

How does Vector Magnitude Obtained from Wrist Worn Actigraphy Relate to Kinetic and Spatiotemporal Measures of Wheelchair Propulsion Technique at Different Speeds

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Abstract

Our study examined associations between wheelchair propulsion technique and vector magnitude (VM) obtained from a wrist worn triaxial accelerometer. Participants who were full time wheelchair users (n= 17) propelled on a treadmill at common (1.34 m/s), and fast (2.0 m/s) speeds in their own wheelchairs with instrumented wheels attached. Accelerometer and energy expenditure (VO2) data were recorded simultaneously. Outcome measures included kinetic and spatiotemporal propulsion technique variables occurring at the wheelchair handrim as well as subject characteristics like shoulder pain (WUSPI) and physical activity level (PASIPD). Regression analysis found peak total force, contact angle, shoulder pain and physical activity level to be predictive of VM at the common speed while stroke frequency, peak total force, and shoulder pain were predictive of VM at the fast speed. Our findings, although preliminary, underscore the increasing potential of wearable sensors to serve as an upper limb preservation tool in MWUs in real world settings.

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Introduction

There are an estimated 2 million manual wheelchair users (MWU) in the United States [1]. Although wheelchairs offer heightened mobility and independence [2,3], they have the potential to overwhelm the upper limbs [4-12]. For example, wheelchair specific activities like propulsion and transferring, although necessary, predispose the upper limbs to high forces repetitively. Consequently, the incidence of upper limb pain and injury in MWU is extremely high, with reports ranging from 49%-78% [6,10,11,13-19]. Since MWU must rely on their upper limbs to perform nearly all activities of daily living, the effects of pain and injury can disrupt daily functioning resulting in marked activity limitations and participation restrictions [9,10,20].

As the consequences of upper limb pain can be severe, considerable efforts have been made to elucidate and rectify the contributing factors. In 2005, the Consortium for Spinal Cord Medicine published a clinical practice guideline summarizing the evidence pertaining to the preservation of upper limb function in wheelchair users. In it, the authors provide evidence based recommendations rooted in ergonomics, equipment selection, training, environmental adaptations, and exercise. Generally speaking, the guidelines promote reduced frequency of upper limb tasks and force minimization to complete these tasks, as well as avoiding extremes of wrist and shoulder motions when possible. In the context of propulsion, MWUs are encouraged to use a low frequency, long and smooth stroke during the propulsive phase to decrease force exerted at a given velocity while allowing the hand to drift down and back below the handrim during recovery [21].

Much of what researchers know about wheelchair propulsion biomechanics has accumulated through the use of specially instrumented data collection tools. For example, the kinetic(forces and moments applied to the hand rim) and spatiotemporal(stroke frequency and timing) features of hand rim propulsion have been routinely examined with inertial dynamometers [22], instrumented force and moment sensing wheels like SMART^{Wheels} and OptiPush, as well as and motion capture systems like ViconTM. Although extremely accurate, these systems have drawbacks including versatility, cost, operational expertise, and feasibility for use outside of laboratory environments. Additionally, because instrumented wheels are used in place of an individual's own wheels they may

alter the mass and inertia of the wheelchair users system, therefore threatening experimentation external validity [23].

More recently, miniaturized wearable sensor technology like accelerometers offer researchers the opportunity to overcome many of the limitations imposed by the aforementioned technologies when studying wheelchair propulsion. Specifically, body worn and wheelchair mounted accelerometers more readily enable data capture in wheelchair users' own environments, without altering the users' configuration or the interface. These further allow for prolonged period of data collection rather than a brief observation.

To date, accelerometers have been used to examine a range of applications pertaining to wheelchair use including the gross aspects of movement, physical activity [24], and energy expenditure. For example, researchers have used wheel mounted accelerometers to identify physical activity metrics like bouts of mobility as well as distance, time, and velocity of wheeling [25]. Arm and wrist worn accelerometers have been used to examine outcomes like energy expenditure [26], activity counts [27] and duration of propulsion [28].

More recently, investigators have begun to explore the feasibility of using wearable sensors to monitor and possibly prevent upper limb injury in MWU. For example, because of the well-established relationship between task repetition and pain/injury development, Ojeda & Ding, 2014 used triaxial arm worn accelerometers with a wheel rotation monitor to accurately assess stroke frequency and stroke number during propulsion [29]. In another study, wheelchair and wrist mounted inertial sensors were used to develop biomechanical parameters for the purposes of improving propulsion technique in junior wheelchair athletes [30].

Study Purpose

The purpose of this study was to determine if there was a relationship between established kinetic and spatiotemporal propulsion technique metrics occurring at the handrim and the accumulation accelerometer counts (Vector Magnitude (VM) at the wrist. While a VM approach has been used to examine energy expenditure (EE) and physical activity (PA) levels in MWU, its potential for measuring propulsion technique remains unclear.

The information gained may help facilitate the role of wearable sensors as practical tools capable of providing health and safety feedback to MWU in real world settings. Based on previous studies we hypothesized spatiotemporal parameters, like stroke frequency and contact angle, would be associated with VM production; however, since there are no related studies pertaining to kinetic parameters this study was exploratory.

Materials and Methods

Study participants

The protocol was approved by a university institutional review board, and all participants provided written informed consent prior to study participation. We recruited twenty-eight participants through direct contact with wheelchair users on a university campus or who had previously taken part in our research. Based on inclusion criteria, all participants were between 18-64 years of ages, used a manual wheelchair as their primary mode of mobility (> 80% ambulation), free of any upper extremity condition or disability that could be worsened by PA, and were, if applicable, a minimum of two years post spinal cord injury. Two of the participants did not

meet the inclusion criteria, one cancelled participation, and one was unable to complete the protocol. Due to random equipment failure associated with our instrumented wheel, seven participants were not included in the study. Of the 17 remaining, data loss occurred in 3 more participants during the fast pace trial resulting in a final sample of 14 for the fast pace condition (6 Female, 8 Male; 30.7 ± 11.1 years) and 17 for the normal pace condition (7 Female, 10 Male; 32.2 ± 11.7 years). Clinically, participants reported having Multiple Sclerosis (n=4), Spina Bifida (n=2), Spinal Cord Injury (n=7), above the knee amputation (n=1), Transverse myelitis (n=1), Arthrogryposis (n=1), and Cerebral Palsy (n=1). Participant demographics are presented in (Table 1).

Wheelchair propulsion

All wheelchair propulsion activities were performed in a laboratory setting on a wheelchair treadmill, equipped with lateral and anterior safety fastenings (Max Mobility, Antioch, TN). Force and moment sensing SMARTwheels (SMARTwheel; Three Rivers Holdings, Mesa, AZ) were used to capture propulsion technique variables at a sampling frequency of 240 Hz [31]. SMARTwheels were fitted bilaterally to participants' personal, daily wheelchairs, however only the right SMARTwheel was used for data collection. The left wheel served as a dummy wheel to equate weight distribution and inertial characteristics. Hand dominance was not considered during data collection as previous studies have reported no significant differences in propulsion technique from dominant to non-dominant limbs while in a lab setting [32,33].

Accelerometer count

Accelerometer counts were measured as VM by wrist worn triaxial ActiGraph accelerometers (GT3X, Health One Technology, Pensacola, FL, USA). The GT3X is designed to measure and record time varying acceleration ranging in magnitude from 0.05 to 2.5 G. The acceleration signal is digitized by a 12-bit analog-to-digital converter, at a sampling rate of thirty times per second (30Hz). The GT3X accelerometers were prepared according to standard procedures [34], and one GT3X accelerometer was worn per wrist, placed posterior to the radial and ulnar styloid process. Information about motion direction and speed are integrated to produce an electrical current with variable magnitude and duration. The electrical current data are stored in the monitor as "activity counts." A single activity count represents 0.000175 gram force unit, or .0017 N. Data were collected from the right wrist only to coincide with data obtained simultaneously from the right Smart Wheel. A previous study found strong correlations between accelerometers worn bilaterally at the wrists during treadmill propulsion [26]. Finally, the accelerometer signal was processed into 30-s epochs, and imported into Microsoft Excel for further processing. Steady-state data for VM were averaged over the same 30-s intervals as per VO₂.

Energy expenditure

Energy expenditure (EE) was measured as oxygen consumption (VO $_2$) using a portable metabolic unit (K4b2, Cosmed, Rome, Italy) [35], and prepared according to the standard procedure [34]. To allow freedom of upper body movements during propulsion activities, the K4b2 unit was placed in a standard shoulder harness located on the sternum with the battery located on the upper back. The data were collected breath-by-breath where 30-s averages we retrieved for further processing in Microsoft Excel. The analyses involved steady-state VO $_2$ in ml kg $^{-1}$ min $^{-1}$ by averaging the 30-s VO $_2$ values over the final 3 min of propulsion bouts and rest periods.

Table 1: Participant demographics.

| # | Subject ID | Gender | Age | Disability Type | Years with Disability | PASIPD | WUSPI | ВМІ |
|----|-----------------|--------|-----|-----------------|-----------------------|--------|-------|-------|
| 1 | 7 | M | 30 | SCI | 26 | 42.89 | 0.0 | 18.43 |
| 2 | 8 | M | 39 | SCI | 19 | 63.62 | 0.0 | 21.10 |
| 3 | 9. | M | 35 | SCI | 10 | 54.34 | 19.3 | 22.0 |
| 4 | 10 | M | 28 | SCI | 11 | 31.78 | 0.80 | 23.32 |
| 5 | 11 | F | 19 | СР | 19 | 42.99 | 10.20 | 23.51 |
| 6 | 12 | M | 30 | Arth | 30 | 28.82 | 12.40 | 22.04 |
| 7 | 13 | M | 26 | SCI | 8 | 30.52 | 1.60 | 26.31 |
| 8 | 14 | M | 23 | SB | 23 | 23.09 | 0.0 | 22.26 |
| 9 | 15 | F | 23 | SCI | 17 | 33.67 | 0.20 | 14.53 |
| 10 | 16 | F | 28 | TM | 23 | 37.31 | 0.0 | 14.52 |
| 11 | 17 | M | 29 | AMP | 7 | 24.17 | 5.70 | 17.99 |
| 12 | 18 | F | 21 | SCI | 11 | 29.20 | 6.90 | 23.96 |
| 13 | 19 | М | 25 | SB | 25 | 38.44 | 5.00 | 23.05 |
| 14 | 20° | M | 27 | MS | 7 | 8.47 | 0.0 | 20 |
| 15 | 21 ⁻ | F | 55 | MS | 24 | 30.6 | 0.0 | 34.6 |
| 16 | 22 | F | 55 | MS | 32 | 53.24 | 0.0 | 23.11 |
| 17 | 23 | F | 54 | MS | 7 | 69.04 | 34.50 | 22.34 |

Note: M: Male; F: Female; SCI: Spinal Cord Injury; CP: Cerebral Palsy; Arth: Arthrogryposis; SB: Spina Bifida; TM: Transverse Myelitis; AMP: Amputee; MS: Muscular Sclerosis; Duration of Disability reported in years.

Pain and Physical activity assessments

After the completion of consent and demographic forms, all participants completed the Physical Activity Scale for Individuals with Physical Disabilities (PASIPD) [36] and the Wheelchair Users Shoulder Pain Index survey (WUSPI) [37,38]. Both the PASIPD and the WUSPI are reliable and validated questionnaires. The PASIPD provides a calculated estimate of a participant's overall daily physical activity level, specific to manual wheelchair propulsion. The PASIPD uses information on leisure, household, and occupational PA levels from the previous seven days to calculate an estimated daily PA score. Scores for the PASIPD range from 0 (no physical activity completed) to 199.45 (maximum levels of PA completed in all of the three categories). Similarly, the WUSPI is used to quantify current levels of shoulder pain during functional activities (e.g., transferring, daily propulsion, lifting objects, etc.). Scores for the WUSPI range from 0 (no pain) to 150 (maximum limitations resulting from pain).

Protoco

On the day of testing, participants completed informed consent and surveys. Participants were measured for height, which was estimated by tibia length [39,40] and weight, which was measured with a wheelchair scale (LW Measurements, Santa Rosa, CA). Participants then received instruction on the propulsion testing protocol. Next SMART wheels were attached to each particpants' own everyday wheelchair and then secured to the wheelchair treadmill. Participants were given 2-3 minutes to acclimate to the treadmill, and then provided with a 10-minute recovery period. For testing, participants completed three 6 minute bouts of propulsion at three steady state speed conditions in random order with 10-minute recovery between each where, slow =0.67m/s, common= 1.34m/s, and fast = 2.0 m/s. Data presented in this manuscript is based on a larger study [41] in which 3 speeds were utilized however significant data loss occurred during the slow trial (0.67m/s) so it was left out of the current analysis. The remaining two speed conditions used for analysis are well supported as those which represent common and fast propulsion speeds [42-44].

Data reduction

(Propulsion Technique).

For analysis of propulsion technique, kinetic variables included Peak Total Force (N), Peak Torque (Nm) and Peak Braking Torque (Nm) which were obtained from the right side SMART^{wheels} and calculated using SMART^{wheels} software, while Contact Angle (CA) [Deg], and Stroke Frequency (SF) [stroke/sec], and Push Period (sec) represented Spatio temporal and timing variables. All variables for each participant were calculated as the mean values for the propulsion period.

Statistical analysis

Differences observed in the propulsion technique variables between the speed conditions are reported. Because of the small sample sizes and the fact that the distributions for many of the variables being investigated were non-normal, a nonparametric approach was used instead of attempting to remove influential cases or transforming the raw data. Specifically, the WIlcoxon Signed Rank tests were employed as a within-subjects' comparison to test if there were differences between speed conditions.

Two stepwise semi-automated regression procedures were used to test if the propulsion related independent variables were related to the VMs (dependent variable) after adjusting for shoulder pain, physical activity level, and EE (VO₂) for each speed condition. Shoulder pain and physical activity were included as covariates because of their potential association with technique. Energy Expenditure was included as a covariate because of its association with VM demonstrated previously [26].

This procedure was chosen to 1) reduce the overall number of comparisons from potentially inflating type-I error that might

^{&#}x27;Participants data not included in fast speed condition due to equipment malfunction

Table 2: Descriptive Statistics: Wheelchair Propulsion.

| | Common (n=17) | | | Fast (n=14) | | | |
|----------------------|---------------|---------|--------|-------------|---------|---------|--------------------|
| Variable | Mean | Md | StD | Mean | Md | StD | p-value† |
| Peak Force Total | 40.14 | 38.48 | 11.11 | 58.72 | 54.02 | 27.46 | 0.005* |
| Peak Torque | 6.30 | 5.41 | 2.79 | 9.10 | 9.05 | 3.07 | 0.004 [*] |
| Contact Angle | 62.93 | 67.70 | 18.83 | 75.05 | 79.39 | 15.40 | 0.056 |
| Braking Torque | -1.21 | -0.74 | 1.32 | -1.97 | -1.30 | 1.92 | 0.001 [*] |
| PushPeriod | 1.65 | 1.57 | 0.49 | 1.12 | 1.13 | 0.35 | 0.001 [*] |
| Stroke Frequency | 0.70 | 0.68 | 0.18 | 1.01 | 0.95 | 0.30 | 0.001 |
| EE(VO ₂) | 7.75 | 7.67 | 1.81 | 15.55 | 14.00 | 5.77 | 0.001° |
| VM | 2196.58 | 1990.85 | 632.23 | 4521.72 | 4162.15 | 1744.98 | 0.001 [*] |

[†]P-values based on nonparametric test, difference between speeds. Indicates significance.

occur by testing every variable individually; 2) help eliminate any multicollinearity seen, as it was expected that some the kinetic variables would be highly correlated with each other; and 3) identify the most parsimonious model that would best predict VMs. The semi-automated procedure was done by entering the three covariates in the first block and then using the automated stepwise procedure after that. The variables included in the stepwise procedure included the aforementioned kinetic and spatiotemporal variables, using a rule in p \leq .05 and a rule out p \geq .1. Statistical significance was set to be p < 0.05. All model assumptions were tested and as stated if violated non-parametric statistics were used. All data were analyzed using SPSS (v.24.0 SPSS Inc. Chicago, IL).

Results

Statistical model

Unfortunately data loss occurred in three individuals during the fast trials, these participant's results were only included in the regression model for the common speed condition. Demographics are presented in (Table 1). Descriptive statistics and condition comparisons for the kinetic variables are presented in (Table 2). As stated previously, the WIlcoxn Signed Rank tests were employed to test if there were differences between speed conditions. All variables, except for Contact angle, were significantly different between the speed conditions, $p < .05. \ \,$

Results for the automated regression for both conditions resulted in a model that included two additional predictors after adjusting for the covariates, for a total of three blocks (Table 3). While normality was an issue bivariately, the regression models met the assumptions for normality, Shapiro Wilk U = .95, p= .60 and Shapiro Wilk U = .92, p= .23. Multicollinearity was not an issue for either model with the highest VIF = 1.82, and lowest Tolerance = .55. Residual analysis did not suggest the presence of heteroscedasticity or overly influential cases.

Demographics

Demographic characteristics are presented in Table 1. After data loss occurred reducing the number of participants from 17(fast speed) to 14(common speed) age, years with diagnosis, sex, disability type, physical activity level(PASPPD), and shoulder pain(WUSPI) were not significantly different between groups t(29)=0.36,p=0.71; t(29)=0.22,p=0.8; $\chi^2(1)=0.009,p=0.92; \chi^2(6)=0.45, p=0.99; t(29)=0.27,p$ 0.78; t(29)=0.04,p=0.96.

Shoulder pain

Results of the PASIPD and WUSPI questionnaires are reported

in (Table 1). Scores for the PASIPD (39.20 \pm 14.06) are similar to those in previous research [45,46]. Participant WUSPI scores (5.52 \pm 9.32) indicated the sample experienced low levels of shoulder pain in comparison to previous research [47-51]. Descriptive results of the propulsion variables are presented in (Table 2).

Wheelchair propulsion

For the common speed condition the final model was significant, F (5,16) = 14.55, p< .001, $_{adj}R^2{=}.81$, and the two additional predictors chosen were peak force and contact angle. The change in R^2 with each step was significant for Peak Total Force, Δ $R^2{=}.29$, F (1,12)=13.78, p=.003, and for Contact Angle , Δ $R^2{=}.12$, F(1,11)=10.28, p=.008. In the final model, shoulder pain and physical activity level were also significant.

For the fast speed condition the final model was significant, F (5,13) = 14.43, p= .001, $_{adj}R^2$ =.84, and the two additional predictors chosen were Stroke Frequency and Peak Total Force. The change in R² with each step was significant for Stroke Frequency, Δ R²=.64, F (1,9)=33.99, p<.001, and for Peak Total Force, Δ R²=.07, F(1,8)=5.66, p=.045. In the final model, shoulder pain was also significant.

Discussion

This study provides insight into associations between wheelchair propulsion technique parameters occurring at the wheel handrim and VM obtained from a wrist worn triaxial accelerometer. Specifically, handrim forces and other established temporal parameters were examined for their predictive value for VM production. To attain this goal, it was first necessary to conduct a laboratory based study under controlled conditions for first stage examination of VM and propulsion metrics. Our findings, although preliminary, underscore increasing potential of wearable sensors to serve as an upper limb preservation tool in MWUs.

The triaxial accelerometers used in the current study provide output of activity counts per unit time (epoch) over three axes. The derivation of VM from the wrist worn device proportionally reflects the net external acceleration generated by the arm during the entire propulsive stroke. This technique has been used previously to ascertain physical activity levels, energy expenditure, and cut off points in MWU [26-28]. However, up until now, VM has not been examined for its association with metrics specific to propulsion technique.

In the current study, application of Peak Total Force was a significant predictor of VM at both common and fast propulsion speeds. More specifically, higher Peak Total Force was associated

Table 3: Stepwise Regression Model Results

| Model | Block | Variable | В | SE | Beta | t | Sig. |
|--------|-------|----------------------|----------|---------|-------|-------|--------------------|
| | | Intercept | 2241.62 | 469.46 | | 4.77 | 0.001 [*] |
| Common | 1 | WUSPI | -29.67 | 9.89 | -0.44 | -3.00 | 0.012 [*] |
| | | PASPPD | -17.04 | 5.39 | -0.41 | -3.16 | 0.009° |
| | | EE(VO ₂) | 79.04 | 39.68 | 0.23 | 1.99 | 0.072 |
| | 2 | Peak Force Total | 148.53 | 28.60 | 0.65 | 5.19 | <0.001° |
| | 3 | Contact Angle | -12.42 | 3.87 | -0.37 | -3.21 | 0.008* |
| | | | | | | | |
| | | (Constant) | -1374.72 | 1136.62 | | -1.21 | 0.261 |
| Fast | 1 | WUSPI | -66.71 | 27.59 | -0.36 | -2.42 | 0.042* |
| | | PASPPD | 6.87 | 18.67 | 0.06 | 0.37 | 0.723 |
| | | EE(VO ₂) | 69.04 | 140.02 | 0.06 | 0.49 | 0.635 |
| | 2 | Stroke Frequency | 4082.16 | 865.57 | 0.70 | 4.72 | 0.002* |
| | 3 | Peak Total Force | 22.19 | 9.33 | 0.35 | 2.38 | 0.045* |

*Indicates significance.

with increased VM. Although more investigation will be necessary to understand which aspects of arm motion contributed to this finding, even basic knowledge of force magnitude obtained indirectly could benefit MWUs. For example, the use of higher forces have been correlated with upper limb pain and injury as well as risk for developing nerve dysfunction [21,52-54]. Moreover, only laboratory based systems are capable of monitoring propulsive forces which has historically constrained kinetic analysis to laboratory environments. A portable device capable of providing some degree of force feedback in the real world could have enormous implications. Future work will be required on larger populations of MWU over more diverse propulsion scenarios to confirm and extend these associations.

Other findings specific to timing and temporal features of propulsion technique where predictive of VM as well. For example, during the common speed condition, Contact Angle (CA) predicted VM where increased CA was associated with decreased VM production. Ultimately, participants using more of the handrim per stroke, which is recommended [52], produced less net external acceleration which may reflect improved propulsion technique. During the faster speed condition, Stroke Frequency (SF) was predictive of VM where increased SF was associated with greater VM. It is likely that VM sensitivity to SF reflects the commonly observed scenario whereby wheelchair users use more strokes to maintain a higher pace which may predispose the upper limbs to pain and injury [55,56].

Shoulder pain and physical activity (PA) level were associated with VM production as well. Specifically, self-reported shoulder pain was associated with reduced VM production at both common and fast propulsion speeds, while PA level was associated with reduced VM at the common speed only. Because historically researchers have not found clear differentiations in propulsion technique as a function of pain [57,58], this finding may be of interest where even low levels of pain contributed to reduced net upper limb movements. The extent to which this finding represents a technique adjustment that was preventative or reactionary to shoulder pain cannot be ascertained from the current design but warrants further investigation. Similarly, the influence of PA on propulsion technique cannot be fully explained however activity level and fitness may have the potential to mediate aspects of propulsion technique and should be explored.

Fortunately, wearable senor technology offers enormous potential for identifying VM correlations with factors like pain and physical activity in real world settings. The size and practicality of wearable sensors more readily permit large scale examination of these factors in MWU's lived environments, over time. To maximize the utility of accelerometers and the VM approach, it will be necessary to determine if the aforementioned relationships persist when MWUs propel at self-selected velocities over more variable terrain. Ultimately these are the conditions in which MWU actually develop injury. Additionally, as researchers continue to accumulate accelerometer data it may be possible to develop more finely tuned algorithms for the detection of injurious propulsion biomechanics.

While more work is needed to determine if VM can serve as a viable tool for propulsion assessment, initial lab based results are encouraging. Specifically, the VM method was sensitive to both kinetic and spatiotemporal aspects of propulsion in a controlled setting. Having already shown promise in measuring PA, EE, and stroke frequency in MWUs, accelerometers continue to offer practicality and diverse functionality in the context of research, rehabilitation, personal use, and athletics. In a rehabilitative context they offer an objective means to study the effects of interventional strategies aimed at improving the wheelchair user interface, but in the real world environment. For example, clinicians delivering propulsion training and or wheelchair seating/configuration evaluations could monitor and assess clients' changes in their home environments.

Limitations

A number of important study limitations should be addressed when interpreting results. For example, although the testing conditions are well documented as speeds that approach common and fast testing velocities, they were not self-selected and therefore may not generalize to all daily life propulsion scenarios. Although it was necessary to begin this line of investigation controlling for speed and terrain, future studies should extend these observations to over ground conditions at self-selected speeds. Additionally, participants' homogeneous characteristics and low pain levels may limit generalizability to broader populations of MWU. Next, while the PASIPD and WUSPI are validated scales, some degree of error inherently accompanies self-reported data. Finally, no measure of upper limb function or wheelchair configuration was performed,

which may have influenced participants' propulsion technique. Researchers must be cognizant of the many factors influencing propulsion technique when designing future studies.

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