Wrist Actimetry Biomarker Development of Paretic Upper Limb Use in Post Stroke Patients for Ecological Monitoring.

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Research

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Wrist actimetry biomarker development of paretic upper limb use in post stroke patients for ecological monitoring.

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Abstract

Background

In post-stroke patients it is unclear which wrist actimetry biomarkers to use to estimate the degree of upper limb hemiparesis. The objective of this study was to develop a general and objective framework for monitoring hemiparetic patients in their home environment via different biomarkers based on 7 days of actimetry data. A secondary objective was to use all of

these biomarkers to better understand the mechanism for potential non-use of the paretic upper limb.

Methods

Accelerometers were worn continuously for a period of 7 days on both wrists of 10 post-stroke hemiparetic patients as well as 6 healthy subjects. Various wrist actimetry biomarkers were calculated, including the Jerk ratio 50 (JR50, cumulative probability that the Jerk Ratio is between 0 and 0.5), absolute and relative amounts of functional use of movements of the upper limbs (FuncUse and FuncUseR) and absolute and relative velocities of the upper limbs during functional use (VUL and VULR). For each biomarker, the values of stroke and healthy groups were compared. The correlations between all the biomarkers were studied.

Results

We studied 10 participants with mild-to-moderate chronic hemiparesis and 6 healthy control participants. FuncUse and VUL of the paretic upper limb of stroke patients were significantly lower than in the non-dominant upper limb of healthy subjects. Similarly, FuncUseR (paretic/non-paretic vs non-dominant/dominant), JR and VULR are significantly lower in stroke patients than in healthy subjects. FuncUseR, VULR and JR50 seem to be complementary biomarkers for monitoring patient strokes.

Conclusion

The stroke patients do not seem to compensate for the decrease in functional movement on the paretic side by an increase on the non-paretic side. The speed of execution of functional movements on the paretic side could be the limiting factor to a normal use of the paretic upper limb. A thorough clinical study is needed to identify the limiting factors. In conclusion, this study for the first time has shown actimetry is a robust and non-obtrusive lightweight

technology for continuously acquiring objective upper limb data of paretic arm use/ non-use over an extended period in a home environment for monitoring stroke patients.

Keywords: Actimetry, Stroke, hemiparesis, biomarkers, upper limb,

1. Background

Stroke is one of the leading causes of disability worldwide, with a global prevalence rate that has been increasing over the past 30 years [Murray et al., 2012]. Despite the accumulated research on rehabilitation of the upper limb (UL) following a stroke, a large majority of patients continue to present non-use of paretic upper limb at the chronic stage which impacts their quality of daily life [Morris et al, 2013]. As such, only 5 to 20% of stroke survivors regain UL function after 6 months [Kwakkel et al, 2003]. Although there are numerous clinically based assessments of paretic arm use/non-use, objective, robust, and reproducible indicators of the amount of UL use in a home environment are needed for better monitoring the paretic UL use and non-use and the response to various proposed treatments aiming at improving motricity and functioning.

Current methods of quantifying movement of the upper limbs rely primarily on clinical deficit scores such as the Fugl-Meyer test [Fugl-Meyer et al, 1975], or on more functional tests like Wolf Motor Function Test (WMFT), Action Research Arm Test (ARAT) or questionnaires (Motor Activity Log - MAL). A more recent work focused on the direct visual observation of stroke patients by hospital practitioners in a clinical environment during 7 days [McLaren et al, 2020]. This work found that the ratio of use activity between the paretic limb and the non-paretic limb is around 0.69 for stroke patients [McLaren et al, 2020] whereas it is 0.95 for

healthy subjects (non-dominant/dominant) [Bailey et al, 2014]. The human assessor method used by McLaren, [McLaren et al, 2020] has the advantage of identifying with certainty the periods of functional use as assessed directly by the clinician. However, the time and human resources costs of performing these measurements reduce its applicability to monitor multiple patients, and moreover, limiting observations in a clinical setting and not in a home environment reduces the ecological validity of these observations.

Alternatively, a commonly used quantitative and objective technique to quantify functional UL movements relies on methods based on actimeters or gyroscopes [Bailey et al, 2014] positioned on the wrists over a period of time ranging from 2 to 7 days. The functional UL movement results of Bailey's work [Bailey et al, 2014; Bailey et al, 2015] are based on the calculation of activity counts directly from the acceleration signals. The authors then obtain activity durations and intensities. However, these metrics have shown limitations, especially since the proprietary activity count algorithms do not allow for validation and standardization of the method. To overcome this, Pan et al, [Pan et al, 2020] developed new accelerometric biomarker based on the Jerk, which is the derivative of acceleration. He showed that the Jerk ratio (JR) has a very high sensitivity to the amount of UL motion as well as a very high correlation with the biomarkers developed by Bailey et al. Leuenberger [Leuenberger et al, 2017] extended the method by using inertial sensors (accelerometer and gyroscope) as inclinometers. This allowed the authors to define functional upper limb movements according to elevation angle and range of motion in a given time space. Leuenberger [Leuenberger et al, 2017] found excellent correlation of these biomarkers with the box and block test. However, Leuenberger's work [Leuenberger et al, 2017] is based on inertial sensors with low energy autonomy, which only allow for measurements over 2 consecutive days. In addition, no comparison was made with healthy subjects.

In this study, we developed a new method to derive a biomarker of functional UL use using two accelerometers positioned at each wrist that couples the calculation of the JR with the elevation angle of the UL over a period of 7 days, in the patients' ecological environment. The new biomarker is termed the execution velocity of functional upper limbs (VUL) movements that is calculated via the temporal derivative of the elevation angle of the UL. We then compared the different accelerometric biomarkers between a population of 10 stroke patients and 6 healthy subjects.

2. Methods

1. Participants

In this study, a sample of 10 stroke survivors and a sample of 6 healthy subjects were recruited by the Physical and Rehabilitation Medicine PRM) department of Montpellier University Hospital. Each participant was asked to sign an informed consent form approved by the Institutional Review Board (the local ethics commission). Patients were recruited in the PRM unit between December 2019 and May 2021. The post-stroke participants met the following inclusion criteria: (1) diagnostic criteria for stroke, (2) people after an ischemic or haemorrhagic stroke that suffered from a paretic arm (defined as a Fugl Meyer -Upper Extremity – FM-UE score >15/66), in the chronic stage of recovery (>6month post-stroke). (2) 18 years or older. The exclusion criteria were the following: (1) Mini-Mental Status Examination score <24 [Bleecker et al, 1988], (2) strong neglect with a Bell's test >15 bells (3) othopedic or rheumatologic injury on the forearm, (3) pregnancy. The controls had no self-reported injuries that would alter or impair their use of either UL.

2. Procedures

Accelerometers (Axivity Ax3, Newcastle upon Tyme, UK) were placed on each wrist for all participants. The patients were asked to wear the accelerometers for 7 days without removing them. Data acquisition was performed at a frequency of 50Hz coupled with a cut off of 8g for

the measurement of acceleration in the three spatial directions. The accelerometers were recovered at the end of the 7 days to extract the data using the OmGui software provided by Axivity. The data were sliced day by day to obtain daily acceleration data values. The data were then saved in csv format so they can be read by any programming language.

3. Biomarkers

Data processing was done using the *python 3.7* programming language. The *numpy* and *scipy* libraries are notably used for numerical calculation operations (derivation, frequency analysis). The *scipy* library allows the application of a low pass filter with a cut-off frequency of 10Hz in order to remove noise. The magnitude of the acceleration vector (SVM: scalar vector magnitude) is then calculated for each time step of the two actimeters (via the acceleration data at a given time t : $a_x(t)$; $a_y(t)$; $a_z(t)$).

$$svm(t) = \sqrt{a_x^2 + a_y^2 + a_z^2} \quad (1)$$

1) Jerk

The time derivative of the acceleration at a given time t allows us to obtain the Jerk, noted J, in the three directions of space via the following calculation (finite difference centered approximation):

$$J_i(t) = \frac{a_i(t+dt) - a_i(t-dt)}{2dt} \quad (2)$$

Where *i* represents the three directions of space *x*, *y* and *z*, *a* is the scalar value of the acceleration and dt the sampling time step (i.e. 50Hz). Physically, the Jerk represents the rate of change of the acceleration vector. It is then possible to calculate the magnitude of the Jerk:

$$Jerk_{Mag} = \sqrt{J_x^2(t) + J_y^2(t) + J_z^2(t)} \quad (3)$$

Pan et al., [Pan,2020] showed that the jerk ratio (JR) is sensitive to the degree of upper limb mobility. The jerk ratio is defined as the ratio of the jerk amplitude of the paretic (non-dominant) limb to the sum of the jerk amplitude of the paretic (non-dominant) limb and the nonparetic (dominant)

limb:

$$Jerk_{Ratio} = \frac{|Jerk_{non-paretic}|}{|Jerk_{paretic}|+|Jerk_{non-paretic}|} \quad (4)$$

Points where the jerk of the paretic or non-paretic side is equal to zero are excluded from the study. A JR close to 0 means a preponderant use of the paretic (non-dominant) arm while a jerk ratio close to 1 means a preponderant use of the non-paretic (dominant) arm. It is then possible to calculate the histogram and probability density function of the JR for each measurement day. The probability density function is normalised to give a total probability distribution of 1.

Following the work of Pan et al, [Pan et al, 2020], the jerk ratio 50 (JR50) was calculated. This metric corresponds to the cumulative probability that the JR is between 0 and 0.5. A JR50 value greater than 0.5 suggests a preponderant non-paretic (dominant) arm mobility.

2) Forearm Elevation angle and speed

In quasi-static condition, the calculation of the angle of elevation of the forearm with respect to the gravity vector takes the form of equation 6, following the trigonometric laws:

$$\alpha(t) = arcos\left(\frac{a_y(t)}{svm(t)}\right) \quad (6)$$

It is then possible to obtain the angular velocity of elevation by the time derivative:

$$\dot{\alpha}(t) = \frac{\alpha(t+dt)-\alpha(t-dt)}{2dt} \quad (7)$$

3) Functional movement

Leuenberger et al., 2017, [Leuenberger et al., 2017] estimates that the upper limbs perform a functional movement when there is a variation in the angle of inclination of the arm greater than 30° and that this same angle of inclination is between ± 30° (to avoid data from walking) all within a time window of 0.5 seconds. The mathematical formulation is as follows:

$$|\alpha| \leq 30° \quad and \; \alpha_{max} - \alpha_{min} \geq 30° \quad (8)$$

A functional movement iteration counter is created for both upper limbs for each day. The counter is updated for each functional movement detected. The absolute values of functional movements and ratio (paretic/non-paretic or non-dominant/dominant) are presented as a boxplot with the median value of the 7 days of measurements.

4. Statistical Analysis

Each biomarker was qualitatively compared between the post-stroke population and the healthy population using boxplots. Depending on the normality or not of the data distribution, identify by the Shapiro test, student test or non-parametric Wilcoxon-Mann-Whitney test was applied. Scatter plots were performed to visualise the relationships between the ratio of upper limb use

or the number of movements on the paretic arm with all the calculated biomarkers. Depending on the distribution of the scatter plot data, linear relationships were established between the upper limb ratio or the number of movements on the paretic side with the rest of the biomarkers. The coefficient of determination is computed to assess the goodness of the fit with the experimental data. Regarding the large number of biomarkers, principal component analysis (PCA) was used for its potential for data reduction and explanation. To overcome the different units of measurement, the data were standardized. Then only the first two principal components were selected to explain the results.

3. Results

1. Patients

In this study, 6 healthy (3 women) and 10 post-stroke patients (6 women) participated. The characteristics of the patients and healthy subjects are summarised in Table 1.

Table 1: Stroke patients and healthy subject characteristics

	Post Stroke patients	Healthy volunteers
Number	10	6
Age in years	67 ± 12 [47-82]	45 ± 18 [18 - 75]
Gender	4 males, 6 females	3 males – 3 females
Affected body side	5 right, 5 left	-
Dominant Side Affected	5 (50%)	-
FM-UE Score (/66)	50.5 ± 14 [27-66]	-

2. Jerk Ratio

Figure 1.A shows the histogram and probability density function (PDF) of the JR for a healthy subject on a representative day. We can see that the histogram is centered on a value of 0.5, which highlights a balance in the movement of the upper limbs. A slight peak can also be seen at a JR value of 0 and 1, highlighting a non-negligible amount of probability of movement of the dominant limb only or non-dominant limb only, respectively. Figure 1.B compares the one-

day JR PDFs of a healthy and a stroke patient. It can be seen that the maximum JR PDF of the stroke patient is positioned at a value of 0.9, highlighting a preponderance of movement of the non-paretic limb. Figure 1.C compares the group median JR50 values between the two populations using a boxplot. The post-stroke population has a median JR50 value of 0.55 which is significantly higher than the median value of 0.51 for healthy subjects (t-test $p<0.05$). In addition, there is a very high inter-patient variability in the stroke population, indeed the range of JR of stroke patients is between 0.5 and 0.63 while the JR of healthy subjects is between 0.49 and 0.53.

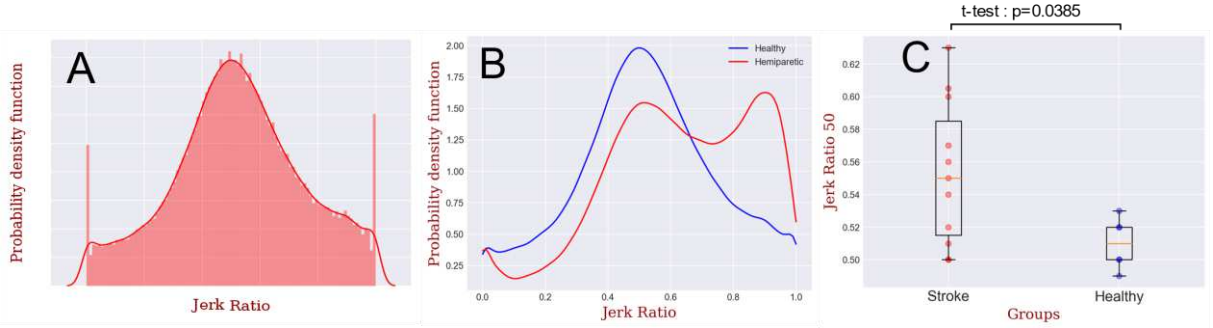

Figure 1: (A) Normalized probability density function of the Jerk ratio JR of a healthy subject. A JR of 0 indicates use of the paretic (non-dominant) limb and a ratio of 1 indicates use of the non-paretic (dominant) limb. (B) Comparison of the JR probability density functions of a healthy subject and a stroke patient. The healthy subject has a maximum probability for a JR of 0.5 (use of both limbs at the same time) while the maximum probability of the JR for the stroke patient is 0.9 (predominant use of the non-paretic limb). (C) Boxplot of the median JerkRatio50 (JR50) values for the stroke and healthy groups. Each point corresponds to the median JR50 value of each subject ***(t test: p value =0.0385).***

3. Functional movements

Figure 2.A shows the median number of functional movements of the paretic (non-dominant) and the non-paretic (dominant) upper limb over a 7-day period for the stroke and healthy participants. It can be observed that the median values of functional movements (FuncUse) of the paretic upper limb of stroke patients (median: 1500, range: [0; 3500] movements) were significantly lower (WMW test: $p<0.001$) than the values of the non-dominant limb of healthy

subjects' movements (median: 5000, range: [4500; 9000]). In contrast, stroke patients compensate with the non-paretic limb where they can reach a median 6000 movements in one day (range: [1500, 13000]) (fig 2.B). Figure 2.C shows the boxplots of the median FuncUseR of the paretic upper limb to the non-paretic upper limb for the stroke and healthy groups (ratio of dominant/non-dominant UL). It can be seen that the median ratio over 7 days of measurement was significantly lower (WMW test $p<0.005$) for the stroke (0 to 0.5, 0 to 50 movements of the paretic limb per 100 of the nonparetic limb) than for the healthy (0.6 to 1.3, 60 to 130 movements of the non-dominant limb per 100 of the dominant limb) population.

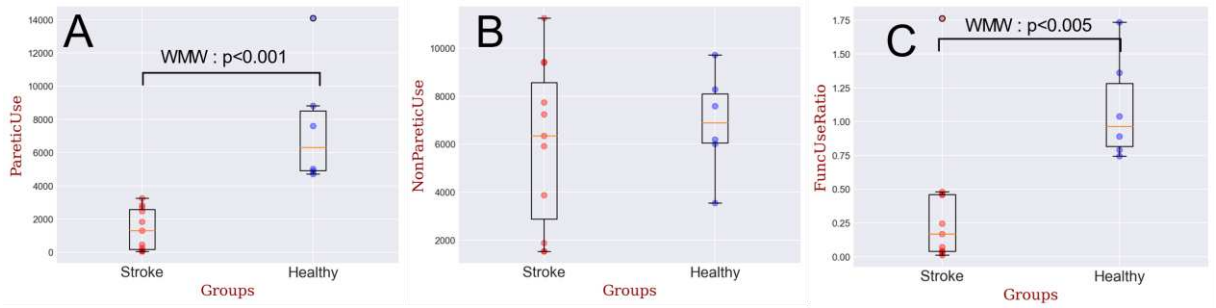

Figure 2: Boxplot of the median functional use of movements (FuncUse) of the (A) paretic and non-dominant (B) non-paretic and dominant UL of the stroke and healthy groups, respectively. (C) Boxplot of the median functional use of movement ratio (FuncUseR) between UL of the stroke (paretic/non-paretic) and health (non-dominant/dominant) groups. As shown in Fig.1A, healthy subjects show a larger number of FuncUse of the non-dominant UL than stroke patients paretic UL. As shown in Fig2B, healthy subjects and stroke patients show a comparable amount of FuncUse of the non-paretic and dominant UL, respectively. As shown in Fig2C, the FuncUseR of the healthy subjects were larger than stroke patients.

4. Functional movement elevation speed

Fig.3a shows the functional movement elevation velocities of the UL (VUL) for the stroke and healthy groups. In figure 3.A we can observe that the VUL of healthy subjects on the non-dominant side are significantly higher ($p<0.05$) than the stroke patients on the paretic side. Indeed, the median VUL over 7 days of measurements are between 135 and 190 for the healthy

subjects and between 110 and 160 for the stroke patients (see figure 3.A, WMW test: $p<0.05$). The VUL of the stroke patients on their non-paretic side were significantly lower than the healthy subjects on their dominant side (Figure 3.B: $p<0.05$). For the stroke patients, the VUL ranged from 105 to 159 and from 138 to 175 for healthy subjects (see figure 3.B). Figure 3.C presents the VULR of paretic/non-paretic (non-dominant/dominant) for the stroke and healthy population. It can be observed for the stroke patients that the VULR of the paretic limb were 10% lower than those of the non-paretic limbs (i.e. speed ratio of 0.83 to 1.22). In comparison, most of the VULR of healthy subjects were greater than 1 (speed ratio interval of [0.95 ;1.12]) (WMW test: $p<0.05$).

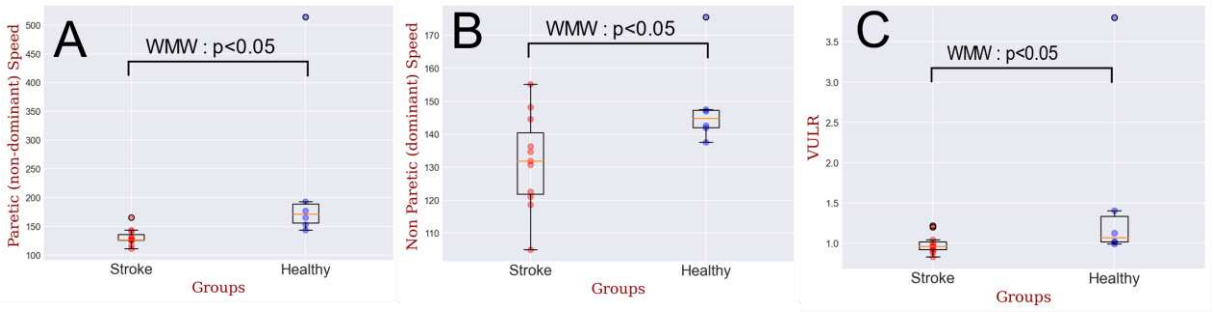

Figure 3: Boxplot of median functional movement elevation speed of the UL (VUL) for the stroke and healthy groups: (A) Paretic vs non-dominant UL, (B) Non-Paretic vs dominant UL, (C) Ratio of UL velocity (VULR). In Fig3a healthy subjects show a greater speed of forearm elevation than stroke patients. In Fig3c. Healthy subjects show a greater ratio than stroke patients.

5. Relationship between biomarkers and functional movements

Figure 4.A shows the linear relationship between FuncUse on the paretic side and the FuncUseR for stroke patients ($r^2=0.36$, $p<0.001$). Indeed, the more a stroke patient tends to use his/her paretic upper limb, the more the FuncUseR tends towards 1. This relationship does not exist for healthy subjects (Fig4a; $p>0.05$). In parallel, Figure 4.B shows that there is a linear relationship

between the amount of FuncUse of the dominant and non-dominant upper limbs for healthy subjects (r^2=0.49, $p<0.001$) whereas this is not the case for stroke patients considering the paretic and non-paretic UL. This means that for healthy subjects, the more they use their dominant limbs the more they use their non-dominant limbs. Furthermore, a very strong correlation was found between VULR and FuncUseR for healthy subjects (Figure 4.C, r^2=0.8, $p<0.001$) but not for stroke patients. This relationship shows that the VULR must reach a value of 1.1 for a healthy subject to have a FuncUseR of 1. At the same time, stroke patients have very high VULR (1.75) without the FuncUseR exceeding 0.25. Finally, Figure 4.D highlights the relationship between two biomarkers of the amount of upper limb functional movement use, the FuncUseR and the JR50. Figure 4.D shows a curve of decreasing exponential appearance where as JR50 increases the FuncUseR decreases. This graph shows the greater sensitivity of the FuncUseR for healthy subjects. Indeed, while the JR50 varies between 0.48 and 0.54 for healthy subjects, the FuncUseR varies in a range from 0.5 to 1.5. On the other hand, the JR50 has a very high sensitivity for subjects with very little movement on the paretic side. Notably, a stroke patient presents a FuncUseR between 0 and 0.05 while his JR50 varies in a range of 0.54 to 0.77

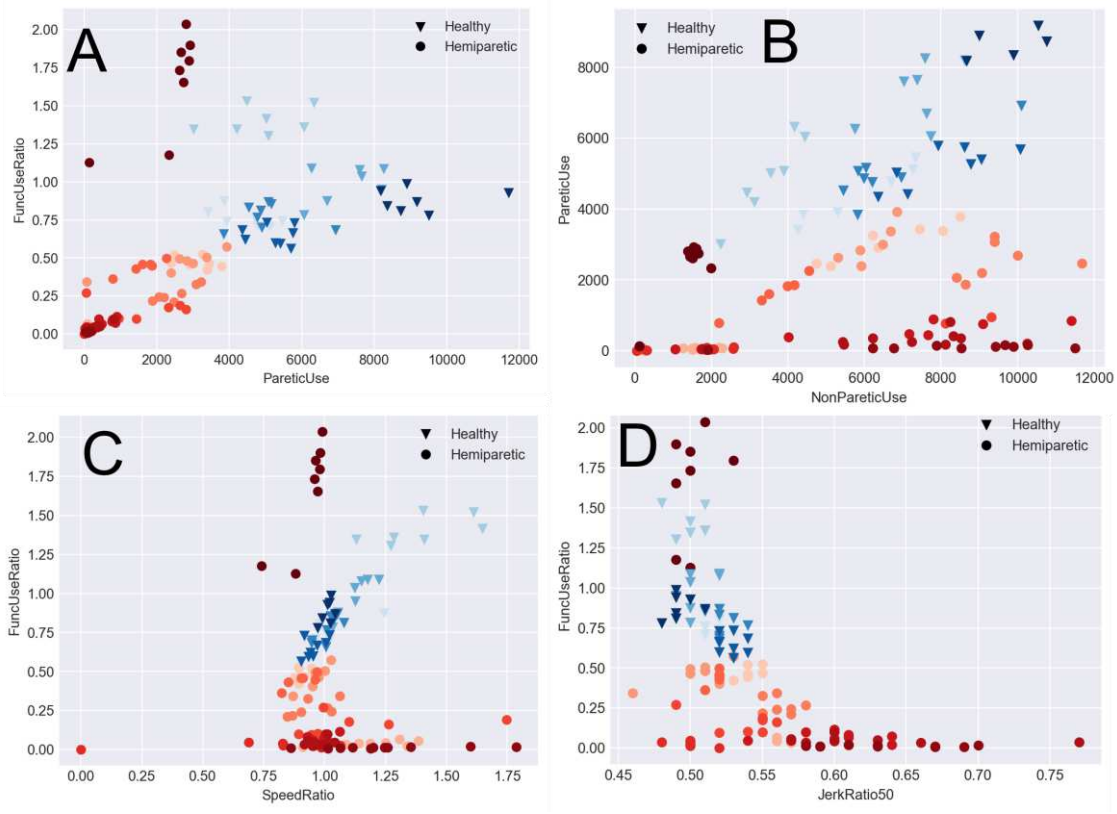

Figure 4: Relationship between functional use of movement of the UL (FuncUse) to derived biomarkers. (A) FuncUseR relationship to FuncUse on the paretic side for stroke patients and non-dominant side for the healthy subjects. (B) FuncUse of the paretic (non-dominant) side in relation to the non-paretic (dominant) side for the stroke (healthy) group. (C) (FuncUseR relationship to VULR. (D) FuncUseR relationship to JR50. Healthy subjects are represented by blue circles and stroke patients by red triangles with a colour gradient differentiating subjects.

6. Principal component analysis

The different biomarker principal component analysis showed that principal components 1 and 2 (PC1 and PC2) accounted for 51% and 24% of the variance in the results, i.e. 75% in total. Figure 5.A shows the position of each study participant in relation to PC1 and PC2. The healthy subjects all have positive PC1 values while the stroke patients all have negative PC1 values except for one subject with a Fugl-Meyer of 66. Figures 5.B and 5.C show the relative importance of each biomarker in PC1 and PC2 respectively. We see the two most important biomarkers in CP1 are related to the FuncUse and VUL of use of the paretic limb while the most important biomarkers in CP2 are related to the FuncUse of the non-paretic limb and the JR50.

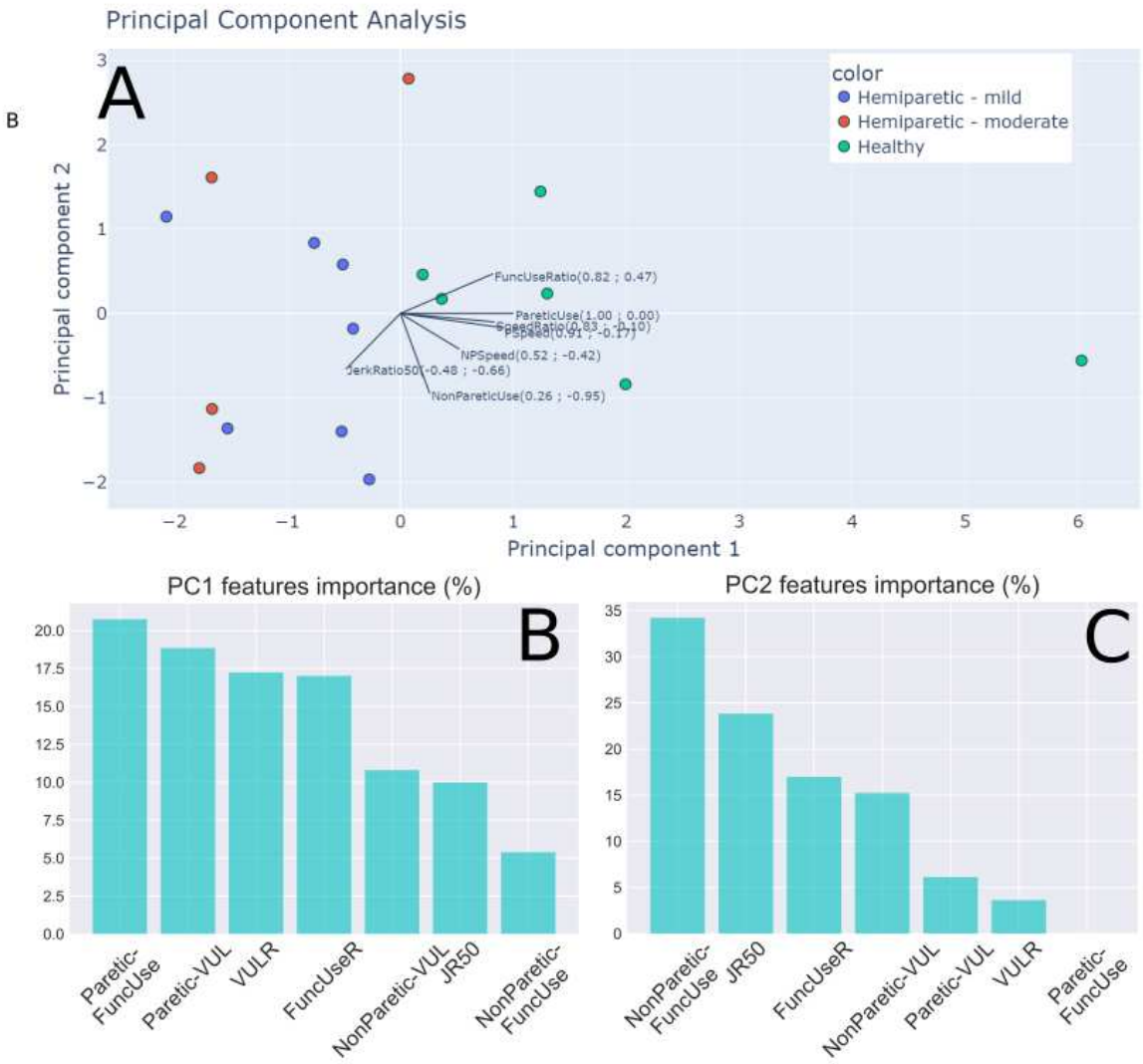

Figure 5 *(A) Different biomarker principal component (PC) analysis scatter and loading plot in the PC1 and PC2 plane. Mild (Fugl-Meyer>40), Moderate (Fugl-Meyer : [21-39]) stroke patients and healthy subjects are represented in blue, red and green dots respectively. (B) PC1 features importance. (C) PC2 features importance.*

4. Discussion

The aim of the study was to calculate multiple wrist actimetry biomarkers of stroke patients over a 7-days period in their home environment and then determine optimal biomarkers to monitor functional paretic arm use (FuncUse). We performed, to our knowledge, the first study

in stroke patients that calculated over an extended 7-days period multiple functional movement biomarkers via two simple and lightweight wrists worn accelerometers, and compared these values with values acquired in a healthy population. Accordingly, we derived new actimetry biomarkers, in particular, we were able to calculate average elevation speed of execution of functional movement (VUL) and the Jerk via the derivation of the elevation angle and the acceleration respectively

Previous studies have measured the amount of functional movement of the upper limb (FuncUse) in an ecological environment via IMUs placed at the wrist for a period of only 48 hours [Leuenberger et al, 2017]. According to our measurements, JR50 has a very low intra-patient variability (standard deviation of plus or minus 0.05) but VULR and FuncUseR have large standard deviations of up ± 0.5 and ± 0.3 respectively. It is then necessary to maximize the number of measurement days to obtain relevant biomarker values. The arm elevation was calculated using the same accelerometric metrics to which the authors added the calculation of the yaw angle to identify movements in the horizontal plane. In our study, we choose to use actimeters with a battery autonomy of more than one week for an acquisition frequency of 50 Hz and thus to be more representative of the patient's ecological behavior. It is noted that [Leuenberger et al, 2017] demonstrated a linear relationship between the Box and Blocks Test and the ratio of movement of the paretic limb to the non-paretic limb.

However, they did not explore other biomarkers. These include average arm raise speed or jerk ratio. In addition, they did not perform a comparison with a healthy population without hemiparesis. A novel finding of the study was the significantly greater use of the non-dominant limb of the healthy subjects compared to the paretic limbs of the stroke patients as well as a significantly greater FuncUseR in the healthy subjects than in the stroke patients. Similarly,

stroke subjects show significantly lower functional movement speeds and speed ratios than controls. Interestingly, a second novel finding was that the movement speed of the non-paretic arm of the stroke patients was significantly slower than the dominant arm of the healthy subject. The healthy subjects show on average three times more daily movement of the non-dominant limb than the paretic limb of the stroke subjects. Indeed, healthy subjects performed approximately 5000 functional movements per day with their non-dominant limb whereas post-stroke patients realized only 1500 movements per day with their paretic limb. Moreover, the healthy subjects show a FuncUseR close to 1, meaning an equal use of the dominant and non-dominant upper limbs while the stroke patients show a very low median FuncUseR close to 0.18, which indicates 18 movements of the non-paretic limb for one movement of the paretic limb. However, patients show an equivalent amount of functional movement of the non-paretic limbs to that of the dominant limb of the volunteer subjects. This suggests that the stroke patient studied here maintain a relatively normal amount of non-paretic UL movement average.

The Jerk Ratio appears to reflect a ratio of the amount of movement in a given time frame between the two limbs. While this ratio is balanced in healthy subjects, it shows a slight imbalance in stroke subjects. These results show that there is a significantly higher probability that stroke patients perform less movement, both functional and non-functional, with their paretic limb than with their non-paretic limb when compared with the healthy population. Furthermore, the study of correlations between the different biomarkers seems to show a decreasing exponential relationship between the FuncUseR and the JR50. This suggests that depending on the degree of deficit of the stroke patients, the two biomarkers would be

complementary in establishing a diagnosis. Indeed, the FuncUseR seems to be more sensitive for patients with upper limb behavior similar to healthy subjects, whereas the JR50 seems to be more sensitive for subjects with significant hemiparesis (Figure 4.D). Furthermore, the results showed that stroke patients had significantly lower average execution speeds of functional movements than healthy subjects. It should be noted that the measured elevation speeds seem to correspond to the values of the literature [Lacquaniti et al, 1982]. It is interesting to note that there is a very strong positive correlation between the FuncUseRatio and the VULR in healthy subjects but not in strokes patients. Finally, the principal component analysis showed that the PC1 allows to differentiate with sufficient sensitivity the actimetric results of healthy and hemiparetic subjects. We also see that the moderate hemiparetic subjects have the lowest PC1 values.

In order to define a functional movement of the upper limbs we have arbitrarily chosen to define an amplitude of elevation of the arm of more or less 30°. However, a large proportion of stroke patients show uncontrolled flexion of the healthy elbow when walking. This phenomenon is called "associated reaction" and may have an influence on the results of our study [Kahn et al, 2020]. This choice remains arbitrary and it would be necessary to explore the evolution of the FuncUseR as well as the functional movement quantities as a function of this elevation amplitude parameter. In particular, we would expect to observe no significant difference between post-stroke and volunteers' subjects for functional movements of plus or minus 10° of elevation. Instead, the difference would tend to increase with the amplitude of the movement. It would then be possible to identify an angular amplitude threshold value for each patient and thus to obtain a new parameter allowing to better identify the patient deficiency.

Another perspective would be to mix experimental method tools based on actimetry and artificial intelligence to identify with more precision what kind of movements is performed by the patients [Sanhudo, 2021]. This identification of the movement will allow to better identify the physical capacities of hemiparetic patients and thus to develop specific patient therapies. In addition, other actimetric markers could be calculated to refine the study. In particular, we think of the quantification of physical activity via the ENMO (Euclidean Norm Minus One) indicator [White et al, 2016] as well as the quantification of smoothness during a functional movement via the study of [Melendez-Calderon et al, 2021]

The wrist actimetry methods developed in this article seems relevant for clinical use. Indeed, while the hemiparetic subjects studied had only mild or moderate deficit, some biomarkers were shown to be sensitive enough to identify significant differences between populations. It is now necessary to carry out an in-depth clinical study to identify different patient patterns, by enlarging the number of patients we involve and by covering a larger panel of different patients. While the FuncUseR developed by [Leumberger et al, 2017] correlates linearly with the BBT, we do not know if this is the case for the FuncUseR developed in our study. Moreover, it would be relevant to study the correlations of all the actimetric parameters present in our study with different clinical parameters. We are thinking in particular of the BBT and the Fugl Meyer score for the upper limbs but also gait speed or 6 minutes walking test. Interestingly, the tool developed in this article should make it possible to identify stroke patients with excellent actimetric results. It would then be relevant to deepen the study by correlating actimetric and clinical variables with other variables identifying motivation, environmental factors, anxiety and depression [Morris et al, 2013]. Such studies would allow the identification of other paths for performance improvement.

5. Conclusions

This study comparing healthy and post-stroke subjects found significant differences in calculated actimetric biomarkers between healthy and post-stroke subjects. While the healthy subjects had an upper extremity functional use ratio close to 1, the post-stroke subjects had a ratio of about 0.2. The post-stroke subjects do not seem to overuse their healthy limb to compensate for the loss of motor skills in the paretic limb. The results of this study show the interest of using different biomarkers for the longitudinal follow-up of patients with upper limb hemiparesis.

- Ethics approval and consent to participate

The part of the study including post-stroke participants was approved by the IRB of the Montpellier University Hospital, Montpellier, France (CPP SUD-EST II). The part of the study including non-disabled healthy participants was approved by the IRB of the University of Montpellier, France. All participants gave their informed consent for participating the study.

- **Consent for publication**

Not applicable.

- **Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

- **Competing interests** : The authors declare that they have no competing interests

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- **Authors' contributions**

GD: conceptualization of model and computational framework, software, formal analysis, data collection and curation, writing—original draft. DM: Conceptualization and design of the study, results interpretation, writing – review and editing. MM: Results interpretation writing – review and editing . IL: Writing – review and editing. KB: Conceptualization and design of the study, data collection, results interpretation, writing – review and editing. All authors read and approved the final manuscript.

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- **Authors' information (optional)**

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