,28] stroke and have shown sized similarity between both devices in the quantification of the neural and extensor carpi radialis (ECR) muscles was measured by EMG using a unidirectional biomechanical model [21,33] based on the force-time traces during passive wrist extension (software program NeuroFlexor Scientific v0.06, Supplementary file 1) The neural component (NF-NC, in Newton) is defined as the immediate resisting force at the end of the fast passive wrist extension movement (i.e., 30° wrist extension) minus the non-neural elastic and viscous components. The elastic component (NF-EC, in Newton) is the length-dependent resisting force recorded 1 s after stopping the slow movement (i.e., 30° wrist extension). The viscous component is the velocity-dependent resisting force of soft tissues to stretch.

2. Methods

2.1. Participants

For this study, patients with chronic stroke and initial upper limb paresis were recruited. Inclusion criteria were: (1) ischemic or haemorrhagic stroke at least six months prior to inclusion; (2) initial upper limb paresis as defined by the National Institutes of Health Stroke Scale (NIHSS) item 5 a/b-score > 0 (i.e. not able to hold the affected arm at a 90° angle for at least 10 s); (3) age 18 years or older, and (4) sufficient cognitive ability to follow test instructions (mini-mental state examination > 17) [31]. Exclusion criteria were: (1) limitations of the arm-hand function of the affected side other than due to stroke; (2) less than 40° of passive wrist extension with extended fingers in order to comply with the NeuroFlexor® protocol and (3) botulinum toxin injections in the affected arm in the previous three months which may have affected wrist hyper-resistance components. Ethical approval was obtained from the Medical Ethics Committee of the VU University medical centre, Amsterdam, The Netherlands (NL47079.029.14). In accordance with the Declaration of Helsinki [32], all participants gave written informed consent.

2.2. Experimental design

In this cross-sectional study, demographic data, stroke characteristics, neurological status (NIHSS and Fugl-Meyer motor assessment of the upper extremity), and medical history were collected. NeuroFlexor® (NF), Wristalyzer (WA), and clinical assessments were performed in an arbitrary sequence on the same day, with at least 10 min in between, or, for practical reasons, on two separate days with a maximum of one day in between. When performed on two separate days, the MAS was performed on the same day as the NF assessment. All assessments were performed on the patients’ impaired arm by a team of five trained researchers according to a standardized protocol.

2.3. NeuroFlexor®

2.3.1. Instrumentation and measurement protocol

The NeuroFlexor® [21], is a motor-driven device which applies isokinetic positional perturbations to the wrist with extended fingers from 20° flexion towards 30° extension at two controlled velocities (5 and 236°/s), see Table 1 for characteristics. Resistance during passive wrist extension is measured in Newton [N] using a force sensor mounted underneath the moveable handle. The patient was seated comfortably beside the device with the shoulder in 45° abduction, 0° of flexion, the elbow in 90° of flexion, with the forearm fastened to the device in pronation, and the hand pronated (facing down) with extended fingers fastened to the movable platform. The axis of the wrist joint was visually aligned with the rotation axis of the device. One measurement consisted of five slow movements, followed by ten fast movements. The first movement at both velocities was excluded from the analysis to avoid bias from startle reflexes and mechanical hysteresis. Two NeuroFlexor® measurements were performed at least 15 min apart and mean values were used for further analysis.

2.3.2. Model description and component calculation

Wrist hyper-resistance components were derived from a unidirectional biomechanical model [21,33] based on the force-time traces during passive wrist extension (software program NeuroFlexor Scientific v0.06, Supplementary file 1) The neural component (NF-NC, in Newton) is defined as the immediate resisting force at the end of the fast passive wrist extension movement (i.e., 30° wrist extension) minus the non-neural elastic and viscous components. The elastic component (NF-EC, in Newton) is the length-dependent resisting force recorded 1 s after stopping the slow movement (i.e., 30° wrist extension). The viscous component is the velocity-dependent resisting force of soft tissues to stretch.

2.4. Wristalyzer

2.4.1. Instrumentation and measurement protocol

The Wristalyzer is a one degree-of-freedom haptic manipulator (MOOG, Nieuw Vennep, The Netherlands) [34] rotating a custom-made handle (Meester Techniek, Leiden, The Netherlands) by a vertically positioned servo motor (Parker SMH100 series, Parker Hannifin, Charlotte, NC, USA), see Table 1 for characteristics. Patients were seated comfortably with the shoulder slightly abducted and elbow in 90° flexion. The forearm was strapped in a lower arm cuff in a neutral position between pronation and supination with the hand in the neutral (parasagittal) plane with extended fingers fastened to the handle. The axis of the wrist joint was visually aligned with the vertical rotation axis of the haptic manipulator. Muscle activity of the flexor carpi radialis (FCR) and extensor carpi radialis (ECR) muscles was measured by EMG using pairs of unipolar electrodes (Blue Sensor N, Ambu, Ballerup, Denmark) placed on the muscle belly [16]. Maximal passive range of wrist
extension and flexion was determined by applying a slow increasing torque with a duration of 15 s up to a maximal torque of 2 Nm in both flexion and extension direction. Subsequently, the wrist was passively extended and flexed over the full recorded passive range of motion (PRoM) minus one degree in both the maximal flexion and extension direction (sweep), including two slow sweep trials at 5°/s, two sweeps at PRoM/s, and two fast sweep trials at 236°/s. Each sweep trial contained a preparatory movement from neutral wrist angle position towards maximal flexion, followed by a sweep towards maximal extension, returning to maximal flexion, and ending towards neutral position respectively.

Wrist angle, torque, and EMG signals of the FCR and ECR were recorded simultaneously at 2048 Hz using a Refa amplifier (TMSi, Oldenzaal, The Netherlands). Matlab R2017b (The Mathworks, Inc., Natick, MA, USA) was subsequently used for offline data analysis. Wrist angle and torque signals were low-pass filtered at 20 Hz (3rd-order Butterworth), EMG signals were band-pass filtered at 20–450 Hz (3rd-order Butterworth), full-wave rectified, and subsequently low-pass filtered at 20 Hz (3rd-order Butterworth), to obtain the EMG envelope. Finally, the minimal EMG value, determined with steps of 8 ms during the total time window, was subtracted from the total EMG to reduce the influence of noise and onset muscle activation.

2.4.2. Model description and component calculation

An EMG-based antagonistic optimization wrist model was used based on a bidirectional wrist model [16] which is derived from an ankle model [28]. Wrist angle, torque, and EMG of the FCR and ECR were used to estimate 12 parameters by a nonlinear least squares optimization algorithm that minimizes the error function, i.e. the difference between the measured torque and predicted torque. The model optimized the parameters over the full duration of the sweep protocol with different joint velocities in both extension and flexion direction. Detailed information about the optimization model is described in Supplementary file 2. After parameter optimization, the neural component induced by the velocity-dependent stretch reflex of the FCR during passive wrist extension (WA-NC, in Newton • meter [Nm]) was calculated based on root mean square values of the modelled variant active torque within the time window of the fast (236°/s) extension sweeps and the elastic tissue component of the FCR during passive wrist extension (WA-EC, in Nm/rad) was taken at 30° wrist extension at a velocity of 5°/s.

2.5. Clinical assessment

Resistance to manually applied passive wrist extension movement with extended fingers was measured using the modified Ashworth scale [35], an ordinal scale with scores ranging from 0 (no increased tone) to 4 (the joint is rigid). The maximal range of passive wrist extension with extended fingers was determined using a goniometer. Mean values of three extension movements were used for further analysis.

2.6. Statistical analysis

In the absence of a gold standard, a priori assumptions for the similarity between outcomes of the NeuroFlexor® and Wristalyzer were formulated [36]. Correlation coefficients above 0.50 were considered as similar constructs, between 0.30–0.50 as related, but distinct constructs, and below 0.30 as unrelated constructs [37]. We expected 1a,b) correlation coefficients above 0.50 between the corresponding components of both devices (convergent validity); 2a,b) correlation coefficients below 0.30 between the different components of both devices (discriminant validity); 3a,b) both devices to separate wrist hyper-resistance in two different components (r < 0.30) (discriminant validity); 4) similar individual ranking of the wrist hyper-resistance components of both devices; 5a,b) neural and elastic components of both devices to relate in the same way to the clinical MAS (0.30 < r < 0.50); 6) higher neural and elastic components in patients with higher MAS scores for both devices (discriminative validity), and 7a,b) the elastic component of both devices to relate in the same way to the range of passive wrist extension, obtained by goniometry and the Wristalyzer respectively (0.30 < r < 0.50).

Study data were analysed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used for demographic and clinical characteristics. Correlation coefficients between components, and with the MAS and range of passive wrist extension, were calculated using Spearman’s rank correlation coefficients to address assumptions 1, 2, 3, 5, and 7, respectively. A Fisher’s z transformation was used to calculate 95% confidence intervals of the correlation coefficients [38]. To test whether components relate in the same way to the MAS and the range of passive wrist extension, 95%
confidence intervals were compared (assumption 5 and 7). Overlapping confidence intervals were considered similar. Percentage explained variance was calculated by $r^2 \times 100\%$.

To deal with the differences in metric units used by both devices, outcomes of each component were ranked in order from the lowest to the highest value (rank 1 to 43 respectively). Wilcoxon signed-ranks tests were used to test the differences between the individual ranks of the neural and elastic components of both devices (assumption 4). In addition, for both components of both devices, patients’ scores were classified into quartiles. The quartile classifications of the two devices were compared at individual level for both the neural and elastic components. A difference of more than one quartile between the two devices were compared for the same component within one patient was classified as divergent.

Patients were classified according to their MAS score. Patients with a MAS score of 1 and 1+ were both classified as MAS\textsubscript{1}. The between MAS group differences in neural and elastic components for both devices were assessed by the Kruskal-Wallis analysis, with Mann-Whitney U post-hoc analyses (assumption 6). The level of significance was set two-tailed at 0.05. To correct for multiple testing in the post-hoc analyses, a Bonferroni correction was applied.

### 3. Results

Of the 46 patients in the study, data of 43 patients were included in the analysis. Two patients could not perform the measurements due to pain during passive wrist extension movement and data of one patient was excluded from analysis due to a technical problem of the NF during wrist extension. For three patients, the second NF measurement was missing and data of one measurement was used for analysis. The main demographic and clinical characteristics of the patient population are summarized in Table 2.

Table 3 shows an overview of the pre-determined assumptions and the results of the similarity between the outcomes of the NF and WA, and their relation with the MAS and range of passive wrist extension.

### 4. Discussion

We performed a head-to-head comparison of the NeuroFlexor® (NF) with the EMG-based Wristalyzer (WA) for the quantification of neural and non-neural elastic components of resistance to passive wrist extension in 43 patients with chronic ischemic or haemorrhagic stroke with initial upper limb paresis. The majority (9/12) of our predetermined assumptions were confirmed by this study, which supports the similarity between the two instrumented assessment methods. Significant associations above 0.50 between the neural components as well as between the elastic components obtained by the two devices were as expected, suggesting that the components measured by both devices represent similar constructs. The remaining unexplained variance (i.e., 63% for the neural components and 72% for the elastic components) is substantial and may evolve from differences in measurement setup and protocol, including the presence or absence of direct determination of muscle activity, the different modelling methods in deriving the components and/or the different states at which both components are determined. In comparison, the NF uses a fixed position of 30° wrist extension after a fast wrist extension movement over a fixed 50-degree perturbation range to obtain the neural component, regardless of the patients’ passive range of motion, whereas the WA estimates the neural component over the patients’ full passive range of motion at a corresponding scatterplots of the correlations are presented in Supplementary file 3. NF-NC showed a significant correlation coefficient with WA-NC (0.61, 95% CI: 0.38 to 0.77) and NF-EC showed a significant correlation coefficient with WA-EC (0.53, 95% CI: 0.28 to 0.72). NF-NC showed significant correlation coefficients with WA-NC (0.36, 95% CI: 0.06 to 0.59) and with NF-EC (0.46, 95% CI: 0.18 to 0.67). WA-NC showed non-significant correlation coefficients with NF-EC (0.15, 95% CI: -0.16 to 0.43) and with WA-EC (0.16, 95% CI: -0.15 to 0.44).

Fig. 1 presents an overview of the rank numbers for each component of both devices per patient, ordered by NF-NC. Wilcoxon signed-ranks tests did not show a difference in individual ranks on the NC and EC between the two devices ($P = 0.57$ and $P = 0.87$, respectively). As illustrated in Fig. 2, for the neural component, 20 of the 43 patients (47%) were categorized in equal quartiles by both devices. Nineteen patients (44%) were categorized into different, but adjacent, quartiles, while four patients (9%) were categorized into divergent quartiles. For the elastic component, 17 of the 43 patients (40%) were categorized into equal quartiles. Nineteen patients (44%) were categorized into adjacent quartiles, while seven patients (16%) were categorized into divergent quartiles.

The neural components of both devices, i.e. NF-NC and WA-NC, showed significant correlation coefficients with overlapping confidence intervals with the MAS (0.58, 95% CI: 0.34 to 0.75 and 0.49, 95% CI: 0.22 to 0.69, respectively) (Table 3). The elastic components NF-EC and WA-EC also showed correlation coefficients with overlapping confidence intervals with the MAS (0.51, 95% CI: 0.25 to 0.70 and 0.30, 95% CI: 0.00 to 0.55, respectively). All components showed a gradual increment with MAS category (Table 4). Kruskal-Wallis analysis revealed a significant difference between the MAS categories for NF-NC ($P = 0.005$), NF-EC ($P = 0.014$), and WA-NC ($P = 0.010$). Post-hoc Mann-Whitney U analyses showed a significantly higher NF-EC for patients with MAS\textsubscript{1} and MAS\textsubscript{2} compared to MAS\textsubscript{0} ($P \leq 0.008$). WA-NC for patients with MAS\textsubscript{1} was significantly higher compared to MAS\textsubscript{0} and MAS\textsubscript{1} ($P \leq 0.008$).

The elastic components of both devices, i.e. NF-EC and WA-EC, showed significant negative correlation coefficients with overlapping confidence intervals with the range of passive wrist extension, as obtained by goniometry (-0.44, 95% CI: -0.65 to -0.16 and -0.74, 95% CI: -0.85 to -0.57, respectively). Significant negative correlation coefficients with non-overlapping confidence intervals were found with the range of passive wrist extension, as obtained by the WA at 2 Nm (-0.54, 95% CI: -0.72 to -0.28 and -0.87, 95% CI: -0.93 to -0.78, respectively) (Table 3).

### Table 2

Demographic and clinical characteristics of the study population, stratified by modified Ashworth scale.

<table>
<thead>
<tr>
<th>Overall</th>
<th>MAS\textsubscript{0}</th>
<th>MAS\textsubscript{2}</th>
<th>MAS\textsubscript{0}</th>
<th>MAS\textsubscript{1}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean ± SD)</td>
<td>60.1 ± 7.2</td>
<td>59.3 ± 7.6</td>
<td>60.3 ± 7.2</td>
<td>60.3 ± 7.2</td>
</tr>
<tr>
<td>Gender, male/female</td>
<td>4/14</td>
<td>10/4</td>
<td>16/6</td>
<td>16/6</td>
</tr>
<tr>
<td>Stroke type, iCVA/hCVA (n)</td>
<td>37/6</td>
<td>7/1</td>
<td>22/2</td>
<td>5/2</td>
</tr>
<tr>
<td>Time post stroke, months (mean ± SD)</td>
<td>61.1 ± 33.9</td>
<td>65.8 ± 33.6</td>
<td>73.2 ± 41.0</td>
<td>71.0 ± 39.2</td>
</tr>
<tr>
<td>Affected side, left/right (n)</td>
<td>23/20</td>
<td>14/10</td>
<td>3/4</td>
<td>3/4</td>
</tr>
<tr>
<td>NIHSS score (mean ± SD)</td>
<td>4.7 ± 3.2</td>
<td>3.9 ± 3.9</td>
<td>6.6 ± 3.9</td>
<td>6.8 ± 3.9</td>
</tr>
<tr>
<td>FM-UE (mean ± SD) (min; max)</td>
<td>34.0 ± 18.4 (6; 46)</td>
<td>31.2 ± 18.4 (6; 46)</td>
<td>24.6 ± 18.4 (6; 46)</td>
<td>15.0 ± 18.4 (6; 46)</td>
</tr>
<tr>
<td>Passive wrist extension,goniometry\textsuperscript{a} (mean ± SD)</td>
<td>73.2 ± 18.4</td>
<td>71.7 ± 18.4</td>
<td>68.6 ± 18.4</td>
<td>71.0 ± 18.4</td>
</tr>
<tr>
<td>Passive wrist extension,goniometry\textsuperscript{a} (mean ± SD)</td>
<td>56.4 ± 18.4</td>
<td>57.4 ± 18.4</td>
<td>51.2 ± 18.4</td>
<td>42.5 ± 18.4</td>
</tr>
<tr>
<td>MAS (median [25th, 75th percentile])</td>
<td>1.5 [1 to 2]</td>
<td>1.5 [1 to 2]</td>
<td>1.5 [1 to 2]</td>
<td>1.5 [1 to 2]</td>
</tr>
</tbody>
</table>

\textsuperscript{a}iCVA: ischemic stroke; hCVA: haemorrhagic stroke; NIHSS: National Institutes of Health Stroke Scale [range: 0–42]; FM-UE: Fugl-Meyer motor assessment of the upper extremity [range: 0–66]; passive wrist extension\textsuperscript{goniometry} obtained by goniometry; passive wrist extension\textsuperscript{goniometry} obtained by the Wristalyzer using 2 Nm; MAS: modified Ashworth scale [range 0–4].

--

A. Andringa et al. Medical Engineering and Physics 98 (2021) 57–64
velocity of 236°/s, using EMG, which will affect the estimate of the reflexive response of muscle activity. Furthermore, the position of the forearm in which the wrist is moved differs per device. In the wrist extension movement in the vertical plane, which is imposed by the NF, the gravitational component of the mass of the hand may influence the exerted force from which the neural and elastic components are

Table 3
Overview of pre-determined assumptions and their results for similarity between the outcomes of the NeuroFlexor® and Wristalyzer.

<table>
<thead>
<tr>
<th>Pre-determined assumptions for similarity</th>
<th>Expected correlation</th>
<th>Results</th>
<th>Assumption confirmed?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a NF-NC vs. WA-NC</td>
<td>$r &gt; 0.50$</td>
<td>0.61 (0.38 to 0.77)</td>
<td>37% √</td>
</tr>
<tr>
<td>b NF-EC vs. WA-EC</td>
<td>$r &gt; 0.50$</td>
<td>0.53 (0.28 to 0.72)</td>
<td>28% √</td>
</tr>
<tr>
<td><strong>2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a NF-NC vs. WA-EC</td>
<td>$r &lt; 0.30$</td>
<td>0.36 (0.06 to 0.59)</td>
<td>13% x</td>
</tr>
<tr>
<td>b WA-NC vs. NF-EC</td>
<td>$r &lt; 0.30$</td>
<td>0.15 (-0.16 to 0.43)</td>
<td>2% √</td>
</tr>
<tr>
<td><strong>3</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a NF-NC vs. NF-EC</td>
<td>$r &lt; 0.30$</td>
<td>0.46 (0.18 to 0.67)</td>
<td>21% x</td>
</tr>
<tr>
<td>b WA-NC vs. WA-EC</td>
<td>$r &lt; 0.30$</td>
<td>0.16 (-0.15 to 0.44)</td>
<td>3% √</td>
</tr>
<tr>
<td><strong>4</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ranking of components per individual is similar in both devices</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>5</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a NF-NC vs. MAS ($r_1$) is equal to WA-NC vs. MAS ($r_2$)</td>
<td>$r_1 = r_2$</td>
<td>$r_1 = 0.58 (0.34 to 0.75)$</td>
<td>√</td>
</tr>
<tr>
<td>b NF-EC vs. MAS ($r_3$) is equal to WA-EC vs. MAS ($r_4$)</td>
<td>$r_3 = r_4$</td>
<td>$r_3 = 0.51 (0.25 to 0.70)$</td>
<td>√</td>
</tr>
<tr>
<td><strong>6</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NC’s and EC’s measured by devices are higher in patients with higher MAS scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>7</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a NF-EC vs. passive wrist extension$<em>{gonio}$ ($r_1$) is equal to WA-EC vs. passive wrist extension$</em>{gonio}$ ($r_2$)</td>
<td>$r_1 = r_2$</td>
<td>$r_1 = -0.44 (-0.65 to -0.16)$</td>
<td>√</td>
</tr>
<tr>
<td>b NF-EC vs. passive wrist extension$<em>{wa}$ ($r_3$) is equal to WA-EC vs. passive wrist extension$</em>{wa}$ ($r_4$)</td>
<td>$r_3 = r_4$</td>
<td>$r_3 = -0.54 (-0.72 to -0.28)$</td>
<td>x</td>
</tr>
</tbody>
</table>

√, assumption confirmed; x, assumption not confirmed; NF-NC: NeuroFlexor®, neural component [N]; NF-EC: NeuroFlexor®, elastic component [N]; WA-NC: Wristalyzer, neural component [Nm]; WA-EC: Wristalyzer, elastic component [Nm/rad]; MAS: modified Ashworth scale [-]; passive wrist extension$_{gonio}$ obtained by goniometry [°]; passive wrist extension$_{wa}$ obtained by the Wristalyzer using 2 Nm [°]. Values are Spearman’s rank correlation coefficients ($r$) with 95% confidence intervals.

Fig. 1. Overview of the ranking of neural and elastic components of both devices per patient, with patients ordered according to the neural component assessed by the NeuroFlexor®. The outcomes of each component were ranked in order from the lowest to the highest value (rank 1 to 43 respectively). NF-NC: NeuroFlexor®, neural component; WA-NC: Wristalyzer, neural component; NF-EC: NeuroFlexor®, elastic component; WA-EC: Wristalyzer, elastic component.
consistent with previous studies that suggest that assessments using components of both devices, while WA-NC showed no association with computationally intensive. Currently still limited as the offline signal analysis is yet complex and Q: quartile.

EMG-related parameters [39,40]. In contrast, EMG-based instrumented be less valid to describe neural components than measurements using neural and elastic component of wrist hyper-resistance. Our findings are WA, using input from EMG, provides better discrimination between the either a non-neural component, such as viscosity, or other neural factors, such as involuntary background activation. Our findings suggest that the non-neural component; WA-EC: Wristalyzer, elastic component; MAS: modified Ashworth scale. NF-NC showed unexpectedly high associations with the elastic components of both devices were moderately associated with the MAS, and the elastic components of both devices showed negative associations with the range of passive wrist extension, suggesting construct validity of both devices for quantification of neural and elastic components of wrist hyper-resistance in patients with chronic stroke. However, these assessment methods that are able to discriminate between components of wrist hyper-resistance have an added value compared to clinical assessment with the MAS alone. Further investigations are required to assess whether muscle activity measurements by EMG are needed to gain a valid, reliable, and accurate discrimination between the neural and non-neural tissue property-related components.

The overall results of our study indicate comparable outcomes for the NF and WA at group level, however, there is misclassification at the individual level seen in Fig. 2. This may lead to different treatment decisions in clinical practice at the individual level. The responsiveness of the neural and non-neural components to different treatments, such as botulinum toxin and orthotics, should be evaluated in future studies to gain insight into treatment options for patients with increased neural and/or non-neural components of wrist hyper-resistance and the associated cut-off values that can be used for patient selection.

As expected, components of both devices were moderately associated with the MAS, and the elastic components of both devices showed negative associations with the range of passive wrist extension, suggesting construct validity of both devices for quantification of neural and elastic components of wrist hyper-resistance in patients with chronic stroke. However, these assessment methods that are able to discriminate between components of wrist hyper-resistance have an added value compared to clinical assessment with the MAS alone.

4.1. Study limitations

Differences in metric units prevented the assessment of absolute agreement. Patients with passive wrist extension of less than 40º had to
be excluded due to the NF protocol, which may have affected the variance in the passive tissue properties of the wrist flexor muscle in the included group of patients. Due to pragmatic reasons, the NF and WA assessments were performed in a semi-randomized order and, in thirteen patients, on different days. As the neural drive can vary from day-to-day and even within a day, these fluctuations could have influenced the variance in the neural component between the devices.

5. Conclusions

The current study shows similarity between two instrumented assessment methods, i.e. NeuroFlexor® and the EMG-based Wristalyzer, for the quantification of neural and non-neural elastic components of wrist hyper-resistance in patients with chronic stroke. The NeuroFlexor® is easier for clinical use, while the EMG-based Wristalyzer may provide a better distinction between the independent components of wrist hyper-resistance. The possible added value of EMG in the discrimination between the neural and non-neural components, as well as the improvement of the classification of wrist hyper-resistance components at the individual level, requires further investigation.

CRediT authorship contribution statement

**Aukje Andringa:** Visualization, Formal analysis, Writing – original draft, Investigation. **Carel Meskers:** Conceptualization, Supervision, Writing – review & editing. **Ingrid van de Port:** Writing – review & editing. **Sarah Zandvliet:** Software, Investigation, Writing – review & editing. **Larissa Scholte:** Data curation, Software, Formal analysis, Writing – review & editing. **Jurriaan de Groot:** Software, Data curation, Writing – review & editing. **Gert Kwakkell:** Conceptualization, Supervision, Writing – review & editing. **Erwin van Wegen:** Conceptualization, Supervision, Writing – review & editing.

Declaration of Competing Interest

None declared.

Acknowledgments

We are grateful to all patients for their participation in the study. We would like to thank Mique Sae, Dirk Hoevenaars, and Robert Croese for their contribution to the data collection and Caroline Terwee for her contribution to the interpretation of the data.

Funding

This work was supported by the European Research Council (Grant No. 291339, 4D-EEG project); The Netherlands Organisation for Health Research and Development (ZonMw) (Grant No. 104003008, PROFITS project); and an unrestricted grant from IPSEN.

Ethical approval

Ethical approval was obtained from the Medical Ethics Committee of the VU University medical centre, Amsterdam, The Netherlands (NL47079.029.14).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.medengphy.2021.10.009.

References


Medical Engineering and Physics 98 (2021) 57–64


