Distribution Agreement

In presenting this thesis as a partial fulfillment of the requirements for a degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis in whole or in part in all forms of media, now or hereafter now, including display on the World Wide Web. I understand that I may select some access restrictions as part of the online submission of this thesis. I retain all ownership rights to the copyright of the thesis. I also retain the right to use in future works (such as articles or books) all or part of this thesis.

Anusha Gadipudi March 23, 2021

A Standardized Method of Detecting Movement Onset in Ballistic Wrist Extension Movements of Stroke Patients

by

Anusha Gadipudi

Dr. Cathrin Buetefisch

Adviser

Neuroscience and Behavioral Biology

Dr. Cathrin Buetefisch

Adviser

Dr. Michael Borich

Committee Member

Dr. Gillian Hue

Committee Member

2021

A Standardized Method of Detecting Movement Onset in Ballistic Wrist Extension Movements of Stroke Patients

By

Anusha Gadipudi

Dr. Cathrin Buetefisch

Adviser

An abstract of
a thesis submitted to the Faculty of Emory College of Arts and Sciences
of Emory University in partial fulfillment
of the requirements of the degree of
Bachelor of Science with Honors

Neuroscience and Behavioral Biology

2021

Abstract
A Standardized Method of Detecting Movement Onset in Ballistic Wrist Extension Movements of Stroke Patients

By Anusha Gadipudi

Ischemic stroke affecting the primary motor cortex (M1), or its corticospinal projections (CST) has been shown to impact hand function in humans and non-human primates. Considering the prevalence of ischemic stroke, it is essential to accurately quantify hand function in order to track post-stroke recovery of movement and guide rehabilitation. The experimental use of kinematic measures of hand movement - including the onset of the movement, peak velocity, and time to peak velocity – has grown rapidly over the past two decades as a method of quantifying behavioral restitution rather than compensation. The purpose of this study is to test the feasibility of a standardized method for determining the onset of movement in ballistic wrist extensions of patients recovering from ischemic stroke in M1 or CST. Currently the onset of movement is determined visual inspection. However, it is subject to a degree of inter-observer variability and may be time-consuming and inefficient to use. Here we employed four methods of estimating the onset of movement– the visual inspection method, and three automated approaches, the sigma factor method, the 5% Max method, and the 10% Max method. The degree of a participant's affectedness was quantified by their scores on the Jebsen-Taylor Hand Function Test (JTHFT). The visually determined onset was treated as the golden standard of determining the onset of movement. The onset time from the sigma factor method was found to be closest to the onset times from the visual-inspection method, and therefore, the most accurate to the true onset. In participants with higher normalized JTHFT scores, the 10% Max method was less accurate to the true onset, and the 5% Max method of determining onset was generally the farthest from the true onset. Furthermore, a negative correlation was established between normalized JTHFT scores and the peak velocity of the ballistic wrist extensions, potentially explaining the failure of the 5% and 10% Max automated methods in participants with more affected hand function. These results indicate that the sigma factor method may have the most merit for use as a standard metric for determining the onset of ballistic wrist extension movements in individuals affected by ischemic stroke.

A Standardized Method of Detecting Movement Onset in Ballistic Wrist Extension Movements of Stroke Patients

By

Anusha Gadipudi

Dr. Cathrin Buetefisch

Adviser

A thesis submitted to the Faculty of Emory College of Arts and Sciences
of Emory University in partial fulfillment
of the requirements of the degree of
Bachelor of Science with Honors

Neuroscience and Behavioral Biology

2021

Acknowledgements

I am extremely grateful to my research advisor, Dr. Cathrin Buetefisch, for her support and guidance throughout my time at the Emory Motor Control Lab. I also thank my committee members, Dr. Michael Borich and Dr. Gillian Hue, for their valuable insights on this project. I would also like to thank Dr. Leah Roesch for all of her help, without which this project would not have been possible. Finally, a special thanks to my parents, Koteswara Rao and Radhika Gadipudi, for their unwavering support and sacrifices.

Table of Contents

Introduction

Ischemic stroke affecting the primary motor cortex (M1) or it's corticospinal projections (CST) has been shown to impair hand function (Israely S and Carmeli E, 2017), and specifically also wrist extension movements in humans (Buetefisch CM et al., 2018;Revill KP et al., 2020). Previous measures of the effect of stroke on hand function have included the Jebsen-Taylor Hand Function Test (JTHFT) (Jebsen RH et al., 1969), the Wolf Motor Function Test (WMFT) (Wolf SL et al., 1989), the Motor Activity Log (MAL) (Uswatte G et al., 2006), and kinematic measures (Buetefisch CM,Revill KP,Haut MW,Kowalski GM,Wischnewski M,Pifer M,Belagaje SR,Nahab F,Cobia DJ,Hu X,Drake D and Hobbs G, 2018;Thrane G et al., 2019). Kinematic measures of hand movements provide information about the onset, position, acceleration, and velocity of a movement (Singer HS et al., 2016). However, although experimental use of kinematic analysis as a measure of hand function has grown rapidly over the past two decades, standardization of hand movement sensorimotor metrics across studies are lacking (Alt Murphy M and Häger CK, 2015;Kwakkel G et al., 2017;Schwarz A et al., 2019).

This study was prompted by a current longitudinal clinical study that seeks to track recovery of hand function following ischemic stroke by measuring the time of onset and the peak velocity of ballistic wrist extension movements at two timepoints during the recovery process. The first time point is recorded within 1-month following the stroke, during the subacute phase of recovery. The second timepoint is recorded about 6-months after stroke as the patient enters the chronic phase of recovery. Ballistic movements are characterized by rapid muscular contractions and high firing rates. Electromyographic (EMG) recordings of ballistic movements show triphasic burst patterns (Zehr EP and Sale DG, 1994) in the agonist and antagonistic muscles involved in executing the movement. The wrist extension movement is necessary for wrist stabilization and recovery of hand and finger function following ischemic stroke in M1 or CST (Zaaimi B et al., 2012). This laboratory based kinematic measure was demonstrated to correlate with hand function as measured by clinical assessments of function, such as the JTHFT (Buetefisch CM,Revill KP,Haut MW,Kowalski GM,Wischnewski M,Pifer M,Belagaje SR,Nahab F,Cobia DJ,Hu X,Drake D and Hobbs G, 2018) in chronic stroke patients with injury to the M1 or its CST which indicates its

relevance for hand function. Furthermore, evidence from non-human primate stroke models indicates that lesions in M1 are correlated with abnormal movement kinematics, further confirming the validity of ballistic wrist extension movements as a measure of function in M1 or CST (Dancause N et al., 2006)

Movement onset has been previously utilized to quantify the kinematics of a movement. It is defined as the time from the 'go' signal to the onset of the movement. Other frequently used measures include the time to maximum velocity and the duration of a movement. These measures cannot be calculated without first determining the movement onset (Schwarz A,Kanzler CM,Lambercy O,Luft AR and Veerbeek JM, 2019). However, methods for determining the movement onset varied across studies. There are three main proposed methods of determining the onset of a movement in a ballistic wrist extension: As a deviation from the resting position (sigma factor) (Wentink EC et al., 2014); as a percentage of the maximum resultant velocity (%Max) (Rousseau C et al., 2016;Wagner JM et al., 2008); and by visual inspection (Waters P and Strick PL, 1981). While %Max has been frequently utilized to calculate the movement onset, the set percentage of the maximum varies greatly across studies: movement onset of reaching and grabbing movements was defined in one study as 2% of the maximum velocity (Thrane G,Sunnerhagen KS,Persson HC,Opheim A and Alt Murphy M, 2019); and as 5% of the maximum velocity in another study (Wagner JM,Rhodes JA and Patten C, 2008). Alternatively, sigma factor has previously been used to determine the onset of movement when EMG was recorded (Corcos DM et al., 1992;Hodges PW and Bui BH, 1996) but is less frequently used in kinematic measurements. Visual inspection has been previously used to rectify results found from %Max (Bundy DT et al., 2018) but is less frequently used independently to determine onset due to its time-consuming nature and high subjectivity between observers.

The current investigation looks to compare the three different methods of determining the onset of movement in patients suffering from impaired hand function due to ischemic stroke affecting M1 or CST to conclusively determine which method is most reliable

Methods:

The data was gathered from participants recruited for an on-going study by Dr. Cathrin Buetefisch from 2015 – 2020. All participants were confirmed to be suffering from ischemic stroke involving M1 and/or CST by the visual inspection of their brain MRI by a board-certified neurologist (C. Buetefisch). 35 individuals (68.5 ± 9.77, 19 females, 37.14% dominant hand affected) were recruited to participate in this study. Of these 35 individuals, 31 participants (59.9 ± 9.01, 17 females, 35.48% dominant hand affected) had kinematic recordings available for analysis. Recordings were completed within 1-month of the ischemic stroke. Subjects completed written informed consent before entering the study. The Institutional Review Board of Emory University approved the study.

Subject Number	Which Hand Affected	Sex	Age	Dominant Hand Affected?	Non-Affected Hand JTHFT Score	Affected Hand JTHFT Score
NAH_003	**L**	F	60	N	0.27	0.63
NAH_004	**L**	F	52	N	0.13	0.49
NAH_005	**L**	F	56	N	0.15	0.49
NAH_006	**L**	F	41	Y	0.14	0.29
NAH_008	**L**	M	71	N	0.01	0.02
NAH_013	**L**	F	64	N	0.08	0.92
NAH_014	**L**	F	54	N	0.25	0.76
NAH_015	**L**	M	72	N	0.31	0.40
NAH_016	**L**	M	59	N	0.22	0.68
NAH_017	**R**	F	51	Y	0.13	0.22
NAH_019	**L**	F	39	N	0.20	0.25
NAH_020	**R**	F	63	Y	-0.03	0.10
NAH_021	**L**	M	62	N	0.18	0.23
NAH_023	**L**	M	53	N	0.25	0.93
NAH_025	**R**	F	72	N	0.08	0.07
NAH_026	**L**	M	60	N	0.11	0.16
NAH_034	**L**	F	57	Y	0.10	0.13
NAH_036	**R**	M	60	N	0.05	0.18
NAH_040	**L**	F	62	N	0.25	0.92
NAH_041	**R**	M	56	Y	0.22	0.22
NAH_048	**L**	F	65	N	0.31	0.44
NAH_049	**L**	M	61	Y	0.20	0.37
NAH_053	**L**	F	65	N	-0.08	0.92
NAH_055	**L**	M	55	N	0.33	0.93
NAH_056	**R**	M	61	Y	0.21	0.60
NAH_059	**R**	F	79	Y	0.28	0.92
NAH_061	**L**	M	42	N	0.16	0.93
NAH_062	**L**	F	65	N	0.15	0.33
NAH_063	**R**	M	74	Y	0.17	0.29
NAH_065	**R**	F	63	Y	0.12	0.34
NAH_066	**R**	M	61	Y	0.16	0.92

Table 1: Characteristics of participants included in this analysis

Motor Tasks

We measured the wrist extension movement of participants (n = 31) in both hands at a 1-month and 6-month time post-stroke. As part of the ongoing longitudinal study, all participants were also tested in single exposures to two different interventions at these time points. The interventions consisted of either rTMS or Sham and were applied in a random order. The measurements were conducted before and after each intervention at 1-month post-stroke and 6-months post-stroke. As a result, all participants had 2 measurement of ballistic wrist extension movement at each time point for a total of 4 measurements. For the measurement, participants were asked to rapidly execute 7 ballistic wrist extension movements following an auditory cue. A 2-dimensional gyrometer was mounted on the dorsum of the hand to measure wrist extension movements. EMG activity was recorded on the extensor carpi ulnaris (ECU) muscle, a muscle that supports wrist extension movements. Kinematic and EMG data were recorded using LabVIEW (National Instruments, CA, USA). Data were sampled at 1 kHz (bandpass 3Hz – 3 kHz) for 1500ms following the auditory cue. The 2-dimensional position data was recorded in the y-axis and the x-axis.

Kinematic and EMG data were stored on a PC for off-line analysis. Data analysis was done in LabVIEW (National Instruments, CA, USA). Peak velocity and movement onset were calculated from the resultant angular velocity of the ballistic wrist extension movement.

Analysis

Movement onset (MO) was determined through 4 different approaches: visual inspection; 5 %Max; 10% Max; and sigma factor). Peak velocity (Vmax) was defined as the maximum resultant angular velocity from the x-axis and y-axis.

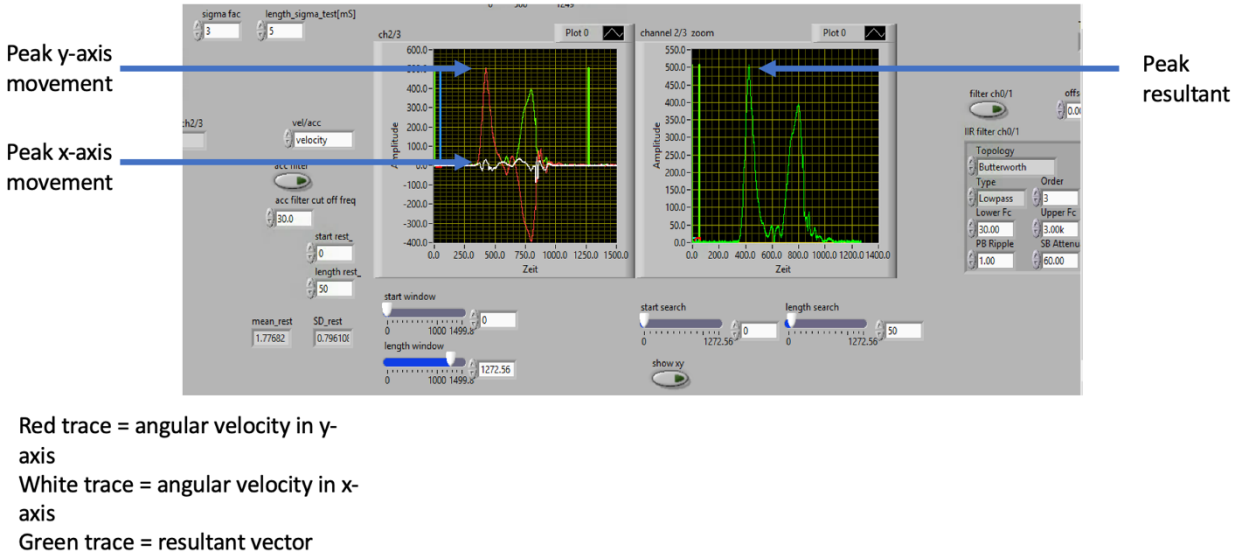


Fig 1: Visualization of the raw data in the labVIEW program. In Ch2/3, the red trace indicates the velocity of the movement in the y-axis. The white trace indicates the velocity of the movement in the x-axis. The green trace indicates the resultant velocity as calculated for the velocity in the x- and y- axes.

Visual Inspection

The onset of the ballistic wrist extension was determined by visually inspecting the kinematic trace of the resultant velocity. A cursor was placed at the time point where the velocity increased from rest, defining the visually determined movement onset. Recordings in which no discernable movement was found during visual inspection were excluded from the analysis.

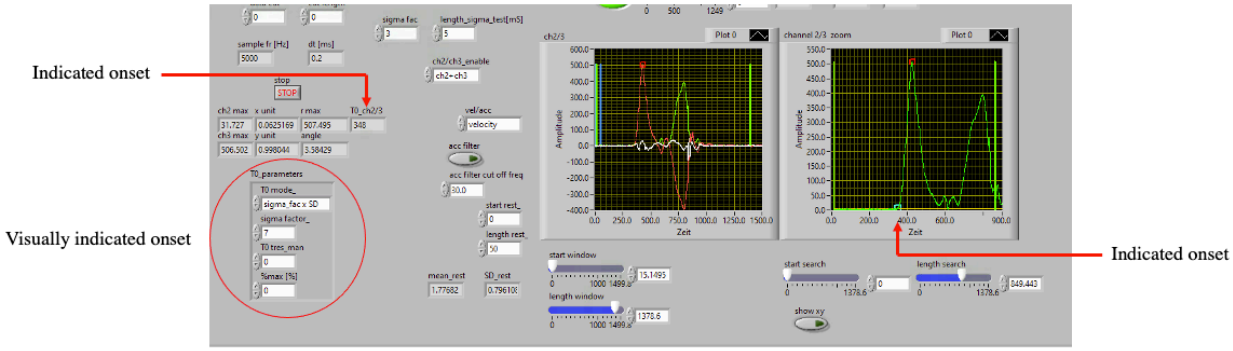


Fig 2: Movement onset by inspection. The cursor (the blue box in the window “Ch 2/3zoom”) was manually moved to the onset of the movement. This time point is extracted and shown under “T0_ch2/3”. In this case, the visually determined onset coincided with a sigma factor value of 7 (indicated in “sigma factor_”)

%Max

In the 5%Max and 10%Max approaches, the movement onset was calculated as a percentage of the maximum resultant velocity of the ballistic wrist extension. Based on previous studies from Bundy et al. and Rousseau et al., the onset of movement was predicted to occur when the velocity of the hand exceeded 10% (Bundy DT,Szrama N,Pahwa M and Leuthardt EC, 2018) or 5% (Rousseau C,Papaxanthis C,Gaveau J,Pozzo T and White O, 2016) of the maximum velocity of the movement.

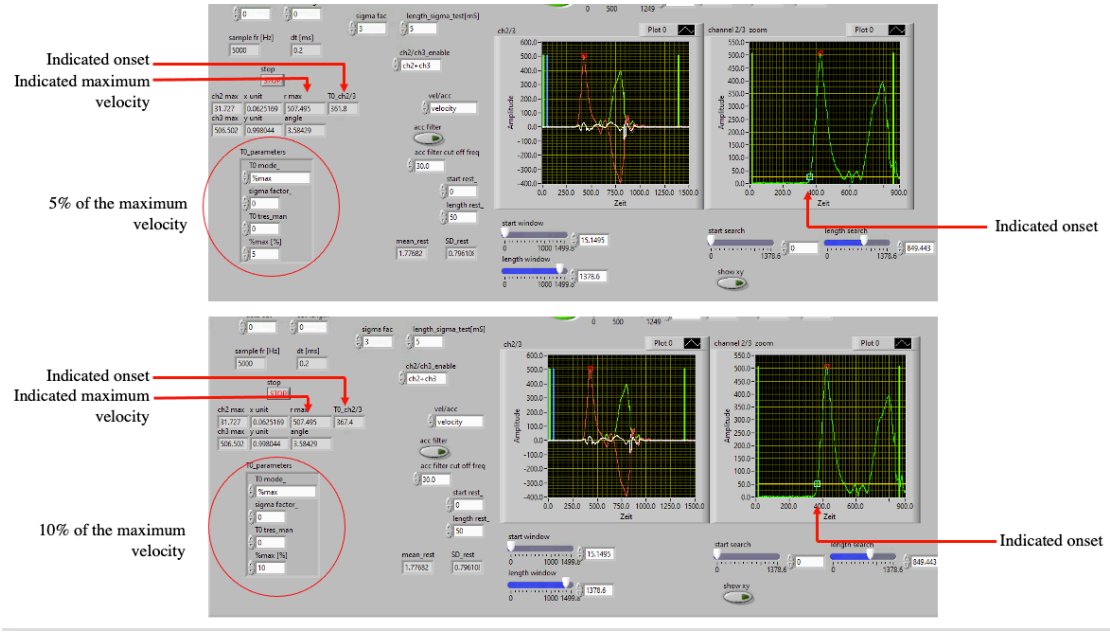


Fig 3: Movement onset by %Max. First, the maximum velocity ("rmax") is marked with the red cursor. The maximum velocity is used to indicate the time ("T0_ch2/3") at 5% or at 10% of the maximum velocity ("%max"). 5% or 10% of the maximum velocity is selected under the "%max" tab.

Sigma Factor

In this approach, the deviation from the mean rest velocity determines the onset of movement. The resting period was defined by the 50 ms following the auditory cue, as in Fig 4. Based on the observed reaction times in healthy adult humans, auditory cued movements are not expected to occur within 100 ms after to go signal (Schlittenlacher J and Ellermeier W, 2015). To determine the sigma factor, the mean amplitude of the angular velocity at rest was calculated. The sigma factor was then defined as a multiple of the standard deviation from the mean resting amplitude.

In order to standardize the analysis, a single sigma factor was chosen to test on the group-level. A sigma factor value that could accurately indicate the onset time across a range of participants had to be defined. In an initial pilot analysis of 17 files, ($n = 6.91 \pm 0.96$) the highest sigma factor was found to be 10. Considering the shape and slope of the trace, a higher sigma factor was deemed to be more accurate to determine the true onset of movement than a lower sigma factor. As indicated in Fig. 5, a steeper slope causes less shift in the indicated onset along the x-axis per unit amplitude. Smaller slopes, which generally indicate more affected movements are associated with an

increased shift along the x-axis per unit amplitude. Furthermore, Fig. 5a. demonstrates the error in underestimating the individual sigma factor. The indicated onset time is much lower than the true onset time. As a higher sigma factor was determined to be more accurate to the true movement onset, the highest sigma factor from the pilot analysis was then chosen to standardize the group-level analysis. The highest sigma factor found in the pilot analysis was 10, so a sigma factor value of 10 was used in this analysis.

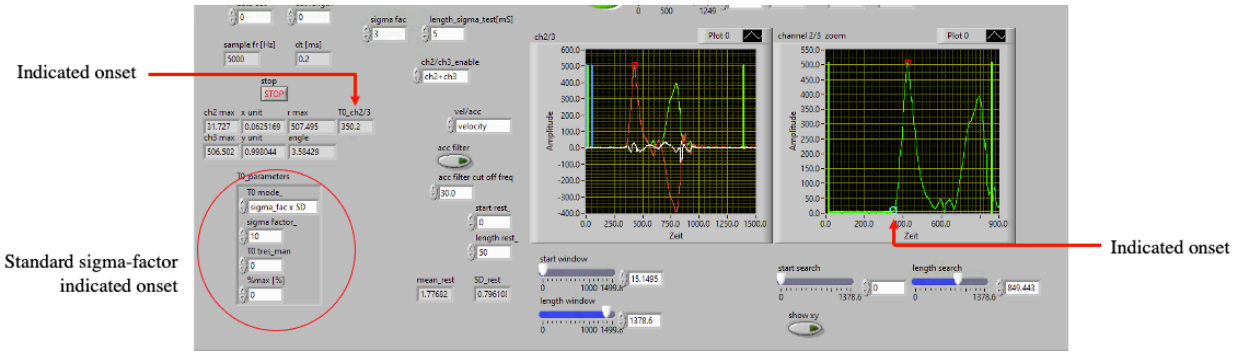


Fig 4: Movement onset by the standard sigma factor method. First, standard sigma factor ("sigma factor") is set to 10. The time at which the resultant angular velocity exceeds 10 standard deviations of the angular velocity at rest is indicated as the onset ("T0_ch2/3").

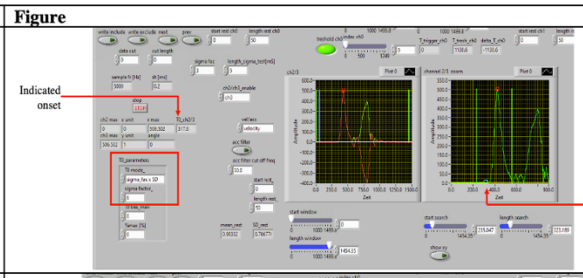
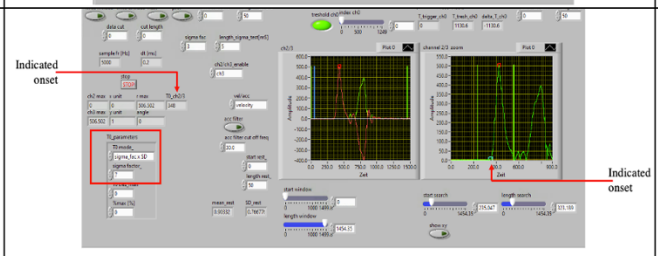
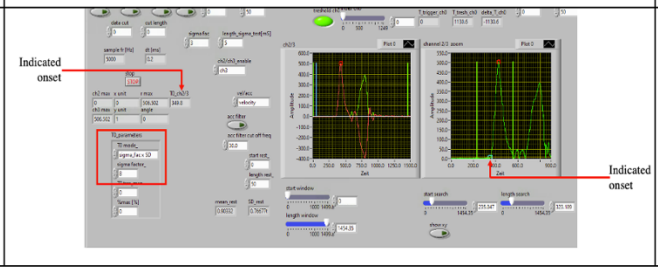
Onset	Figure	Time Difference
Early onset		$348\ ms - 317.8\ ms = 30.2ms$
Correct visual onset		$348\ ms - 348\ ms = 0\ ms$
Late onset		$348\ ms - 349.8\ ms = -1.8\ ms$

Fig 5: Using a higher sigma factor is more accurate to the true onset time than using a lower sigma factor

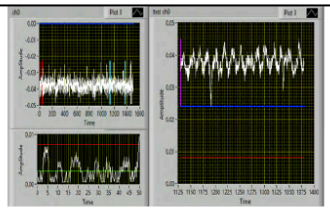
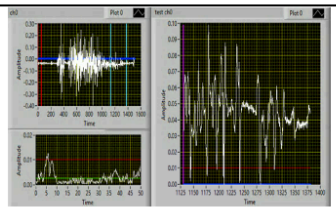
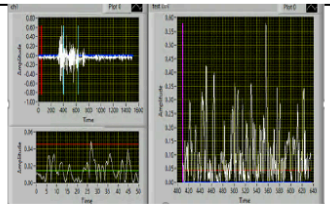
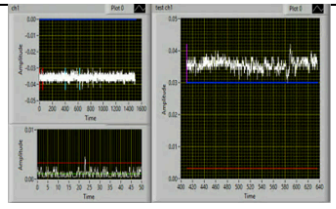
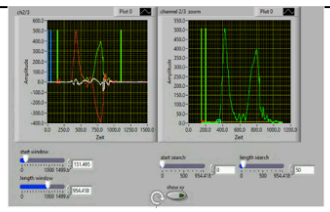
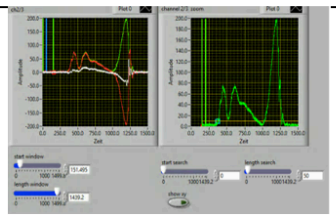
	Less affected Participant	More affected Participant
EMG Ch 0 – right hand		
EMG Ch 1 – left hand		
Ballistic movement trace		

Fig 6: Comparing the EMG, peak velocity, and slope – or the time to reach maximum velocity, in less affected and more affected movements

Unclear Onset

EMG Method

The sigma factor method of determining onset depends on setting a determined rest period. In this study, the rest period was set to the first 50ms after the auditory tone. However, movements recorded from more affected participants may not have a clear resting period. These participants may have unwanted movements or overflow from other movements that confounds the recordings and precludes defining the onset of the movement. An example is depicted below in Fig. 7. In these participants, the standardized sigma factor approach fails to accurately determine the onset of the movement. In such cases, it becomes necessary to use the EMG of an agonist muscle to estimate and visually correct the onset of the movement. The agonist muscle for this ballistic wrist extension movement is the ECU (Fig 7. Upper left panel). Using the onset of the EMG burst we are able to estimate the onset of movement based on ECU muscle activation (Buetefisch CM,Revill KP,Haut MW,Kowalski GM,Wischnewski M,Pifer M,Belagaje SR,Nahab F,Cobia DJ,Hu X,Drake D and Hobbs G, 2018). Any movement recorded before the EMG burst is ascribed to another muscle and is not considered the target movement. The temporal relationship between M1 pyramidal tract neuron discharges, EMG activity, and execution of voluntary movements was previously established in non-human primate studies (Kalaska JF, 2009). PTN firing occurred 100-200 ms before EMG activity, which was found to proceed the onset of kinematic movement (Crammond DJ and Kalaska JF, 2000). In the contraction of skeletal muscles in humans, the delay between the onset of electrical activity and measurable muscle tension was found to be between 30 – 100 ms (Cavanagh PR and Komi PV, 1979).

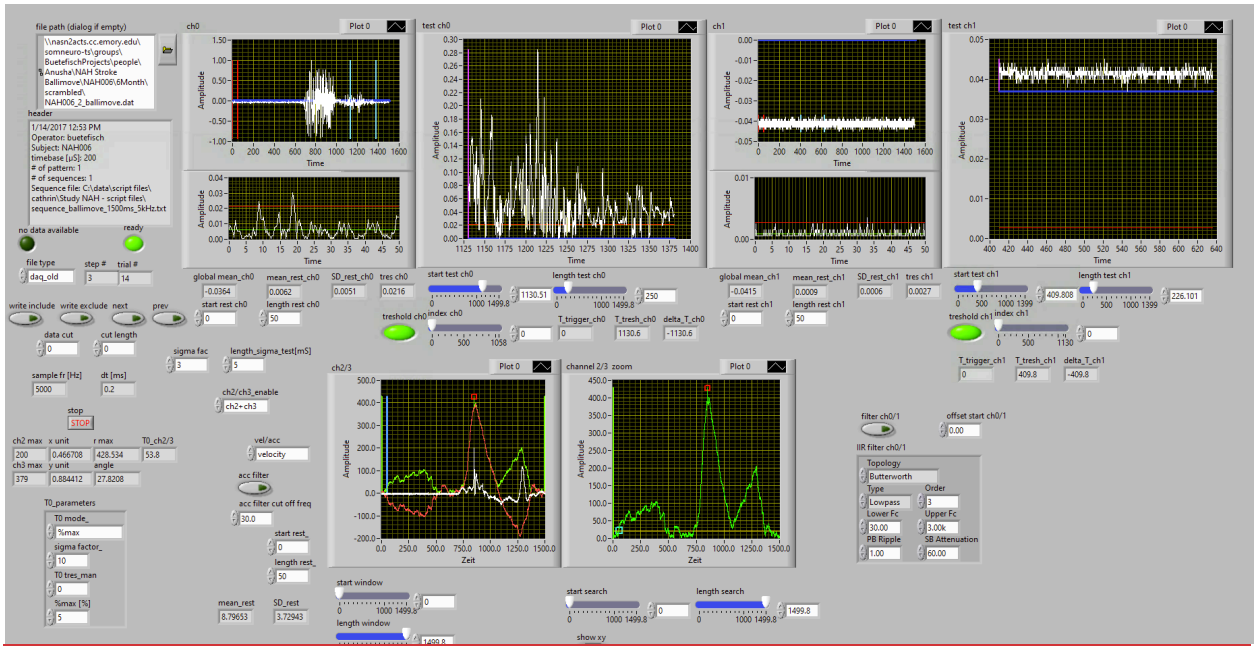


Fig 7: Affected ballistic wrist extension movement. EMG burst pattern is observed in Ch 0. Kinematic movement trace is observed in Ch 2/3.

In the movement depicted in Fig. 7, the participant appears to be unable to keep their wrist still during the expected rest period. As the sigma factor method of onset depends on marking the beginning of the movement as a deviation from the set resting period, that method is not sufficient to determine the onset here. By observing the EMG in Fig. 7, the characteristic burst pattern of a ballistic movement occurs between 600-800 ms. Setting the sigma factor to 10 indicates the onset at 63.2 ms, which is lower than the expected onset range. Narrowing the search window to 600 ms - 800 ms yields an onset at 741 ms, which is within the expected onset range.

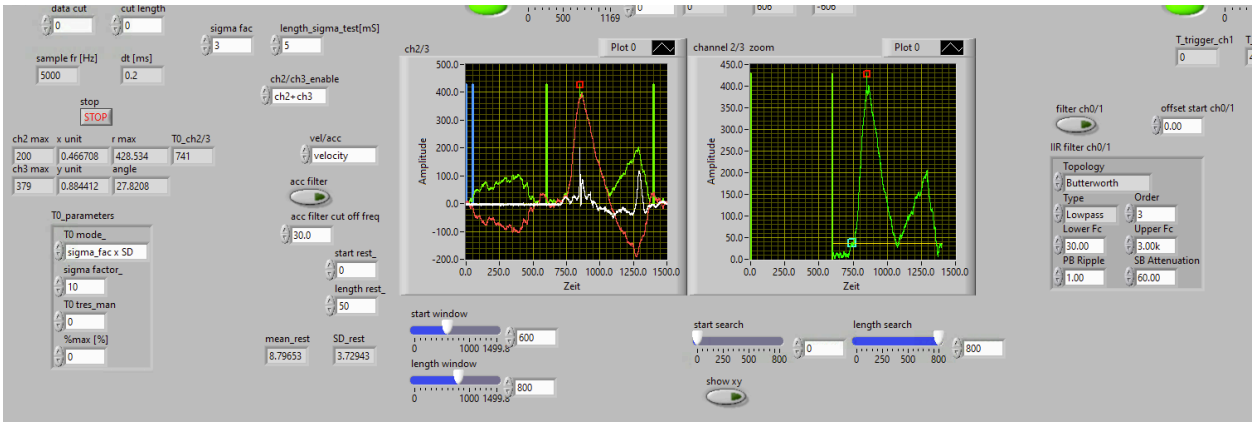


Fig 8: The predicted onset when the sigma factor is set to 10 and the search window is shortened to 600 ms – 800 ms after the stimulus, this range marks the predicted onset indicated by the EMG

Additionally, while the onset can be usually determined from the resultant velocity (between the x-axis and y-axis), there may be instances where the onset is more clearly indicated through the x-axis or the y-axis movement alone. In the example depicted in Fig. 8 and Fig. 9, the excessive movement appears to be on the y-axis (the red trace only). It may be possible to estimate the onset by using the data from the x-axis rather than the resultant. With this method, the onset occurs at 725 ms which is also within the range of the expected onset.

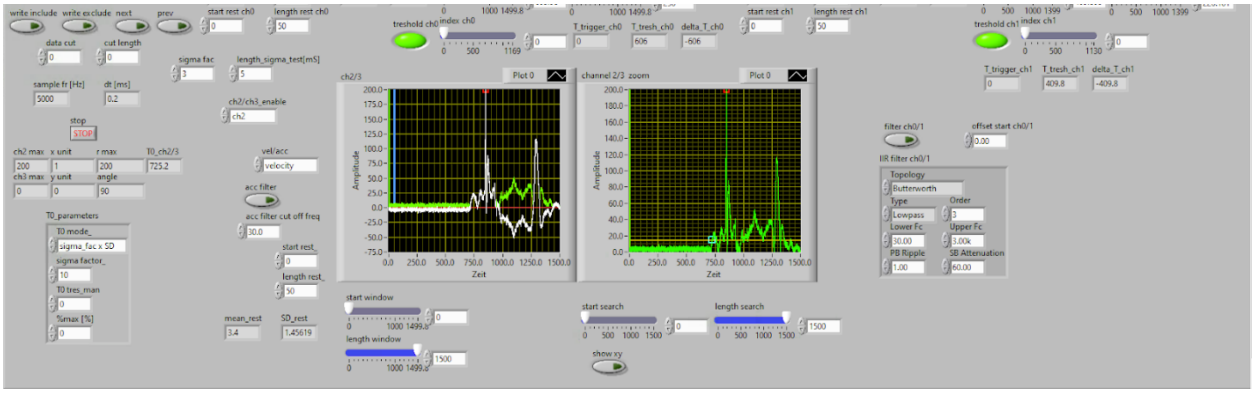


Fig 9: Predicted onset when the sigma factor is set to 10 and the search window is not shortened when only the x-axis trace is used

Although these movements pose a weakness to the sigma factor method of determining onset, they are also a liability to the %Max method of determining onset. The first instance where the movement crosses 5% of the maximum velocity occurs at 53.8ms (Fig. 10). Similarly, the onset at 10% of the maximum is at 64.2 ms.

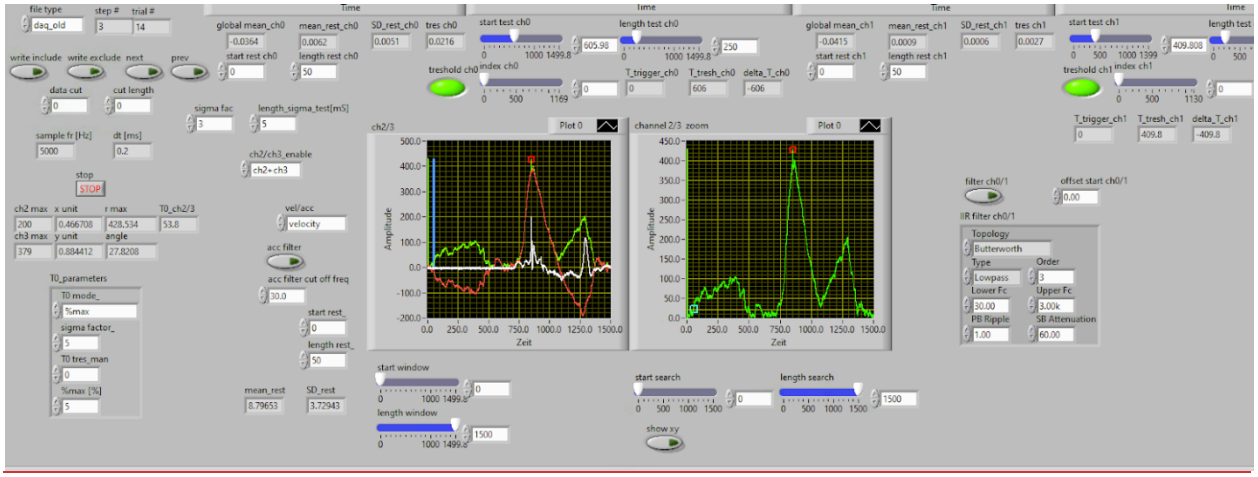


Fig 10: Movement onset as determined by the %Max method

If the search window is shortened, the movement onset at 5% of the maximum is 726.6 ms and at 10% of the maximum is 760.6 ms. If the window is expanded and only x-axis data is considered, the onset of movement at 5% of the maximum is 719.8 ms and at 10% of the maximum is 733.2 ms. Both methods yield onset times within the expected range.

Jebsen-Taylor Hand Function Test

With the ultimate goal of operationalizing a standardized method of determining movement onset, we also utilized the JTHFT to explore association between impaired hand function and validity of our automatic analysis approaches. A strong association between these two measures, i.e., greater impairment in hand function correlates with greater inaccuracy of the automated method, may allow us to set a cutoff score after which a ballistic movement would not be analyzed using the standardized method and would have to be analyzed visually. The Jebsen-Taylor Hand Function Test is a standardized timed measure of hand function (Jebsen RH,Taylor N,Trieschmann RB,Trotter MJ and Howard LA, 1969). JTHFT is a reliable and valid test of hand function (Bovend'Eerdt TJ et al., 2004;Sığırtmaç İ C and Öksüz Ç, 2020). The JTHFT score is calculated based on the norm scores that Jebsen defined in 1969 (Jebsen RH,Taylor N,Trieschmann RB,Trotter MJ and Howard LA, 1969). In the present study, the test was administered by a trained research physical therapist. Patients were asked to complete 7 motor tasks within 120 s. However,

two tests – for writing and stimulated feeding, were excluded from analysis due to low test-retest reliability (Stern EB, 1992). Ultimately, the time taken for the patient to complete 5 motor tasks was summed to derive a RAW score. The RAW score was normalized to age- and sex- matched controls. The test was repeated in the ipsilesional and contralesional hands, and the final value was normalized for hand dominance. A larger score on the JTHFT indicated more abnormal hand movement.

Results

1. The range of sigma factors that indicated the true onset

The sigma factor indicating onset was recorded in a pilot study of 17 measurement sessions with 7 trials each. The highest occurring sigma factor was found to be 10 (Fig. 11). Based on these preliminary results, the standardized sigma factor value was set to 10. After completing the analysis of the entire data set (n = 31), there was only one trial with a higher sigma factor of 17 for the affected hand measurements. For the non- affected hand, 4 trials had greater than 10 sigma factor (Fig. 12). The average sigma factor was found to be 6.62±1.23 in the affected hand, and 6.59±1.31 in the non-affected hand.

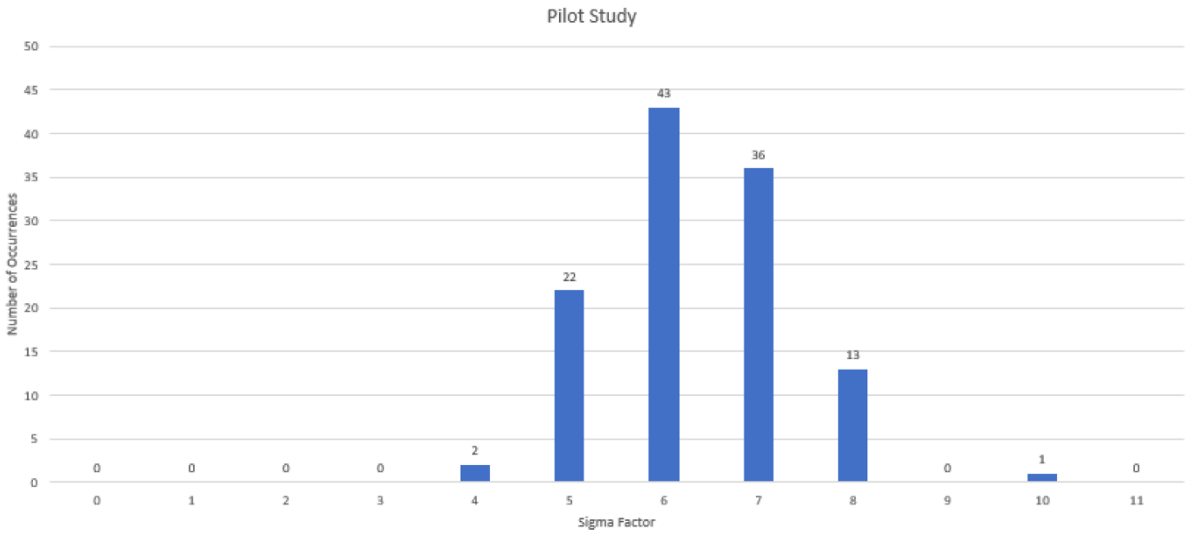


Fig 11: The range of sigma factors that indicated the true, visually determined onset of 17 measurement sessions, each with 7 trials. Recordings in which no discernable movement was detected through visual inspection were excluded from the analysis

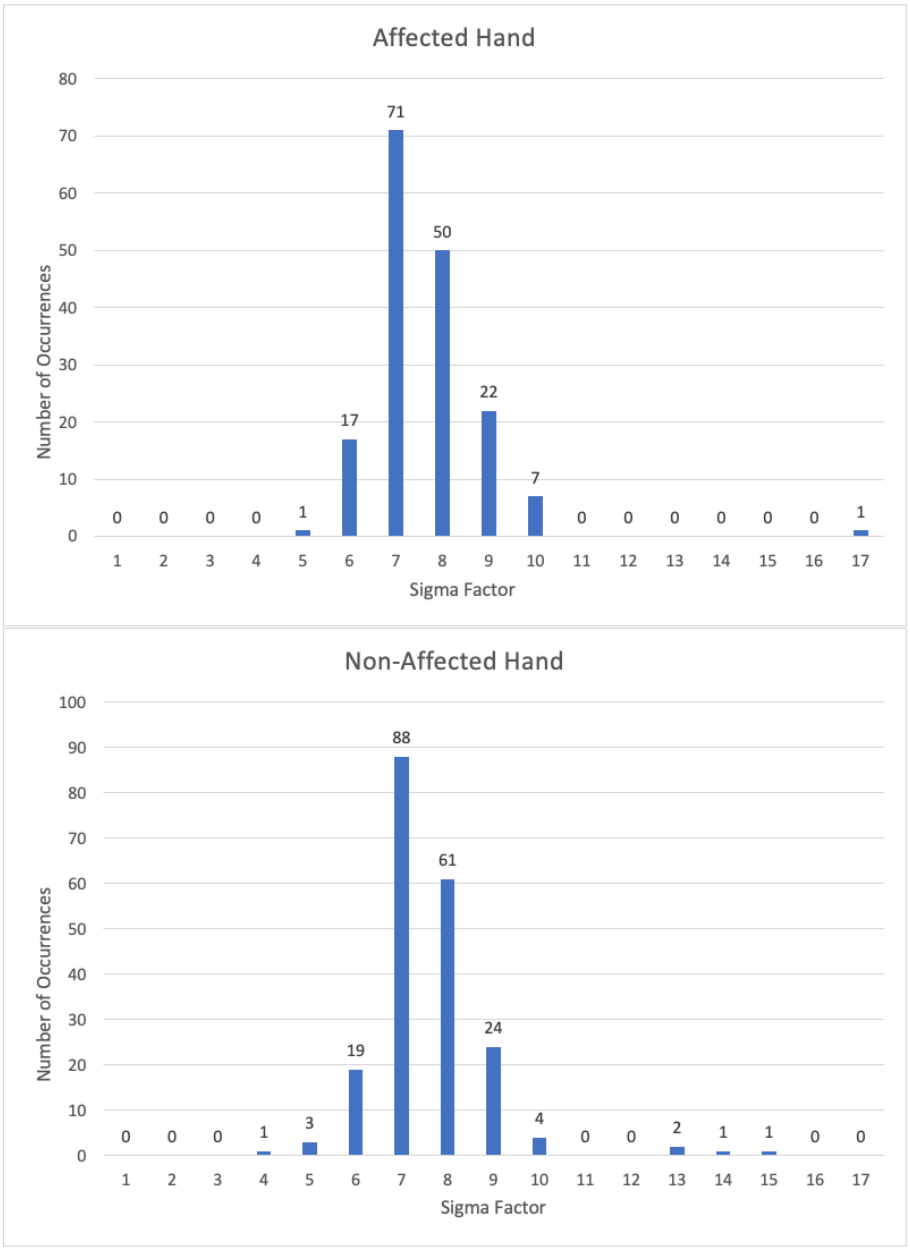


Fig 12: The range of sigma factors that indicated the true, visually determined onset in the affected hand and the non-affected hand (n = 31). Each file has 7 trials. Recordings in which no discernable movement was detected through visual inspection were excluded from the analysis

2. Movement onset determined by different approaches

Figure 13 shows the range of the indicated onset times in the affected hand and in the non-affected hand. Figure 14 shows the average indicated onset time in both hands and compares the different methods of detecting the onset of movement. In the affected hand, the average indicated onset time

of the visual ($387.07 \pm 16.60ms$), sigma factor ($396.26 \pm 17.34ms$), 5% max ($353.80 \pm 30.60ms$), and 10% max ($380.67 \pm 26.20ms$) methods are shown. The average indicated onset time using the 5% max method is much lower than the visually indicated true onset time, suggesting that the 5% Max method is less accurate than the 10% Max method or the sigma factor method. In the non-affected hand, the average indicated time of the visual ($381.00 \pm 11.56ms$), sigma factor ($377.13 \pm 11.86ms$), 5% max ($392.90 \pm 17.14ms$), and 10% max ($406.87 \pm 17.82ms$) methods are shown.

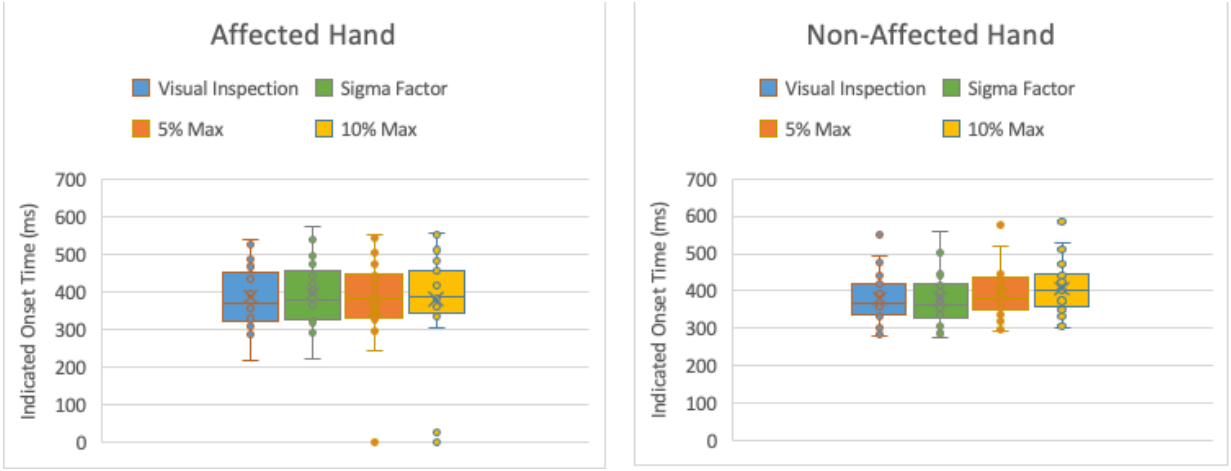


Fig 13: The range of indicated onset times by the 4 different methods employed in the affected hand and the non-affected hand.

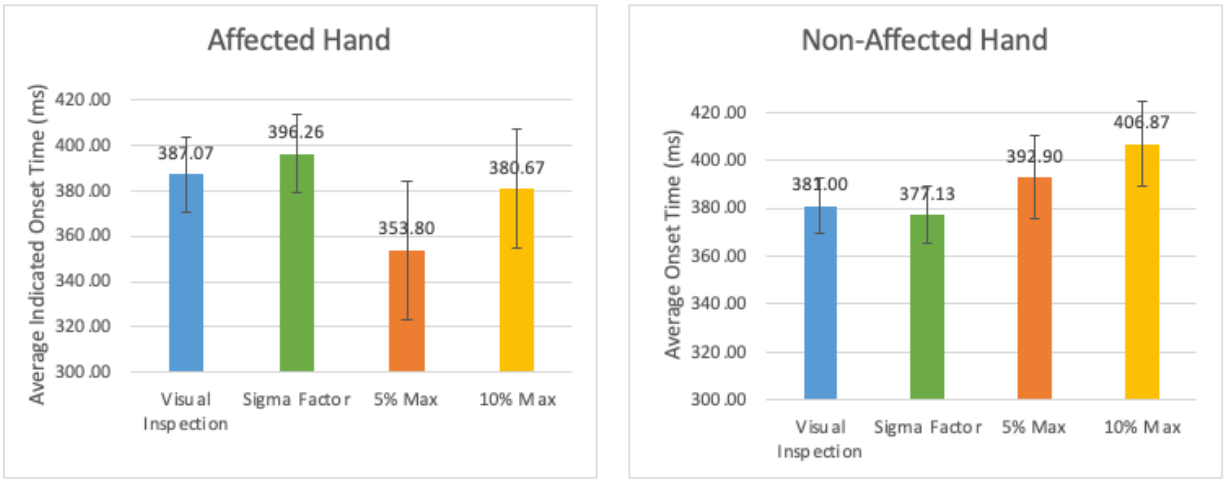


Fig 14: The average indicated onset time and the standard deviation across all participants in the affected and non-affected hand.

3. Relationship between peak velocity and JTHFT

The peak velocity of a kinematic movement is lower in more affected subjects, who have higher normative scores on the JTHFT. As the 5% max method fails in participants with lower peak velocities, it is possible that the 5% max method may not be an appropriate method for standardizing a method of finding the movement onset in more affected individuals. The JTHFT was used as a clinical method of determining how an individual's movement quality is affected by ischemic stroke. More affected participants have higher JTHFT scores than less affected participants. A JTHFT score of 0 indicates a normal hand function.

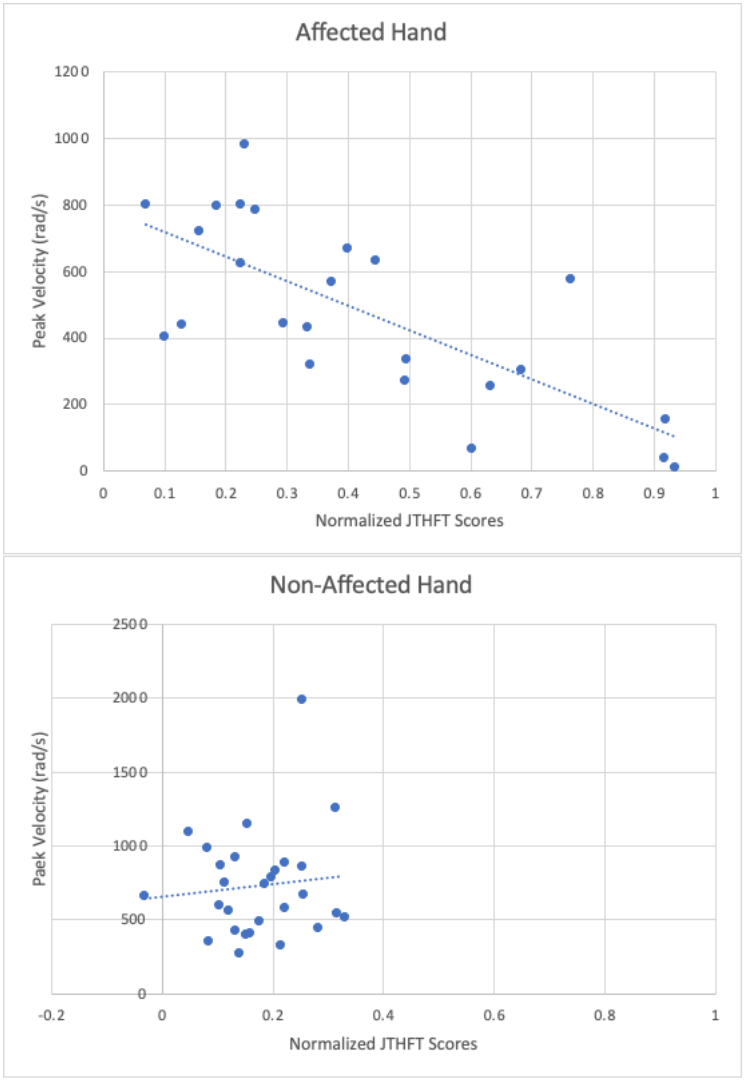


Fig 15: The correlation between JTHFT scores and the peak velocity reached in the ballistitic wrist extension movement, in the affected and non-affected hands

4. Relationship between JTHFT scores and the time difference

We found a clear correlation between degree of impairment in hand function and the time difference from the true onset in the 5% and 10% max methods of determining the onset. The time difference was calculated by taking the absolute value of the difference between the indicated onset time in the standardized method and the indicated onset time in the visually determined method. The more affected a participant was, the less accurate the 5% and 10% methods were (Fig. 16).

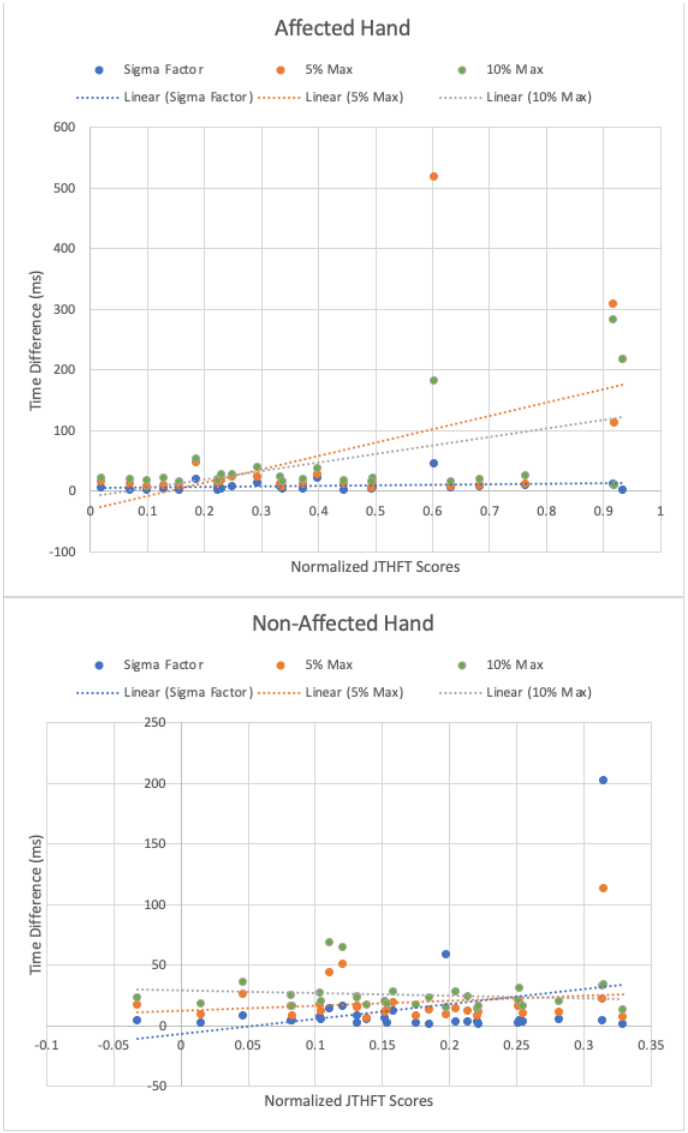


Fig 16: The correlation between JTHFT scores and the time difference from the indicated onset in the affected and non-affected hands.

Discussion

The sigma factor method is generally the most accurate to the true movement onset as defined by visual inspection. This effect was consistent across all subjects. The 5% Max and 10% Max method of standardizing the movement onset were found to be inaccurate in more affected subjects with higher JTHFT scores. These results indicate that the %Max method may not be appropriate in determining onset of movement in studies of people with impaired hand function such as patients recovering from ischemic stroke in M1 or CST.

This study uses 2-dimensional inertial recording. The current recommendation from the Stroke Recovery and Rehabilitation Roundtable is to conduct recordings in 3-dimensions using high-speed optoelectronic recording devices. In this study, the 2-dimensional recording system still allows for analysis of resultant movements. In addition, the use of inertial systems may be valid for capturing ballistic wrist extension movements (Wirth MA et al., 2019) . Furthermore, the use of optoelectronic systems is subject to a degree of interobserver variability, and the recording apparatus can be expensive and time-consuming to set-up. Future investigation may seek to compare the results in determining the onset of a movement using optoelectronic recording as opposed to inertial recording systems. Future studies may also include recordings captured in 3-dimensions rather than 2-dimensions.

The failure of the 5% and 10% Max methods in patients suffering from ischemic stroke is of particular note. The greater a participant's JTHFT score, the worse the 5% and 10% Max methods were at finding the true onset accurately. Furthermore, the high degree of variation in the onsets determined by the 5% and 10% Max methods suggest that this effect may be driven by a few highly affected subjects, for whom this method is simply insufficient for determining the movement onset. In such cases, visual inspection may be needed to correct the movement onset to accurately reflect the true onset. Alternatively, these results also make the case for implementing a 'cut-off' JTHFT score beyond which the determination of the movement onset cannot be standardized and automated. Beyond this score, visual inspection would be needed to determine the movement onset.

Furthermore, a sigma factor value of 10 was chosen for this study based on the results from analyzing a pilot group. However, the highest sigma factor in the complete sample was found to be 17 for one trial for the affected hand and greater than 10 in 4 trials of the non- affected hand (max. 14). Potential future investigation may consider testing the effect on accuracy when choosing different sigma factors in order to further understand the most accurate standardized method of finding the movement onset.

Future investigation may look to compare the inter- and intra- observer reliabilities of the kinematic approach to the clinical approach. This investigation may also compare the reliability of the visually determined onset method to the standardized method. Additional investigation may be conducted to develop a method of automating this analysis.

I have received IRB approval on the following protocol:
IRB ID: CR001-IRB00081238

References:

Alt Murphy M, Häger CK (2015), Kinematic analysis of the upper extremity after stroke – how far have we reached and what have we grasped? Physical Therapy Reviews 20:137-155.

Barany DA, Revill KP, Caliban A, Vernon I, Shukla A, Sathian K, Buetefisch CM (2020), Primary motor cortical activity during unimanual movements with increasing demand on precision. J Neurophysiol 124:728-739.

Bovend'Eerdt TJ, Dawes H, Johansen-Berg H, Wade DT (2004), Evaluation of the Modified Jebsen Test of Hand Function and the University of Maryland Arm Questionnaire for Stroke. Clin Rehabil 18:195-202.

Buetefisch CM, Howard C, Korb C, Haut MW, Shuster L, Pergami P, Smith C, Hobbs G (2015), Conditions for enhancing the encoding of an elementary motor memory by rTMS. Clin Neurophysiol 126:581-593.

Buetefisch CM, Revill KP, Haut MW, Kowalski GM, Wischnewski M, Pifer M, Belagaje SR, Nahab F, et al. (2018), Abnormally reduced primary motor cortex output is related to impaired hand function in chronic stroke. J Neurophysiol 120:1680-1694.

Bundy DT, Szrama N, Pahwa M, Leuthardt EC (2018), Unilateral, 3D Arm Movement Kinematics Are Encoded in Ipsilateral Human Cortex. J Neurosci 38:10042-10056.

Cavanagh PR, Komi PV (1979), Electromechanical delay in human skeletal muscle under concentric and eccentric contractions. Eur J Appl Physiol Occup Physiol 42:159-163.

Corcos DM, Gottlieb GL, Latash ML, Almeida GL, Agarwal GC (1992), Electromechanical delay: An experimental artifact. J Electromyogr Kinesiol 2:59-68.

Crammond DJ, Kalaska JF (2000), Prior information in motor and premotor cortex: activity during the delay period and effect on pre-movement activity. J Neurophysiol 84:986-1005.

Dancause N, Barbay S, Frost SB, Zoubina EV, Plautz EJ, Mahnken JD, Nudo RJ (2006), Effects of small ischemic lesions in the primary motor cortex on neurophysiological organization in ventral premotor cortex. J Neurophysiol 96:3506-3511.

Hodges PW, Bui BH (1996), A comparison of computer-based methods for the determination of onset of muscle contraction using electromyography. Electroencephalogr Clin Neurophysiol 101:511-519.

Israely S, Carmeli E (2017), Handwriting performance versus arm forward reach and grasp abilities among post-stroke patients, a case-control study. Top Stroke Rehabil 24:5-11.

Jebsen RH, Taylor N, Trieschmann RB, Trotter MJ, Howard LA (1969), An objective and standardized test of hand function. Arch Phys Med Rehabil 50:311-319.

Kalaska JF (2009), From intention to action: motor cortex and the control of reaching movements. Adv Exp Med Biol 629:139-178.

Kesar TM, Belagaje SR, Pergami P, Haut MW, Hobbs G, Buetefisch CM (2017), Effects of monoaminergic drugs on training-induced motor cortex plasticity in older adults. Brain Res 1670:106-117.

Kwakkel G, Lannin NA, Borschmann K, English C, Ali M, Churilov L, Saposnik G, Winstein C, et al. (2017), Standardized measurement of sensorimotor recovery in stroke trials: Consensus-based core recommendations from the Stroke Recovery and Rehabilitation Roundtable. Int J Stroke 12:451-461.

Revill KP, Haut MW, Belagaje SR, Nahab F, Drake D, Buetefisch CM (2020), Hebbian-Type Primary Motor Cortex Stimulation: A Potential Treatment of Impaired Hand Function in Chronic Stroke Patients. Neurorehabil Neural Repair 34:159-171.

Rousseau C, Papaxanthis C, Gaveau J, Pozzo T, White O (2016), Initial information prior to movement onset influences kinematics of upward arm pointing movements. J Neurophysiol 116:1673-1683.

Schlittenlacher J, Ellermeier W (2015), Simple reaction time to the onset of time-varying sounds. Atten Percept Psychophys 77:2424-2437.

Schwarz A, Kanzler CM, Lambercy O, Luft AR, Veerbeek JM (2019), Systematic Review on Kinematic Assessments of Upper Limb Movements After Stroke. Stroke 50:718-727.

Sığırtmaç İ C, Öksüz Ç (2020), Investigation of reliability, validity, and cutoff value of the Jebsen-Taylor Hand Function Test. J Hand Ther.

Singer HS, Mink JW, Gilbert DL, Jankovic J (2016) Chapter 5 - Motor Assessments. In: Movement Disorders in Childhood (Second Edition), vol. (Singer HS, Mink JW, Gilbert DL, Jankovic J, eds), pp. 57-66. Boston: Academic Press.

Stern EB (1992), Stability of the Jebsen-Taylor Hand Function Test across three test sessions. Am J Occup Ther 46:647-649.

Thrane G, Sunnerhagen KS, Persson HC, Opheim A, Alt Murphy M (2019), Kinematic upper extremity performance in people with near or fully recovered sensorimotor function after stroke. Physiother Theory Pract 35:822-832.

Uswatte G, Taub E, Morris D, Light K, Thompson PA (2006), The Motor Activity Log-28: assessing daily use of the hemiparetic arm after stroke. Neurology 67:1189-1194.

Wagner JM, Rhodes JA, Patten C (2008), Reproducibility and minimal detectable change of three-dimensional kinematic analysis of reaching tasks in people with hemiparesis after stroke. Phys Ther 88:652-663.

Waters P, Strick PL (1981), Influence of 'strategy' on muscle activity during ballistic movements. Brain Res 207:189-194.

Wentink EC, Schut VG, Prinsen EC, Rietman JS, Veltink PH (2014), Detection of the onset of gait initiation using kinematic sensors and EMG in transfemoral amputees. Gait Posture 39:391-396.

Wirth MA, Fischer G, Verdú J, Reissner L, Balocco S, Calcagni M (2019), Comparison of a New Inertial Sensor Based System with an Optoelectronic Motion Capture System for Motion Analysis of Healthy Human Wrist Joints. Sensors (Basel) 19.

Wolf SL, Lecraw DE, Barton LA, Jann BB (1989), Forced use of hemiplegic upper extremities to reverse the effect of learned nonuse among chronic stroke and head-injured patients. Exp Neurol 104:125-132.

Zaaimi B, Edgley SA, Soteropoulos DS, Baker SN (2012), Changes in descending motor pathway connectivity after corticospinal tract lesion in macaque monkey. Brain 135:2277-2289.

Zehr EP, Sale DG (1994), Ballistic movement: muscle activation and neuromuscular adaptation. Can J Appl Physiol 19:363-378.