31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Predication of Reflex Recovery After Stroke Using Quantitative Assessments of Motor Impairment at 1 Month

M.M. Mirbagheri[1,2] and W.Z. Rymer[1,2]

[1]Department of Physical Medicine and Rehabilitation, Northwestern University Medical School;
[2]Sensory Motor Performance Program, Rehabilitation Institute of Chicago

Abstract— **The objective of this study was to characterize the time-course of changes reflex stiffness after stroke, and to use the Fugl-Meyer Assessment (FMA) at 1 month to predict the ensuing recovery patterns over 1 year. We quantified the modulation of reflex stiffness as a function of elbow joint angles at 1, 2, 3, 6, and 12 months after stroke, using a parallel cascade system identification technique. We then used the "growth mixture" and logistic regression models to characterize recovery patterns over 1 year and to predict these patterns, based on the FMA score at 1 month. We observed two major distinct recovery classes for the relationship between reflex stiffness and elbow angle. The FMA at 1 month was a significant predictor of reflex stiffness as a function of elbow angle at different time points in the first year. The logistical regression class membership may enable us to accurately predict reflex behavior during the first year, information of great potential value for planning targeted therapeutic interventions. Finally, the findings suggest that abnormal reflex function could contribute to functional motor impairment.**

Keywords—**stroke recovery, stiffness, reflex, prediction, natural history**

I. INTRODUCTION

Both the impairment and functional limitation that follows stroke are caused by the direct effects of altered cortical commands on visuomotor control [1-3], but there are also changes in neuromuscular properties secondary to stroke [4, 5]. A clear understanding of contributions of these different impairment mechanisms to clinical function is a prerequisite for the rational development of effective therapies [6].

Furthermore, if these "secondary" changes to muscle mechanical properties can be minimized, an optimum recovery can theoretically be achieved. However, to achieve this outcome, there will need to be properly timed interventions to preempt muscle atrophy and damage. Such treatments, ideally, would require precise knowledge of the natural history and development of neuromuscular abnormalities, i.e. a quantitative time-course analysis, which has yet to be provided. The lack of such quantitative data is due primarily to the general lack of accurate and sensitive tools for separating forces generated by reflex mechanisms from those generated by mechanical properties of musculo-tendon mechanisms [7, 8].

To address these deficiencies, we have recently developed and utilized a parallel cascade identification technique [7, 9], to characterize mechanical abnormalities associated with the spastic joint [4, 5].

In this study, we used this technique to quantify the changes in reflex mechanical properties associated with spasticity in the upper extremity of hemiparetic stroke survivors at different time intervals over a period of 1 year following a stroke. We also used the growth mixture models [10, 11] to characterize the reflex recovery patterns. In addition, using the logistic regression model [10, 11], we explored the effects of Fugl-Meyer Assessment[6] (FMA) at 1 month after stroke on class membership.

II. EXPERIMENTAL PROTOCOL

Twenty-one hemiparetic stroke subjects with different degrees of spasticity were recruited within 4-weeks following stroke. the subjects had approximately even side distribution (11 left hemisphere/ 10 right hemisphere) and different type of stroke (14 hemorrhage/ 7ischemia).

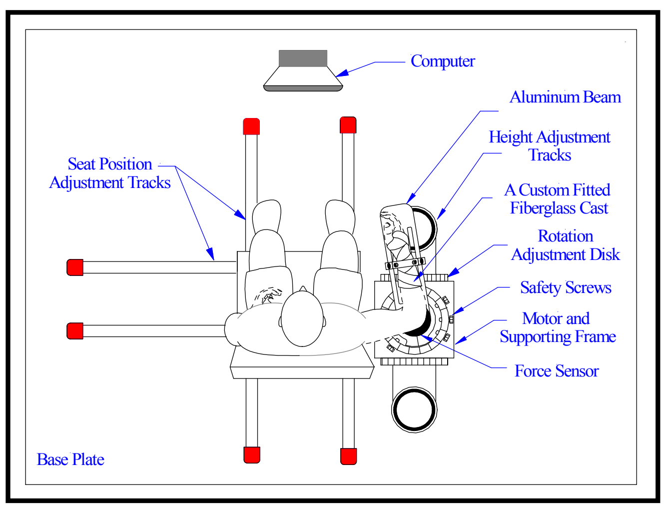


Figure 1: Experimental setup

Subjects were seated on an adjustable chair with their forearm attached to the beam of a stiff, PID controlled motor by a custom fitted fiberglass cast. The seat was adjusted to provide shoulder adduction of 80^o and align the elbow axis of the rotation with axis of the torque sensor and the motor shaft (Figure 1).

Joint position, velocity and torque were recorded by a potentiometer, tachometer & torque transducer, respectively. Electromyograms (EMGs) from biceps, brachoradialis, and triceps were recorded using bipolar surface electrodes.

A series of pseudorandom binary sequences with the amplitude of 0.03 rad and a switching-rate of 150ms were used to perturb the elbow at different positions from 45^o flexion to 75^o extension, at 15^o intervals. A 90^o angle of the elbow joint was considered to be the neutral position (NP) and defined as zero. The subjects were examined at five intervals following stroke, i.e. at 1, 2, 3 6 and 12 months after stroke.

These experiments were conducted on the paretic side, while subjects were relaxed. Flexion is considered negative by convention.

III. Analysis Methods

A. Identification of Reflex Stiffness

Intrinsic and reflex contributions to the elbow stiffness dynamics were separated using the parallel-cascade identification technique [7, 9].

Reflex stiffness dynamics were modeled as a differentiator, in series with a delay, a static nonlinear element (which is half-wave rectifier) and then a dynamic linear element. Reflex stiffness dynamics were estimated by determining the impulse response function, between velocity as the input and the reflex-torque as the output, using Hammerstein identification methods [9].

Non-linear least squares methods were used to fit parametric models to the reflex IRFs. The linear, dynamics of the reflex stiffness were well described by a third order system.

B. Statistical Analysis

We used the growth mixture model [10-12] to extract the recovery patterns (class) for reflex stiffness parameter over one year. This model assumes that the population can be divided into several latent classes (subpopulations) and that there is a unique random effects model characterizing the associations between the longitudinal responses and a set of predictors in each subpopulation. Furthermore, the growth mixture modeling allows the membership of the latent classes to be associated with a group of baseline factors, via a multinomial logistic regression model.

In the fitted growth mixture model, the multinomial (polytomous) logistic regression [10, 11] was used to characterize the association between the membership and FMA. Results with *p*-values less than 0.05 were considered significant.

IV. Results

A. Time-course of Changes in Reflex Stiffness

We studied the time-course of changes in reflex stiffness gain (*G*) of the paretic elbow over a range of elbow angles, at five different time points over the year after stroke. Our results showed that *G* was strongly position dependent ($p<0.01$) (Figure 2); *G* increased progressively when the elbow was moved from full flexion to full extension. However, the slope of changes in *G* with increasing elbow angle varied among subjects, and was different at the different time points.

G was also strongly time-dependent ($p<0.01$). Our results showed two distinct time-dependent patterns. In 14 subjects, *G* increased progressively with time from 1 month to 12 months (Fig 2A), whereas in 7 subjects it decreased with time (Fig. 2B).

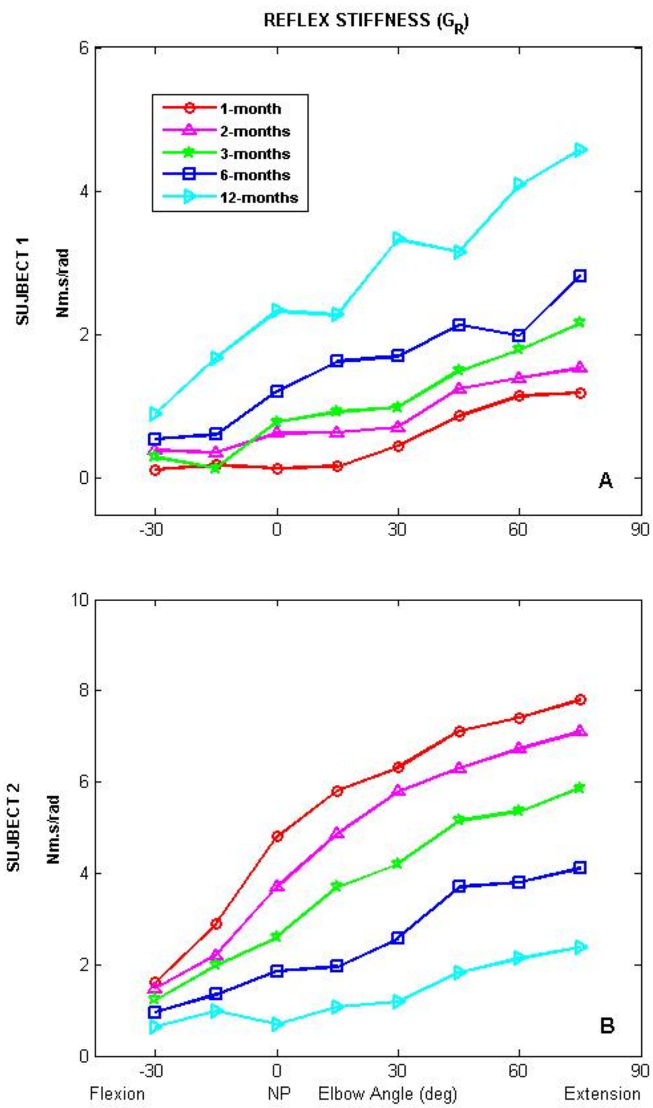
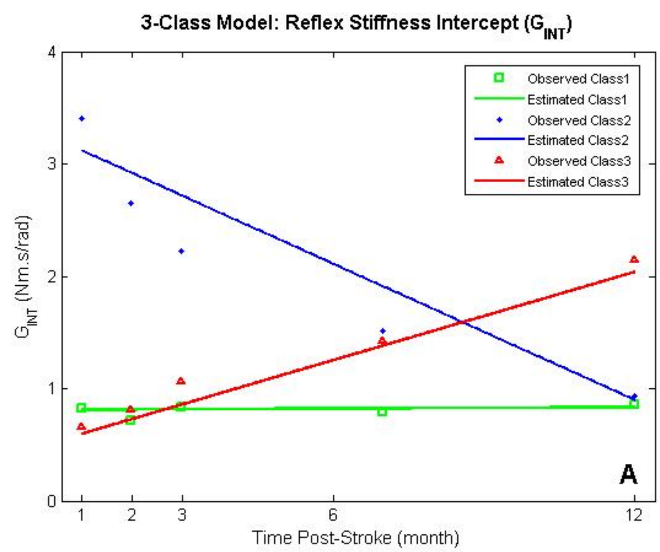


Figure 2: Time course of changes in reflex stiffness (G_R) vs. elbow angle over one year after stroke for two different stroke survivors with different neuromuscular recovery pattern. NP: Neutral Position (90^o).

B. Recovery of Reflex Stiffness

To characterize the modulation of G with elbow angle over 1 year after stroke, we fit a regression line to the changes of G vs. the elbow postion at each time point for each subject. We then used the "growth mixture" model to characterize recovery of these measures over 1 year; i.e. Reflex Intercept (G_{INT}), and Reflex Slope (G_{SLP}).

We identified three classes of recovery patterns for G_{INT} and G_{SLP} . These classes are defined using the growth mixture model of the relation between elapsed time and these reflex parameters. Classification of individuals based on their most likely class membership resulted in class sample size of 33% for class 1, 48% for class 2 and 19% for class 3, for both G_{INT} and G_{SLP} .



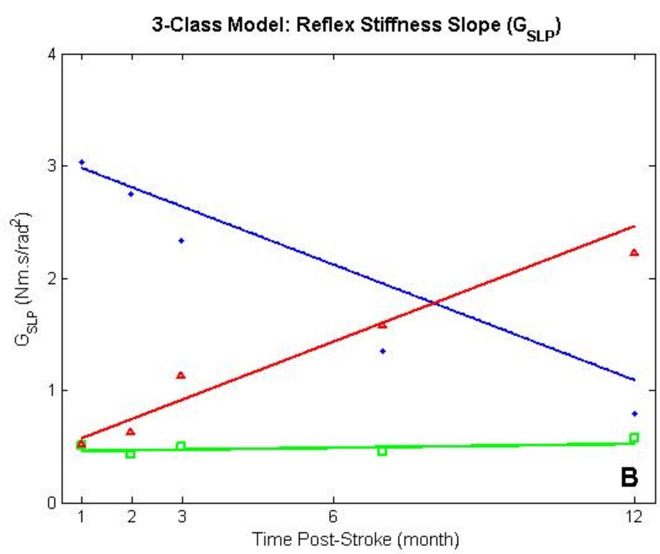


Figure 3*:* Recovery patterns of reflex intercept (G_{INT}), and reflex slope (G_{SLP}). **A** G_{INT} ; **B** G_{SLP} . Class 1 in green, Class 2 in blue and Class 3 in red.

Fig. 3A shows the observed and estimated mean G_{INT} for all classes. For class 1, the growth mixture model provides an intercept of 0.812 Nm.s/rad (p<0.01), indicating that a significant level of G_{INT} was observed at 1 month post stroke. However, the slope of this (G_{INT} -Time) relation was 0.002 Nm.s/rad.month (p, NS) which is non-significant at 0.05 level. For class 2, the intercept was 3.12 Nm.s/rad (p<0.01), indicating that a very high level of G_{INT} was observed at 1 month post stroke. However, the slope was -0.202 Nm.s/rad.month (p<0.01), indicating that a significant decrease in G_{INT} occurred in 5 measurements taken over 1 year post stroke. For class 3, our estimate for the intercept and slope were 0.6 Nm.s/rad (p<0.01) and 0.13 Nm.s/rad.month (p<0.01), respectively, indicating that a significant increase in G_{INT} at 1 month, which followed by significant growth in G_{INT} over 1 year post stroke. Similar classes were observed for G_{SLP} (Fig. 3B).

C. Relation between Reflex Stiffness and Functional Assessment of Motor Impairment (FMA)

The logistic regression was used to explore the effects of FMA score at 1 month post stroke on class membership using class 1 as the reference group. The estimated coefficient for the FMA score was -4.42 (p<0.01) and 0.02 (p, NS) for class 2 and 3, respectively, indicating that the logit and thus probability for class 2 membership decreases as FMA score increases.

The logistic analysis showed that FMA at 1 month is a significant predictor for G_{SLP} class membership. Thus, subjects with an FMA score of >18 at 1 month after stroke were more likely belong to class 1. Subjects with FMA score of ≤4 were more likely to belong to class 2, and other subjects with FMA score between 5 and 18 were likely belong to class 3.

Similarly, based on our analysis, FMA measure at 1 month was a significant predictor for G_{INT} class membership.

V. Discussion and Conclusions

Our results demonstrate that both G_{INT} and G_{SLP} changed significantly over time, indicating that stroke affects both reflex stiffness magnitude (offset) and its modulation with the joint angle. This addresses controversy in literature regarding the nature of changes in reflex properties (threshold [13-16] or gain [4, 5, 8, 17-19]) post-stroke, revealing changes in both with time.

Our results reveal that FMA measured at 1 month is a significant predictor for the reflex recovery patterns. In fact, we find an inverse relationship between the FMA at 1 month and reflex patterns. From a practical standpoint, these findings for subjects who display high initial values of G_{INT} , and G_{SLP} , this forewarns the treating clinician that high initial levels of the FMA may predict declining levels of hyper-reflexia with time, and that pharmacologic treatments may not be warranted long-term. Conversely, subjects with midrange FMA at the initial evaluation will often develop hyper-reflexia, and warrant careful tracking of their clinical status.

ACKNOWLEDGEMENT

Supported by grants from American Heart Association (AHA), National Institute of Health (NIH/NINDS), and National Science Foundation (NSF) awards to MMM.

REFERENCES

[1] R. T. Katz and W. Z. Rymer, "Spastic hypertonia: Mechanisms and measurement," *Arch Phys Med Rehabil,* vol. 70, pp. 144-155, 1989.

[2] A. D. Pandyan, M. Gregoric, M. P. Barnes, D. E. Wood, F. M. Van Wijck, J. H. Burridge, and e. al., "Spasticity: clinical perceptions, neurological realities and meaningful measurment," *Disabil Rehabil,* vol. 27, pp. 2-6, 2005.

[3] R. R. Young, "Spasticity: a review," *Neurology,* vol. 44, pp. S12-20, 1994.

[4] M. M. Mirbagheri, L. Alibiglou, M. Thajchayapong, and W. Z. Rymer, "Muscle and reflex changes with varying joint angle in hemiparetic stroke," *J Neuroeng Rehabil,* vol. 5, pp. 1-16, 2008.

[5] M. M. Mirbagheri, K. Settle, R. Harvey, and W. Z. Rymer, "Neuromuscular abnormalities associated with spasticity of upper extremity muscle in hemiparetic stroke," *J Neurophysiol,* vol. 98, pp. 629-637, 2007.

[6] M. M. Mirbagheri, M. Ladouceur, H. Barbearu, and K. R. E., "The effects of long-term FES-assisted walking on intrinsic and reflex dynamic stiffness in spastic SCI subjects," *IEEE Trans Neural System Rehabil Eng,* vol. 10, pp. 280-289, 2002.

[7] M. M. Mirbagheri, H. Barbeau, and R. E. Kearney, "Intrinsic and reflex contributions to human ankle stiffness: Variation with activation level and position," *Exp Brain Res,* vol. 135, pp. 423-436, 2000.

[8] M. M. Mirbagheri, M. Ladouceur, H. Barbeau, and R. E. Kearney, "Intrinsic and reflex stiffness in normal and spastic spinal cord injured subjects," *Exp Brain Res,* vol. 141, pp. 446-459, 2001.

[9] R. E. Kearney, R. B. Stein, and L. Parameswaran, "Identification of intrinsic and reflex contributions to human ankle stiffness dynamics.," *IEEE Trans Biomed Eng,* vol. 44, pp. 493-504, 1997.

[10] F. Li, T. E. Duncan, and H. Hops, "Piecewise growth mixture modeling of adolescent alcohol use data," *struct equation model,* vol. 8, pp. 175-204, 2001.

[11] C. Proust-Lima, L. Leternneur, and H. Jacqmin-Gadda, "A nonlinear latent class model for joint analysis of multivariate longitudinal data and a binary outcome," *Stat Med,* vol. 26, pp. 2229-2245, 2006.

[12] B. Muthen, "Latent variable analysis: Growth mixture modeling and related techniques for longitudinal data," in *Hand book of quantitative methodology for the social sciences*, D. Kaplan, Ed. Newbury Park: Sage Publications, 2004, pp. 345-368.

[13] W. A. Lee, A. Boughton, and W. Z. Rymer, "Absence of stretch reflex gain enhancement in voluntarily activated spastic muscle," *Exp Neurol,* vol. 98, pp. 317-335, 1987.

[14] M. F. Levin, "On the nature and measurement of spasticity," *Clin Neurophysiol,* vol. 116, pp. 1754-55, 2005.

[15] R. K. Powers, D. L. Campbell, and W. Z. Rymer, "Stretch reflex dynamics in spastic elbow flexor muscles," *Ann Neurol,* vol. 25, pp. 32-42, 1989.

[16] R. K. Powers, J. Marder-Meyer, and W. Z. Rymer, "Quantitative relations between hypertonia and stretch reflex threshold in spastic hemiparesis," *Ann Neurol,* vol. 23, pp. 115-124, 1988.

[17] V. Dietz, M. Trippel, and W. Berger, "Reflex activity and muscle tone during elbow movements in patients with spastic paresis," *Ann Neurol,* vol. 30, pp. 767-779, 1991.

[18] G. L. Gottlieb, G. C. Agarwal, and R. Penn, "Sinusoidal oscillation of the ankle as a means of evaluating the spastic patient," *J Neurol Neurosurg Psychiatry,* vol. 41, pp. 32-39, 1978.

[19] A. F. Thilmann and S. J. Fellows, "The time-course of bilateral changes in the reflex excitability of relaxed triceps surae muscle in human hemiparetic spasticity," *J Neuorl,* vol. 238, pp. 293-298, 1991.