Test-Retest Reliability of Cardiorespiratory Parameters Assessed by Metamax3B During Walking in Persons with Stroke

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Abstract

Introduction: No studies have explored the reliability of the test re-test of the portable respiratory gas exchange analyzer (Metamax3B) in stroke patients despite its increasing use in clinical research. The objective was to evaluate the test-retest reliability of the cardiopulmonary parameters measured by Metamax3B during walking at self-selected speed in individuals with stroke.

Material and Methods: This study included stroke individuals able to walk without human assistance. The participants were equipped with the Metamax3B, calibrated and installed according to the manufacturer's recommendations. The parameters, i.e. oxygen uptake (VO₂), oxygen uptake by weight (VO₂.kg⁻¹), carbon dioxide production (VCO₂), respiratory exchange ratio (RER), expiratory flow rate...
(VE), tidal volume (VT) and respiratory frequency (BF) were measured twice during 6 minutes of walking at self-selected speed in tests performed 2 days apart. The test-retest reliability of these parameters was evaluated using Bland-Altman analysis.

**Results:** Sixteen individuals with stroke sequelae were included (mean age 64.5±14.3 years). No significant difference was observed between the test retest measurements for all parameters except for RER (mean difference=0.02; p=0.01). The Bland Altman analyses showed a mean bias of less than 5% between the test retest measurements.

**Discussion and Conclusions:** The reliability of the cardiorespiratory parameters measured by Metamax3B during walking at self-selected speed in individuals with stroke was high, which encourages the use of this device in this population.

**Keywords:** Reliability; Stroke; Metamax3B; Metabolic cart; Physical activity; Walking

1. **Introduction**

International organizations recommend the use of oxygen uptake (\(\dot{V}O_2\)) to individualize the exercise intensities recommended for individuals with stroke [1]. Controlling the intensity of exercises has been proven to improve the benefits on the cardiorespiratory and functional abilities of stroke patients [2].

Over the past decade, a wide range of portable devices have been developed such as Oxycon Mobile (Carefusion, San Diego, CL, USA) Metamax3B (Cortex Medical, Leipzig, Germany), or Cosmed K4b [2] (Cosmed, Chicago IL, USA). The main interest of this type of monitor is to allow measurements of \(\dot{V}O_2\) outside of laboratory conditions to determine the metabolic solicitation of individuals during ecological activities. These devices therefore facilitate the measurement of respiratory gas exchanges during common physical activities such as walking on flat or irregular ground, walking up or down stairs, manual activities and sports activities. The main appeal of these devices is their reduced weight and size of the systems thanks to miniature sensors for measuring O\(_2\) and CO\(_2\) concentrations, as well as the development of smaller flowmeters [3]. In addition, the recording of variables requires an instant wireless connection with a central computer. Such drastic modifications in spiroergometry and data exchange systems may alter the measurement values compared to larger devices [4].

Reliability describes the ability of a device to accurately repeat a measurement of a given parameter on repeated trials. This is one of the parameters of the validity of a measuring device, along with accuracy. Reliability is fundamental because it is essential to know if a difference observed between two tests represents a real change or simply a measurement error [5].

The Metamax3B (Cortex, Leipzig, Germany) is a portable respiratory gas exchange analyzer consisting of a measuring module, a battery module and a wireless connection system. It is one of the 3 main respiratory gas exchange analyzers used in clinical practice and research [6], the two others being Oxycon Mobile (Carefusion, San Diego, CL, USA) and Cosmed K4b[2] (Cosmed, Chicago IL, USA). Although the Metamax3B is frequently described as
less precise than Oxycon Mobile and Cosmed K4b [2, 6], it is widely used in healthy subjects and in individuals with chronic diseases such as strokes [7-11]. The reliability of the Metamax3B has been evaluated by numerous studies in healthy subjects [6, 12-14]. Perkins et al. (2004) evaluated the reliability of the Metamax3B in healthy subjects on 2 separate days. The authors reported a high test-retest reliability (intraclass correlation coefficient = 0.97, standard error measure = 0.03 – 0.08 L.min⁻¹) [15]. Macfarlane et al. (2012) have also evaluated its validity using the Gas Exchange System Validator test (MedGraphics, MA, USA). This test has been carried out twice and resulted in a high test-retest reliability (ICC=1) with a technical measurement error (TEM) of 1.5% for \( \dot{V}O_2 \) [14].

Although this device has shown high accuracy and reliability in healthy subjects, our experience shows that several factors can compromise its reliability in stroke patients. First, each individual present variable levels of impairment such as spasticity over time [16]. Some of these variations are not related to their recovery but may be related to attention level, stress, medication or intercurrent medical issues [17]. In addition, individuals affected with a stroke feel the effects of fatigue more than healthy subjects, which may set boundaries in their involvement [18]. Moreover, some complications of stroke, such as facial paralysis, can also complicate the use of breathing masks. All these factors can impact the reliability of the exploration of cardiorespiratory parameters carried out by portable respiratory gas exchange analyzers in this population.

To our knowledge, no work has evaluated the reliability of the measurement of \( \dot{V}O_2 \) by Metamax3B during walking at self-selected speed in stroke individuals despite the publication of numerous studies on related topics [8-11]. Measuring cardiorespiratory parameters of walking is essential in stroke individuals because they have a prognostic value in terms of functional ability and social participation [19, 20]. Moreover, recent study reported that the required walking activity necessary to reach physical activity level recommended by the World Health Organization could be adjusted with the oxygen consumption during walking [8].

The objective of this work was to evaluate the reliability of the measurement of cardiorespiratory parameters measured by Metamax3B in individuals with stroke during walking at self-selected speed on flat ground.

2. Materials and Methods

2.1 Study design

This work is a cross-sectional study evaluating the test re-test reliability of the cardiorespiratory parameters reported by Metamax3B during a 6-minute walking activity in individuals with stroke sequelae.

2.2 Population

Participants were recruited in the Physical Medicine and Rehabilitation Department. The inclusion criteria were the following: a single stroke in any area of the brain confirmed by brain imaging, and the ability to walk without human assistance. The non-inclusion criteria were the following: acute cardiac or respiratory pathologies or decompensated chronic pathologies. Cardiac disorders were searched using the complementary examinations usually carried out...
in post-stroke assessment, i.e. electrocardiogram and cardiac ultrasound.

Motor function was evaluated using the Demeurisse motricity index [21], which quickly assesses a patient’s motor function using three tests per deficient limb and which is validated in stroke patients. The patient’s score is calculated from five stages of voluntary motor control from a scale to 0-100, in which a score of 100 is considered healthy [21, 22]. Spasticity was evaluated using the Modified Ashworth Scale (MAS) [23]. Autonomy related to activities of daily living was evaluated using the Barthel Index [24]. Each patient’s walking speed was estimated during the walking task by dividing the distance walked by the duration of the task, which was established at 6 minutes. All of these evaluations were performed by the same examiner for all participants.

The health professional responsible for the data collection informed the participants himself of the details of the protocol before registering their consent. This consent was transcribed in the database. The research protocol and this method of consent were accepted by an ethics committee (RCB: 2012-A01456-37).

2.3 Metabolic cart

The Metamax3B (Cortex Medical, Leipzig, Germany) is a device which measures gas volume using a bidirectional digital turbine [25]. The O2 and CO2 concentrations are measured using an electrochemical cell and an infrared analyzer. VO2 and VCO2 were calculated using standard metabolic algorithms based on the Haldane transformation [26]. Respiratory volume data and respiratory gas concentrations were transmitted live by telemetry to a computer. The system was paired to the Metasoft 3 software, version 3.7.0 SR2. The device was switched on at least 20 min before each use. It was calibrated according to the manufacturer’s recommendations with the following procedure: calibrating the gas analyzers every 14 days by using a reference gas (14.97% O2, 4.96% CO2, balance N2: ±0.02% absolute, Hong Kong Specialty Gases) and checking the calibration exposed to ambient air. Additionally, a volume calibration was performed every day using a standardized 3L syringe (5530 series, HansRudolph, Inc., MO, USA) [25].

2.4 Protocol

We tested the reliability of the measurement of cardiorespiratory parameters measured by Metamax3B in stroke individuals during a walking activity at self-selected speed, which is considered as a moderate-intensity physical activity (6). We have selected this activity as it is both the most common activity performed by stroke individuals in our department because of its impact on functional capacities and social participation. In addition, the metabolic intensity it requires [27] makes it a main activity for physical activity programs offered to our patients. We have selected a duration of the walk of 6 minutes in order to achieve metabolic stability in each subject [28]. Each walk was preceded by 5-10 minutes of rest in a sitting position on a chair to ensure a stable metabolic state. The test was carried out a few hours after meals and in the absence of exciting products that could cause a change in respiratory gas exchanges. The testing protocol was then carried out a second time, ideally 2 days after the first, with equivalent schedules and medical context (nursing, medical care, physical therapy) to avoid
confounding factors that could modify the cardiorespiratory parameters measured during the test.

2.5 Cardiorespiratory parameters
The following physiological parameters were used as they are the most frequently reported in scientific work in the field [28, 29]: \( \dot{V}O_2 \) (L min\(^{-1}\)); \( O_2 \) uptake by weight (mL kg\(^{-1}\)min\(^{-1}\)); \( \dot{V}CO_2 \) (L min\(^{-1}\)); respiratory quotient (RER); expiratory flow rate (VE) (L min\(^{-1}\)); tidal volume (VT) (L); breath frequency (BF) (b min\(^{-1}\)).

2.6 Statistical analysis
We calculated the number of subjects required from the reliability results of the research by Vogler et al. 2010 [13]. The mean difference in the test retest was 2.3% IC95%(1.9-2.6%) for \( \dot{V}O_2 \). Taking into account this mean difference and dispersion we calculated a number of subjects of 12 individuals to obtain a statistically significant difference between the 2 test/re-test measures. Considering the risk of dropping individuals due to intolerance to wearing Metamax3B or medical problems in the interval between the test/re-test measures, we decided to include 15 individuals with stroke.

We calculated the difference between the 2 tests and its significance by means of a t-test in the case of a normal distribution and a Wilcoxon test for matched samples in the case of a non-normal distribution. Pearson correlation coefficients were calculated. The rule of thumb for interpreting the size of a correlation coefficient was: .90 to 1.00, very high correlation; .70 to .90, high correlation; .50 to .70, moderate correlation; .30 to .50, low correlation; .00 to .30, negligible correlation [30]. A Bland-Altman analysis was also carried out to assess the test retest reliability as recommended by Berchtold 2016 [31]. The significance rate was 0.05 for all statistical analyses. All the analyses were carried out by “blandr” and “tidyverse” packages in Rstudio (Version 1.2.5033) © 2009-2019 RStudio, Inc.

3. Results
16 patients with stroke sequelae were included in the test protocol. All participants were in the chronic phase of their stroke with moderate impairments (mean Demeurisse score in lower limb = 81 (43 – 100) ; MAS = 1 (0 – 3)). Their walking speed was 0.83±0.31 ms\(^{-1}\) for the 1st test and 0.84±0.32 ms\(^{-1}\) for the 2nd test. The 2nd test took place on average 1.5±0.8 days after the first. We did not find any statistical difference between the 2 evaluations on the different impairments and autonomy scores collected (Table 1).

No specific adverse events were recorded and there was no discontinuation of the evaluation due to poor tolerance of Metamax3B.

A statistically significant difference was found between the 2 tests for the RER (mean difference=0.02; p=0.01). No statistical differences were found for all other comparisons. (Table 2).
### Table 1: Characteristics of the population. SD: standard deviation; BMI: Body Mass Index; FACm: Functional Ambulation Classification modified; Speed (walking at self-selected speed) D0: first exploration; D1: second exploration; N/A: Not adapted.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>D0</th>
<th>D1</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.6 (56.8-73.5)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>BMI (kgm⁻²)</td>
<td>25 (23-29)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Stroke side (L/R)</td>
<td>9/7</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Time since stroke (day)</td>
<td>37 (30-285)</td>
<td>38 (31-286)</td>
<td>0.74</td>
</tr>
<tr>
<td>Index of Motricity of Demeurisse Lower Limb (/100)</td>
<td>78 (59-100)</td>
<td>81 (59-100)</td>
<td>0.98</td>
</tr>
<tr>
<td>Index of Motricity of Demeurisse Upper Limb (/100)</td>
<td>80 (69-100)</td>
<td>80 (69-100)</td>
<td>0.96</td>
</tr>
<tr>
<td>Spasticity (Ashworth scale modified) (/4)</td>
<td>1 (0-2)</td>
<td>1 (0-2)</td>
<td>0.78</td>
</tr>
<tr>
<td>Barthel Index (/100)</td>
<td>88 (69-100)</td>
<td>88 (69-100)</td>
<td>0.88</td>
</tr>
<tr>
<td>FACm (/8)</td>
<td>6 (4-7)</td>
<td>6 (4-7)</td>
<td>0.96</td>
</tr>
<tr>
<td>Speed (m.s⁻¹)</td>
<td>0.83 (0.31)</td>
<td>0.84 (0.32)</td>
<td>0.43</td>
</tr>
</tbody>
</table>

### Table 2: Test-retest reliability of cardiorespiratory parameters measured by Metamax3B in individuals with stroke. (VO₂: oxygen consumption; VCO₂: carbon dioxide production; VO₂kg⁻¹: oxygen consumption per kilogram; RER: 

<table>
<thead>
<tr>
<th>Parameter</th>
<th>D0</th>
<th>D1</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO₂ (L.min⁻¹)</td>
<td>0.91 (0.28)</td>
<td>0.93 (0.29)</td>
<td>0.53</td>
</tr>
<tr>
<td>VCO₂ (L.min⁻¹)</td>
<td>0.77 (0.26)</td>
<td>0.80 (0.27)</td>
<td>0.18</td>
</tr>
<tr>
<td>VO₂kg⁻¹ (mL.kg⁻¹.min⁻¹)</td>
<td>12.04 (2.77)</td>
<td>12.45 (2.89)</td>
<td>0.50</td>
</tr>
<tr>
<td>RER</td>
<td>0.84 (0.05)</td>
<td>0.86 (0.05)</td>
<td>0.98</td>
</tr>
<tr>
<td>VE (L.min⁻¹)</td>
<td>31.76 (11.57)</td>
<td>33.03 (11.79)</td>
<td>0.25</td>
</tr>
<tr>
<td>VT (L.min⁻¹)</td>
<td>1.20 (0.37)</td>
<td>1.23 (0.37)</td>
<td>0.35</td>
</tr>
<tr>
<td>BF (b.min⁻¹)</td>
<td>26.60 (3.73)</td>
<td>27.16 (4.58)</td>
<td>0.35</td>
</tr>
</tbody>
</table>

| MB                               | -0.05 (-5.4%)           | -0.03 (-3.7%)           | 0.98    |
| MB%                              | -0.40 (-3.2%)           | -0.01 (-1.1%)           | 0.97    |
| MB%                              | -1.26 (-3.9%)           | -0.03 (-2.4%)           | 0.94    |
| MB%                              | -0.55 (-2.0%)           |                     |         |
| Upper LoA                        | 0.09 (0.09)             | 1.48 (0.02)             | 0.09    |
| Lower LoA                        | -0.14 (-1.05)           | -2.28 (-0.05)           | 0.07    |
| RMSE                             | 0.06 (0.07)             | 0.97 (0.02)             | 0.06    |
| %RMSE                            | 6.6% (8.5%)             | 8.0% (8.0%)             | 0.06    |

(VO₂: oxygen consumption; VCO₂: carbon dioxide production; VO₂kg⁻¹: oxygen consumption per kilogram; RER: 

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respiratory exchange ratio; VE: expiratory flow; VT: Tidal volume; BF: breath frequency; r: Pearson correlation coefficient; IC: confidence interval; MB : Mean Bias of Bland-Altman analysis ; MB% : Mean Bias expressed in percentage of the mean of the variable assessed ; Upper LoA : Upper limits of agreement of Bland-Altman analysis ; Lower LoA : Lower limits of agreement of Bland-Altman analysis ; RMSE: root mean square error; % RMSE: RMSE expressed as a percentage of the measured value. D0: First exploration; D1: second exploration).

The Bland-Altman analysis showed mean bias below 5% for all measured parameters. (Table 2 ; Figure 1)

**Figure 1:** Bland-Altman plots for each parameter measured by Metamax3B between first exploration (D0) and second exploration (D1).
4. Discussion

This work showed high test retest reliability of $\dot{V}O_2$(L.min$^{-1}$), $\dot{V}O_2$.kg$^{-1}$ (mL.min$^{-1}$.kg$^{-1}$), VT, VE and BF measured by Metamax3B in individuals with stroke during walking tests at self-selected speed. The reliability parameters were high with mean bias of Bland Altman analysis below 5% between the 2 evaluations performed 2 days apart.

These results are in line with previous work on the validity of Metamax3B for this type of exploration. Indeed, Macfarlane and Wong reported excellent reliability values (ICC=1) in a study comparing the values of $\dot{V}O_2$, $\dot{V}CO_2$ and VE between Metamax3B and a gas calibrator [14]. Other similar studies have reported equivalent reliability parameters [32-34]. This reinforces the evidence that the Metamax3B is a reliable device for measuring respiratory gas exchange parameters.

Our main concern before this study was that the stroke sequelae would lead to a lack of reliability in the measurement of cardiorespiratory parameters due to numerous reports that stroke individuals have variable impairments [17], ways of walking [35], and show increased fatigue during exercise [36]. Several studies reported similar results regarding portable respiratory gas exchanges analyzers from other manufacturers. Eng et al. reported an ICC of 0.96 for $\dot{V}O_2$ values measured by the KB1-C portable respiratory gas exchange analyzer (KB1-C, Aerosport) during a six-minute walk test (6MWT) in 12 stroke subjects [37]. Stookey et al. also reported an ICC of 0.90 for $\dot{V}O_2$ values measured by the K4b2 portable respiratory gas exchange analyzer (K4b2; COSMED USA, Chicago IL) during a 6MWT in 23 stroke subjects [38]. Our results confirm the reliability of this type of exploration in stroke individuals; furthermore, for the first time, it provides reliability results for Metamax3B in stroke individuals, which encourages its use in this population.

We found a significant difference between the 2 trials for the RER (MD=0.02; p=0.01). However, the RER is considered by many works as the least reliable parameter. Indeed, Tang et al. reported an ICC of 0.58 for the RER peak during stress tests in 20 stroke subjects [39]. Stookey et al. also reported an ICC of 0.64 (0.33-0.82) for RER in a 6MWT test in 23 stroke subjects [38]. Nonetheless, the ICC of RER was better in our study than in the aforementioned studies. We believe that this parameter has a lower reliability because it is calculated from $\dot{V}O_2$ and $\dot{V}CO_2$, and thus multiplies the reliability errors of both $\dot{V}O_2$ and $\dot{V}CO_2$.

This study boasts several research and clinical practice interests. Indeed, in recent years, many studies have been published based on the validity of Metamax3B on healthy or non-stroke pathological populations [8-10, 27, 40, 41]. This work is the first to explore the reliability of Metamax3B and thus confirms the validity of the previously studies which used the Metamax3B in their explorations in stroke individuals. In addition, on a clinical point of view, this device could be used routinely as it is well-tolerated by patients. Of the 32 explorations we performed, there was no complaint about wearing Metamax3B. It is also easy to use and can be installed in minutes. Its use in common clinical practice would enable medical practitioners to evaluate the $\dot{V}O_2$ during walking at the beginning and end of rehabilitation programs, for example. It would thus make it possible to assess the improvements in the oxygen cost of walking, a parameter calculated by dividing $\dot{V}O_2$ by the self-selected walking speed at the
metabolic plateau which reflects a patient’s recovery of walking efficiency [20]. The oxygen cost of walking has a high prognostic value in terms of walking ability [42] and social participation in stroke patients [43, 44].

5. Limitations
There were several limitations to this work. First, the small number of included subjects (16 patients) limits its generalization to the entire stroke patient population. However, this number of participants was determined on the basis of previous work [13] to obtain sufficient power to show statistically significant differences. This is what was found for the RER parameter despite a very small difference between the 2 measures (mean difference=0.02; p=0.01). Another limitation is the type of physical activity we have chosen. On the one hand, walking at self-selected speed has the advantage of being an ecological activity that is well tolerated by patients and crucial in terms of autonomy and social participation [45, 46]. On the other hand, it could be interesting to include various physical activities, e.g. walking up and down stairs or manual activities to assess the reliability of the Metamax3B during activities with variable stress intensities. The incorporation of various activities represents an interesting lead in future work investigating the reliability of portable respiratory gas exchange analyzers. Finally, regarding the choice of parameters, we could also have integrated the heart rate and thus the O2 pulse. However, many studies have shown the extreme variability of heart rate [47] in stroke patients due to cardiac co-morbidities and cardiotropic treatments [48], which explains why this parameter is rarely used in clinical practice.

6. Conclusions
This work showed that the measurement of cardiorespiratory parameters such as $\dot{V}O_2$, $\dot{V}O_2$.kg$^{-1}$, $\dot{V}CO_2$, VE, BF and VT by Metamax3B during a walk at self-selected speed in individuals with stroke shows satisfying reliability. These results encourage the use of portable respiratory gas exchange analyzers in stroke population to assess the cardiorespiratory parameters.

Disclosure
The authors have no competing interest to declare.

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