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ABSTRACT

Learning to control forces is known to reduce the amount of movement variability (e.g. standard deviation; SD) while also altering the temporal structure of movement variability (e.g., approximate entropy; ApEn). Such variability control has not been explored in stroke survivors during reaching movements in dynamic environments. Whether augmented feedback affects such variability control, is also unknown. Chronic stroke survivors, assigned randomly to a control/experimental group, learned reaching movements in a dynamically changing environment while receiving either true feedback of their movement (control) or augmented visual feedback (experimental). Hand movement variability was analyzed using SD and ApEn. A significant change in variability was determined for both SD and ApEn. Post-hoc tests revealed that the significant decrease in SD was not retained after a week. However, the significant increase in ApEn, determined on both days of training, showed significant retention effects. In dynamically changing environments, chronic stroke survivors reduced the amount of movement variability and made their movement patterns less repeatable and possibly more flexible. These changes were not affected by augmented visual feedback. Moreover, the learning patterns characteristically involved the control of the nonlinear dynamics rather than the amount of hand movement variability. The absence of transfer effects demonstrated that variability control of hand movement after a stroke is specific to the task and the environment.

Keywords: augmented feedback, approximate entropy, upper extremity, nonlinear dynamics, force fields, robotics

INTRODUCTION

As people age, there is a loss of sensorimotor ability. It is known that decrement in sensorimotor performance with aging is associated with a significant increase in the amount of variability (Enoka et al., 2003; Sosnoff and Newell, 2006). In diseases like stroke in which the sensorimotor status of the individual is further compromised, such a decrement in performance is even more pronounced. Stroke is a leading cause of disability (CDC, 2009) and may result in severe impairment of the affected upper extremity despite intensive rehabilitation (Nakayama et al., 1994). This limits the ability to regain functional independence in the activities of daily living. Therefore, the requirement of more effective rehabilitation strategies is strongly desired both by the patients and their caregivers.

Robot-aided therapy has been studied in recent times as a promising tool in stroke rehabilitation (Volpe et al., 2005). The advantages of robot-aided therapy include accuracy, repetitiveness and consistency of movement training; the ability to customize according to individual requirements; and a reduction in the time for clinical supervision. Robot-aided therapy can be customized to provide either assistive or resistive forces according to the individual requirement of the subjects. In addition to creating different types of force fields for improving outcome, robot aided therapy can be customized for the upper limb or the lower limb, as well as programmed to overcome different levels of weakness, stiffness or spasticity for practicing movement. It can also be programmed to provide directional force fields depending on the patient's directional limitations.

It is known that with practice elderly subjects can improve sensorimotor performance (Bock and Schneider, 2002; Seidler, 2007), and change both the associated amount (i.e. standard deviation; Christou et al., 2007; Kornatz et al., 2005) and the temporal structure of variability

(i.e. approximate entropy; Sosnoff and Voudrie, 2009). With practice, elderly subjects demonstrate a decrease in the amount of variability irrespective of the task whereas the change in the temporal structure of variability is task-dependent (Sosnoff and Voudrie, 2009). This raises the question – do such characteristic changes also occur in chronic stroke survivors? In particular, what would happen to the amount and the temporal structure of variability as chronic stroke survivors learn to perform reaching movements in a novel dynamically changing environment?

Robot-aided therapy can provide adaptive training to stroke survivors. During adaptive training the subject encounters novel force fields or altered visual feedback and is required to make error corrections during goal directed movements. Recent studies (Mukherjee et al., 2012; Patton et al., 2005) have shown that manipulating the environment to enhance reaching errors in stroke survivors may have potential benefit in stroke rehabilitation. These studies utilized the manipulation of haptic and proprioceptive feedback through the use of velocity dependent (Mukherjee and Liu, 2012; Patton et al., 2005) force fields to show that stroke survivors can learn and improve reaching movements in dynamic environments. However, it is not known how such learning will affect the variability of reaching movements. Augmented feedback, comprising of the utilization of extrinsic information that supplements the subject's internal feedback, has led to promising results in the past in stroke survivors (Frasinetti et al., 2002; Rossetti et al., 1998). However, it is not known whether augmented feedback has an effect on variability during motor learning in stroke survivors.

Motor behavior in humans can be explained in terms of the entropy conservation principle (Hong and Newell, 2008). In this principle, within the task-organism-environment framework, entropy is a conserved quantity. During motor task performance, as the task becomes

difficult to perform (increased task entropy) and/or when the information from the environment (e.g. visual feedback) is reduced (increased environmental entropy), healthy human subjects show reduced entropy (organism entropy). This reduced entropy is indicative of a constricted approach in which the degrees of freedom of the system are reduced. However, with learning and practice, as the likelihood of meeting the demands of the task are increased due to an improved capacity to utilize available information, the organism entropy increases. Our objective was to determine how the presence of a dynamic task and environmental information could affect the approximate entropy of reaching movements in chronic stroke survivors. This is not only innovative but also clinically important because understanding the interactions between the task, the environment and the chronic stroke survivor is critical from both a mechanistic as well as a rehabilitation standpoint.

In this study, we recruited chronic stroke survivors to learn reaching movements with a robotic manipulandum in a velocity-dependent force field. Our first goal was to determine if the training of reaching movements in the novel dynamically changing environment in chronic stroke survivors affected the amount and the temporal structure of hand movement variability. Our second goal was to test if augmented visual feedback affected the amount and the temporal structure of hand movement variability in chronic stroke survivors.

METHODOLOGY

Study subjects: Twelve chronic stroke survivors were selected from the local community who attended the stroke clinic of our Medical Center. Before participating in the experiment, all subjects signed an informed consent approved by the Institutional Review Board of our Medical Center. The mean age of the subjects was 62.92±8.07 years and the mean duration of stroke was 18.58±12.47 months (table 2). The Fugl-Meyer Assessment[23], which is a stroke-specific and performance-based clinical evaluation and is used to assess motor functioning, sensation and joint proprioception, was performed prior to the experiment (table 2). All subjects were right-hand dominant and four of the subjects were affected on the right side. *Inclusion criteria:* The inclusion criteria included first time diagnosed carotid distribution ischemic, hemorrhagic, or brainstem stroke, at least three months after the incidence, age between 50 and 75 years, a Folstein Mini-Mental score greater than 25 (Folstein et al., 1975) and free of major post-stroke complications (e.g. recurrent stroke, upper limb dislocation or fracture, myocardial infarction). Subjects were screened to select those who had a unilateral lesion and who had at least 20/40 corrected vision. *Exclusion criteria:* These included subjects who had subarachnoid hemorrhage, asomatognosia/unilateral neglect, obtunded or comatose, history of fractures or injuries in the upper limb of less than 6 months duration, undergoing botox treatment, a Florida apraxia score less than 27, more than one stroke episode, pain at the time of screening, poorly controlled diabetes, progressive neurological diseases (e.g. Parkinson's disease), peripheral nerve pathology and lived more than 60 miles from our Medical Center.

Study protocol: The subjects were randomly placed in either an experimental or a control group so that each group had six subjects. Subjects in the experimental group received augmented visual feedback during performance of the motor task but not the subjects in the

control group. The subjects were blinded to which group they were randomly assigned. Each subject made two visits to the laboratory on consecutive days followed by a follow up visit within a week of the second visit. Subjects performed target-reaching tasks with the affected hand on all three visiting days. During the experiment, the subject was seated on a chair (figure 1) while holding the InMotion2 robotic manipulandum (Interactive Motion Technology, Inc., Cambridge, MA) with the affected hand. The subject was strapped onto the chair to prevent motion of the trunk while performing the reaching movements. During the experiment, the room was darkened to prevent the subject from viewing the arm position. The subject rested the forearm on a plastic piece that was connected to the manipulandum. This allowed motion only at the shoulder and elbow on a 2-D plane. A computer monitor was placed in front of the subject at a distance of approximately one meter. The subject saw the start position at the center of the screen, 8 target positions (figure 1B) located peripherally and the instantaneous hand position (manipulandum position). Each of these positions was represented by 12mm diameter circles displayed on the computer monitor. On day one, the subject performed the following trials (table 1): *familiarization, practice, baseline and experimental trials*. During the *familiarization trials*, the subject was familiarized with the surroundings and the feel of the robotic manipulandum. *Practice trials* were performed so that the subject could make the reaching movement in the desired time of one second. During the *baseline trials* the subject performed reaching movements without any visual/force manipulation of the task. On the second day, the subject performed only the *experimental trials*. Within five days of the second visit, the subject performed *normal reaching trials*, which were similar to the *baseline trials*, as well as *dynamic retention trials*, which tested the retention of motor learning of the reaching movements in the dynamic environment.

INSERT FIGURE 1 HERE

The subject made center out reaching movements to 8 radial targets 15 cm from the start position (figure 1b). Targets were presented one at a time, in a counterclockwise sequence in increments of 45° starting from 0° (target 1) to form a cycle of target reaching movements. In this study, a cycle is defined as a set of 8 target reaching movements or trials, once toward each target in a counterclockwise order of target appearance. *Baseline trials*: The subject performed 5 cycles of reaching movements for a total of 40 baseline trials. Movements were made without any visual or dynamic transformation of the motor task. *Experimental trials*: After the manipulandum was brought to the start position by the robot, an auditory cue "ready" was given to the subject. After 3 seconds the target changed color from red to blue and that was the cue to start the movement. After a period of 1 second the target reverted back to the original color (red). The instruction to the subject was to make a single quick movement to the target. The subject was instructed to finish the movement before the target changed color back to red. Practice trials were performed to achieve the required movement in a time of 1 second. Feedback was provided to the subject to indicate whether the movement was successful, 'too fast' (<0.75s) or 'too slow' (>1s). After each trial, the robot automatically returned the manipulandum to the start position during which the cursor feedback was absent. This was meant to prevent reinforcing the subject's internal feedback. There were 30 cycles for a total of 240 experimental trials. *Normal reaching trials*: On the third day, the subject performed 5 cycles of reaching movements for a total of 40 trials similar to the *baseline trials*, without any visual or dynamic transformation of the motor task. *Dynamic Retention trials*: Also on the third day, the subject performed 5 cycles of reaching movements for a total of 40 trials with the force fields. *The force field:* Subjects in both experimental and control groups performed reaching tasks in velocity dependent viscous

curl field (Patton et al., 2005). The force field was always orthogonal to the hand velocity and formed a counterclockwise circulating pattern. Forces applied at the hand during the reaching movement are given by the following equation:

$$\begin{bmatrix} Fx \\ Fy \end{bmatrix} = \begin{bmatrix} 0 & -\lambda \\ \lambda & 0 \end{bmatrix} \begin{bmatrix} \dot{x} \\ \dot{y} \end{bmatrix}$$

where x, y are the two components of the hand velocity along the medial/lateral (x) and proximal/distal (y) directions, Fx and Fy are the x and y components of the force applied by the robot, and λ is a constant whose value is 20 Ns/m (Mukherjee and Liu, 2012).

The augmented visual sensory feedback of movement error: Only subjects in the experimental group received augmented visual feedback during performance of the reaching task in the velocity dependent force field. The visual feedback augmentation was designed to cause an enhancement of the visual feedback of movement errors. As the subject made the reaching movement in a given trial, the 2-dimensional instantaneous hand position (x and y-axes) was sensed by position sensors in the robot handle. The instantaneous perpendicular deviation from the straight-line path to the target was doubled to create the augmented feedback. In the augmented feedback group, the hand position value in the direction of the target remained the same. The augmented instantaneous hand position was shown to the subject on the visual display monitor.

Data recording: The manipulandum position in a two-dimensional horizontal plane was recorded at 200 Hz. Data recording started when the visual cue for movement was provided to the subject. *Data processing and analysis:* Raw data was processed using MATLAB (MathWorks, Natick, MA) code developed in our laboratory and statistically analyzed using the SPSS statistical software (SPSS Inc.). The amount of movement variability was analyzed using

the standard deviation (SD) of deviation, perpendicular to the direction of movement in each trial (figure 1C). In addition to analyzing the amount of variability, the temporal structure of variability was also explored using nonlinear analysis (Stergiou et al., 2004). The temporal structure of variability was investigated using the nonlinear measure of Approximate Entropy (ApEn).

ApEn is a measure of quantifying the predictability or regularity of a time series (Pincus and Goldberger, 1994). The term entropy is defined as the loss of information in a time series or a signal. Over several years, the use of entropy methods to characterize periodicity or regularity in biological data has become popular. In brief, given a time series $f(n) = f(1), f(2), \ldots f(N)$, where N is the total number of data points equally spaced in time, a sequence of m-length vectors (a data segment of length m) is formed. Each m-length vector within the time series is then compared. If the tail and head of the vector fall within a set tolerance, r, or noise filter, the vectors are considered alike. The next procedure is to divide the sum of the logarithm of the total number of like vectors by $N-m+1$. This process is repeated by increasing m by $1(m+1)$. Subtracting the conditional probabilities of $m+1$ from m then gives us the ApEn value. Practically, ApEn calculates the logarithmic probability that a series of data points, a certain distance apart, exhibit similar relative characteristics on the next incremental comparison within the state space (Pincus and Goldberger, 1994). A time series with similar distances between data points results in lower ApEn values, while large differences in distances between data points results in higher ApEn values. Thus, completely random data will exhibit a value close to two, while completely periodic data (i.e. sine wave) will exhibit a value of zero. Behaviorally, values close to zero represent a behavior that is inflexible and with reduced capacity to adapt characterized by extremely regular movement patterns over time. On the other hand, larger

values represent a behavior that is less repeatable and possibly more flexible. The ApEn algorithm was implemented in MatLab where all time series were analyzed (with m, the number of observation windows to be compared = 2 and r, the tolerance factor = 0.2 and N, the number of data points = 200). The perpendicular deviation time series in each trial was used to calculate the ApEn for that trial. Although there are several analytical tools to evaluate the temporal structure of variability like the Lyapunov Exponent (LyE) and Detrended Fluctuation Analysis (DFA), these tools generally require large amounts of data to provide stable results. For example, the number of data points required for LyE calculations vary between 1000 and 10000 and sometimes even higher numbers have been used (Timmer et al., 2000). The number of data points required for ApEn calculation, on the other hand, is much smaller varying between 50 and 5000 (Pincus, 2000). This is advantageous when data sets are small like those in the present study.

For statistical analysis, the independent variables were the subject group [2 levels – with (experimental group) or without augmented feedback (control group)] and trial type [8 levels – baseline (no forces), early and late trials on day one (with forces), early and late trials on day two (with forces), washout effect on day two (no forces), transfer effect to normal reaching on day three (no forces), retention effect of dynamic control on day three (with forces)]. In each case, the mean of 16 experimental trials was calculated for further analysis. The two dependent variables were the normalized SD and ApEn of deviation perpendicular to direction of movement in each trial. Each subject's data was normalized from the baseline performance of that subject. A 2X8 mixed factor ANOVA (group – between subject factor; trial type – within subject factor) was used to identify overall significant differences followed by post-hoc least squared difference tests for determining specific differences. The alpha level was set at 0.05.

Due to the small size of our time series we also explored whether the source of variations present in the time series data used for analysis, was deterministic in nature. Surrogation was performed for this purpose (Theiler et al., 1992; Stergiou et al., 2004). In this technique, surrogate data was generated which preserved the structure of the original data set having the same mean, variance and power spectra. Theiler's algorithm was used to generate surrogate data series. Algorithm 0 generated a randomly shuffled data series, Algorithm 1 generated a Fourier transform surrogate and Algorithm 2 generated an amplitude adjusted Fourier transform surrogate. Subsequently ApEn of the original data series was compared with each of the surrogate data series. Significant differences would indicate that the original time series was not randomly derived and therefore was deterministic in nature despite their relatively small length.

RESULTS

There was no significant difference (p=0.868) between the mean age of the subjects in the experimental group (62.5±7.79 years) and the control group (63.33±9.07 years). In addition, there was no significant difference (p=0.529) between the mean duration of stroke in the experimental group (16.17±9.70 months) and in the control group (21.00±15.32 months). The mean Fugl-Mayer score for the upper limb was 60.50±18.37 (sensory and motor) in the experimental group and 61.83±16.47 in the control group. These scores were not significantly different (p=0.885). In order to determine if movement time was affected by subject groups or trial type, a 2X8 mixed factor ANOVA revealed that there was no main affect of trial type (p=0.075) or group (p=0.603) and there was no interaction affect (p=0.351). The overall movement time at baseline was 0.92±0.32s, at early training on day one, 0.98±0.02s, at late training on day two, 0.93±0.04s and at retention was 0.90±0.08s.

The raw data representing perpendicular distance (in meters) from the straight line path to the target for a set of 240 trials in one stroke subject (figure 2A) reveal a reducing trend in amplitude over time. The amount of variability in the system shown by the SD of the data series in figure 2A, also shows a reducing trend over time (figure 2B). However, the temporal structure of movement variability, shown by calculating the ApEn of the data series in figure 2A, shows an increasing trend over time (figure 2C), demonstrating the two different aspects of variability and how important is to study both since they behave in strikingly different manners.

INSERT FIGURE 2 HERE

A significant main effect of trial type was shown ($F_{7,35}$=3.911; p=0.001) for normalized SD; however, there was no group or interaction effect. A significant main effect of trial type was also shown ($F_{7,35}$=4.889; p=0.000) for ApEn; however, there was no group or interaction effect.

Post-hoc tests (Figure 4) revealed that there was a borderline increase in the normalized ApEn from baseline to the late trials of day one (p=0.052) and the early trials of day two (p=0.052), from the early to late trials of day one (p=0.015), from early trials of day one to that of day two (p=0.001) and from early trials of day one to late trials of day two (p=0.024). An increase in ApEn means that movement patterns became less repeatable or more predictable with time. There was a significant washout, i.e., a decrease in normalized ApEn from late trials of day two to washout trials (p=0.008) and retention, i.e., an increase in normalized ApEn from the early trials of day one to the retention trials (p=0.039). There was no significant transfer effect i.e., an increase in normalized ApEn from baseline to the normal reaching trials.

Tests of normality were done for the processed SD and ApEn values. Normality was rejected for SD but not ApEn. Therefore nonparametric statistical analysis was done for the SD values. Friedman's test was performed to determine a significant effect of the trial type. A significant effect of the trial type was determined (χ^2 [7]=31.500, p=0.000). A *post-hoc* analysis with Wilcoxon Signed-Rank Tests was conducted (Figure 3). Post-hoc tests revealed that there was an increase in normalized SD from baseline to the early trials of day one (p=0.003) and day two (p=0.032). There was a decrease in normalized SD from the early to late trials of day one (p=0.012), from the early trials of day one to that of day two (p=0.016), and from the early trials of day one to the late trials of day two (p=0.038). A reduction in normalized SD means that the amount of variability reduced over time. There was a significant washout effect i.e., an increase in normalized SD from late trials of day two to washout trials (p=0.026). There were no significant retention or transfer effects. In fact the retention trials showed a significant increase from the late trials of day two to the retention trials (p=0.006), which meant that the significant reduction in normalized ApEn attained at the end of day two was not retained after one week.

INSERT FIGURES 3 AND 4 HERE

Surrogate data were obtained by Applying Theiler's algorithm to the dependent variable - perpendicular distance (in meters) from the straight line path to the target (figure 5). After obtaining the surrogate data sets for each trial, ApEn values were calculated for the raw and Algorithm 0, Algorithm 1 and Algorithm 2 generated surrogate data. A comparison of the mean ApEn values for the raw and surrogate data of all the subjects revealed that the ApEn values derived from the original data were significantly smaller ($p<0.001$) than the ApEn values calculated for the surrogated data sets (figure 6). This was evident in all comparisons. This result demonstrates that the original data are deterministic in nature and justified the exploration of the temporal structure of variability.

INSERT FIGURES 5 AND 6 HERE

DISCUSSION

Our first goal was to determine if motor training of reaching movements in the novel dynamic environment in chronic stroke survivors affected the amount and structure of hand movement variability. Our second goal was to test if augmented visual feedback affected the amount and the temporal structure of hand movement variability in chronic stroke survivors.

Changes in the amount of hand movement variability: In terms of changes in the amount of variability with motor training, the chronic stroke survivors demonstrated reduction in variability on the first day and were able to retain this reduction on the second day. However, they did not show retention of the reduction in the amount of variability on the third visit or its transfer to a task without the force field. In fact the retention trials were significantly increased in comparison to the reduction in normalized SD achieved after two days of training. These results demonstrate that for this specific task, motor training does not lead to a reduction in the amount of variability. However, this could also mean that the affected arm of the stroke subject made controlling the amount of variability difficult. Chronic stroke survivors demonstrate significantly high amounts of variability during upper limb motor tasks (Scheidt and Stoekmann, 2007; Reinkensmeyer et al., 2003). One of the reasons why the amount of force variability is high is because of enhanced motor unit firing rate variability (Laidlaw et al., 2000; Moritz et al., 2005). Moreover, practice/training of an upper limb task has been shown to reduce the motor unit firing rate variability in older adults (Griffin et al., 2009). However, the specific task of target reaching by overcoming a deviating force field in chronic stroke survivors may depend on a control mechanism that requires more than a mere reduction of the amount of variability. We believe that this information may arise from investigating the temporal structure of motor variability and

the nonlinear dynamics of these movement patterns which has been known to provide important information about the function of the neuromuscular system (Stergiou et al., 2004).

Changes in the temporal structure of hand movement variability: Significant changes in the repeatability of hand movement patterns were demonstrated not only for the individual days but in addition, retention effects were also shown. This shows that the temporal structure (instead of the amount) of hand movement variability is a more sensitive indicator in chronic stroke survivors of motor training of reaching movements in dynamic environments. However, these observations may also be specific to the type of task given to the chronic stroke survivors. Specifically because transfer effects were absent for both variability measures. It has been shown previously that the temporal structure of variability during an upper limb motor task may follow separate tendencies depending upon the task (Sosnoff and Voudrie, 2009). In that study, it was shown that if the task comprised of maintaining a constant force, the temporal structure of variability changed as revealed by an increase in ApEn (the motor output became less repeatable) whereas, if the task was cyclic or rhythmic, it lead to a decrease in ApEn (the motor output became more repeatable). The reasoning behind these observations is that each specific task has its inherent degrees of freedom (Newell and Vaillancourt, 2001) and to perform each task successfully, the motor output needs to be specific for the given task. Tasks that require a constant motor output need lower levels of dynamics than those tasks that are cyclic (Newell, Broderick, Deutsch, and Slifkin, 2003; Sosnoff and Voudrie, 2009). Although our task did not require a constant motor output (e.g., constant force) to perform the task successfully, it was not a cyclic task either. This was because the subject had to reach a different target on each trial. However, before starting the experiment, the subject had been given practice to complete the reaching movement in a constant time (not too fast/slow). This meant that the subject maintained

the same velocity profile on each trial. Since the force field was velocity-dependent, this meant that in each trial, the subject encountered similar force field patterns. This may be the reason why the stroke survivors in our study demonstrated similar temporal structure of movement variability to the static force and not the sinusoidal force experiments of Sosnoff and Voudrie (2009). With aging the patterns of physiological functions become more repeatable (Lipsitz and Goldberger, 1992). However, with practice, motor output patterns can be made less repeatable and this effect depends on the type of task performed (Sosnoff and Voudrie, 2009). Our data demonstrates that even chronic stroke survivors, with practice, can learn to make movement patterns less repeatable and possibly more flexible.

The effect of augmented feedback on the amount and temporal structure of hand movement variability: When extrinsic information is provided to a subject, motor output patterns become less repeatable (Hong and Newell, 2008). Conversely, when less information is available or when the resolution of this external/augmented information is low, movement patterns become more repeatable and regular (Kuznetsov and Riley, 2010). In our study, there was no effect of augmented feedback on either the amount or the temporal structure of hand movement variability. The reason for this could be the nature of the available information. In the three cited studies (Hong and Newell, 2008; Kuznetsov and Riley, 2010), the environmental information was specific to the magnitude of isometric force. As the subject increased or reduced the isometric force, the feedback shifted proportionately. The feedback was specific to the task, which was to maintain a constant force. Our feedback was instead an indirect effect of force perturbation. What the subject visualized was the hand deviation during the reaching task as a result of the force perturbation. Although the visual feedback of hand position was manipulated

between the groups, the magnitude of information was not manipulated. Moreover, our task was dynamic as opposed to those studies, which had static tasks.

Human motor behavior has been shown to conserve entropy within the task-organism-environment framework (Hong and Newell, 2008). In those studies it was shown when healthy human subjects performed isometric contractions matched to a target force with their index finger, the approximate entropy of their force output was related to the entropy of the environmental feedback and the entropy of the task. When the task became difficult to perform as in matching variable forces (increased task entropy) or when the information from the environment (e.g. frequency of visual feedback) was reduced (increased environmental entropy), healthy human subjects showed reduced entropy. This reduced entropy is demonstrative of the subjects employing limited coordination patterns or reduced degrees of freedom for performing the specific task. However, with learning and practice, the same task with the same environmental information can lead to increased entropy. This is because as the likelihood of meeting the demands of the task are increased due to an improved capacity to utilize available information.

During the training paradigm, as the context of the environment changes, e.g., from dynamic to non-dynamic and vice versa, we observe changes in both the amount and structure of variability. Specifically for patient populations, as they try to learn "new" movement patterns, they must move from the present state of abnormal movements to a different state where movement is performed more normally. It has been proposed that in rehabilitation, for new stable movements to emerge from learned abnormal movements, it must pass through a critical threshold where instability is high (Harbourne and Stergiou, 2009). It is at this critical threshold where "new" sensorimotor relationships are being learned for the novel dynamic environment, a

highly unstable region, that variability control may play a crucial role. In addition, it is also proposed that normal human movements require an optimal level of variability (Harbourne and Stergiou, 2009). Patient populations, in order to get rehabilitated, need to strive towards their optimal level of variability.

In summary, we have shown that chronic stroke survivors use similar control strategies as healthy individuals for learning reaching tasks in dynamically changing environments by reducing the amount of movement variability and making the hand movement patterns less repeatable during dynamic tasks. We also demonstrated that the control of hand movement as it is revealed by the variability analysis may not be affected by augmented visual feedback. Moreover, the learning of reaching tasks in dynamically changing environments for chronic stroke survivors may involve to a larger extent the control of the nonlinear dynamics of the movement patterns performed rather than simply the amount of hand movement variability. Finally, variability control of hand movement after a stroke is specific to the task and the environment. A limitation in this study is that healthy control data is absent for comparisons however, current studies are investigating this question. It would be interesting to investigate how the control of nonlinear dynamics of the movement patterns is affected in variable environments; however, this will be a future line of research.

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REFERENCES

1. Bock, O., and Schneider, S. (2002). Sensorimotor adaptation in young and elderly humans. *Neuroscience Biobehavioral Reviews, 26,* 761–767.
2. Centers for Disease Control and Prevention (CDC). Prevalence and most common causes of disability among adults–United States, 2005. *MMWR Morb Mortal Wkly Rep.* 2009;58:421–426.
3. Christou, E. A., Poston, B., Enoka, J. A., and Enoka, R. M. (2007). Different neural adjustments improve endpoint accuracy with practice in young and old adults. *Journal of Neurophysiology, 97,* 3340–3350.
4. Enoka, R. M., Christou, E. A., Hunter, S. K., Kornatz, K. W., Semmler, J. G., Taylor, A. M., et al. (2003). Mechanisms that contribute to differences in motor performance between young and old adults. *Journal of Electromyography and Kinesiology,1,* 1–12.
5. Folstein MF, Folstein SE, McHugh PR. "mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12:189-198
6. Frassinetti F, Angeli V, Meneghello F, Avanzi S, Ladavas E. Long-lasting amelioration of visuospatial neglect by prism adaptation. *Brain*. 2002;125:608-623
7. Griffin L, Painter PE, Wadhwa A, Spirduso WW. Motor unit firing variability and synchronization during short-term light-load training in older adults. Exp Brain Res. 2009 Aug;197(4):337-45. Epub 2009 Jul 4.
8. Harbourne RT, Stergiou N. Movement variability and the use of nonlinear tools:principles to guide physical therapist practice. *Phys Ther*. 2009;89:267-82.
9. Hong SL, Newell KM. Entropy conservation in the control of human action. Nonlinear Dynamics Psychol Life Sci. 2008 Apr;12(2):163-90.
10. Kornatz, K. W., Christou, E. A., and Enoka, R. M. (2005). Practice reduces motor unit discharge variability in a hand muscle and improves manual dexterity in old adults. *Journal of Applied Physiology, 98,* 2072–2080.
11. Kuznetsov NA, Riley MA. Spatial resolution of visual feedback affects variability and structure of isometric force. *Neurosci Lett.* 2010 Feb 12;470(2):121-5. Epub 2010 Jan 5.
12. Laidlaw, D. H., Bilodeau, M., and Enoka, R. M. (2000). Steadiness is reduced and motor unit discharge is more variable in old adults. *Muscle Nerve, 23,* 600–610.
13. Lipsitz, L. A., and Goldberger, A. L. (1992). Loss of "complexity" and aging: Potential applications of fractals and chaos theory to senescence. *Journal of the American Medical Association, 267,* 1806–1809.
14. Moritz, C. T., Barry, B. K., Pascoe, M. A., and Enoka, R. M. (2005). Discharge rate variability influences the variation in force fluctuations across the working range of a hand muscle. *Journal of Neurophysiology, 93,* 2449–2459.
15. Mukherjee M, Liu W. Muscle Activation Patterns in Healthy Subjects and Stroke Survivors in an Unpredictable Robotic Environment. *International Journal of Mechatronics and Automation* (In press).
16. Nakayama H, Jorgensen HS, Raaschou HO, Olsen TS. Compensation in recovery of upper extremity function after stroke: The copenhagen stroke study. *Arch Phys Med Rehabil*. 1994;75:852-857
17. Newell, K. M., and Vaillancourt, D. E. (2001). Dimensional change in motor learning. *Human Movement Science, 20,* 695–715.

18. Newell, K. M., Broderick, M. P., Deutsch, K. M., and Slifkin, A. B. (2003). Task goals and change in dynamical degrees of freedom with motor learning. *Journal of Experimental Psychology: Human Perception and Performance, 29,* 379–387.
19. Parker VM, Wade DT, Langton Hewer R. Loss of arm function after stroke: Measurement, frequency, and recovery. *Int Rehabil Med*. 1986;8:69-73
20. Patton JL, Stoykov ME, Kovic M, Mussa-Ivaldi FA. Evaluation of robotic training forces that either enhance or reduce error in chronic hemiparetic stroke survivors. *Exp Brain Res*. 2005:1-16
21. Pincus SM, Goldberger AL. Physiological time-series analysis: what does regularity quantify? Am J Physiol. 1994 Apr;266(4 Pt 2):H1643-56.
22. Pincus, S.M. Irregularity and asynchrony in biologic network signals. *Methods in Enzymology, 2000;321:*149-182.
23. Reinkensmeyer DJ, Iobbi MG, Kahn LE, Kamper DG, Takahashi CD. Modeling reaching impairment after stroke using a population vector model of movement control that incorporates neural firing-rate variability. Neural Comput. 2003 Nov;15(11):2619-42.
24. Rossetti Y, Rode G, Pisella L, Farne A, Li L, Boisson D, Perenin MT. Prism adaptation to a rightward optical deviation rehabilitates left hemispatial neglect. *Nature*. 1998;395:166-169
25. Scheidt RA, Stoeckmann T. Reach adaptation and final position control amid environmental uncertainty after stroke. J Neurophysiol. 2007 Apr;97(4):2824-36. Epub 2007 Jan 31.
26. Seidler R. D. (2007). Older adults can learn to learn new motor skills. *Behavioral Brain Research, 183,* 118–122.
27. Sosnoff JJ, Voudrie SJ.J Mot Behav. 2009. Practice and age-related loss of adaptability in sensorimotor performance. Mar;41(2):137-46.
28. Sosnoff, J. J., and Newell, K. M. (2006). The generalization of perceptual- motor intra-individual variability in young and old adults. *Journal of Gerontology B: Psychological Science, 6,* P304–P310.
29. Stergiou, N; Buzzi, UH; Kurz, MJ; Heidel, J. Nonlinear tools in human movement. In: Stergiou N., editor. *Innovative Analysis of Human Movement. Champaign*, Illinois: Human Kinetics; 2004.
30. Theiler J, Eubank S, Longtin A, Galdrikian B, Farmer JD. Testing for nonlinearity in time series: the method of surrogate data. *Physica D: Nonlinear Phenomena*, 1992;Sep:58:77-94.
31. Timmer J, Häussler S, Lauk M, Lücking CH. Pathological tremors: Deterministic chaos or nonlinear stochastic oscillators? *Chaos.* 2000; 10, 278.
32. Volpe BT, Ferraro M, Lynch D, Christos P, Krol J, Trudell C, Krebs HI, Hogan N. Robotics and other devices in the treatment of patients recovering from stroke. *Curr Neurol Neurosci Rep*. 2005;5:465-470.

Table 1. The description of trials performed in the study.

S.No.	TRIAL TYPE	Description	Number of trials
1.	Familiarization (Day 1)	The subjects were familiarized with the feel of moving the manipulandum within the workspace and also interacting with the visual display.	******
2.	Practice Trials (Day 1)	Training was provided to perform the reaching task within a specific time period.	80 trials
3.	Baseline Trials (Day 1)	Subjects performed target-reaching movements in an environment without any force fields.	40 trials
4.	Experimental Trials (Day 1)	Subjects performed target-reaching movements in an environment having a velocity-dependent force field. Those in the experimental group received augmented visual feedback.	240 trials
5.	Experimental Trials (Day 2)	**********same as above**********	240 trials
6.	Washout Trials (Day 2)	The trials were similar to baseline trials (no force-fields) and were done to test de-adaptive/context switching ability. They were also done for the testing of reaching ability (1 week later) without any influence of the force fields.	40 trials
7.	Normal Reaching Trials (Day 3) *Transfer Effects*	The transfer effect tested any improvement in reaching ability in a non-dynamic environment (without any force fields) as a result of training in a dynamic environment. These trials were similar to the baseline trials and were performed a week after Day 2.	40 trials
8.	Dynamic Retention (Day 3)	This was any improvement in reaching ability in the dynamic environment determined a week after Day 2.	40 trials

Table 2. Demographics of the chronic stroke survivors in the study. The study groups are Control and Augmented Feedback (Aug-Fdbk). The last column indicates the Fugl-Mayer score for the upper limb. The maximum possible sensory + motor score for the upper limb is 78.

Subject No.	Age (yrs)	Sex	Stroke duration (months)	Type of stroke	Side Affected	Study Group	FM Score
s1001	51	M	43	Ischaemic	L	Control	31
s1002	53	M	28	Haemorrhagic	L	Aug-Fdbk	43
s1003	53	M	9	Ischaemic	R	Aug-Fdbk	69
s1004	68	M	21	Ischaemic	L	Control	59
s1005	65	F	13	Ischaemic	L	Aug-Fdbk	77
s1006	60	M	8	Ischaemic	L	Control	62
s1007	71	M	35	Ischaemic	L	Control	75
s1008	74	M	15	Ischaemic	R	Control	69
s1009	71	M	29	Ischaemic	R	Aug-Fdbk	32
s1010	64	M	10	Ischaemic	R	Aug-Fdbk	67
s1011	69	F	8	Ischaemic	L	Aug-Fdbk	74
s1012	56	M	4	Ischaemic	R	Control	75

Figure Captions

Figure 1. A) A schematic view from the top of the subject showing the orientation of the arm and forearm segments, the trunk strapped on to the chair, and the hand holding the manipulandum which is connected to the robot. B) A grid of 8 targets for center-out reaching movements in counterclockwise order from 1 to 8 (increments of 45˚) holding the 2-joint robotic manipulandum. C) Top view of a subject holding the manipulandum. D) Side view of a subject holding the manipulandum and viewing the display monitor. E) The perpendicular deviation from the straight line path to the actual trajectory of the trial is used to calculate the dependent variables – standard deviation and approximate entropy. F) Trajectory Figures of one stroke subject in the *Baseline, Early Training* and *Late Training* Conditions.

Figure 2. A single stroke subjects data. A) *Raw Data:* Perpendicular distance (in meters) from the straight line path to the target for a set of 240 trials. Each trial consisted of 200 data points. 48000 data points are shown for a single subject on one day of the experiment. B) *Standard Deviation:* Each circle represents the standard deviation of the perpendicular distance data series for each trial. C) *Approximate Entropy:* Each circle represents the Approximate Entropy of the perpendicular distance data series for each trial.

Figure 3. Bar chart showing the mean of the normalized standard deviation values of all the subjects (both groups combined) for all the experimental conditions: early and late trials on day one and two, washout effect on day two, transfer effect to normal reaching and dynamic retention on day three. Error bars are standard deviation. *In comparison to the baseline, #In comparison to the early trials of day one, ϕIn comparison to the late trials of day two, single symbols indicate $p<0.05$, double symbols indicate $p<0.005$.

Figure 4. Bar chart showing the mean of the normalized Approximate Entropy values of all the subjects (both groups combined) for all the experimental conditions: early and late trials on day one and two, washout effect on day two, transfer effect to normal reaching and dynamic retention on day three. Error bars are standard deviation. *In comparison to the baseline, #In comparison to the early trials of day one, ϕIn comparison to the late trials of day two, single symbols indicate $p<0.05$, double symbols indicate $p<0.005$, triple symbols indicate $p<0.001$.

Figure 5. A single stroke subjects data. A) *Raw Data:* Perpendicular distance (in meters) from the straight-line path to the target for a set of 240 trials. Each trial consisted of 200 data points. 48000 data points are shown for a single subject on one day of the experiment. B) *Theiler's Surrogation:* The A0 surrogate data series obtained from the raw data shown in A. C) *Theiler's Surrogation:* The A1 surrogate data series obtained from the raw data shown in A. D) *Theiler's Surrogation:* The A2 surrogate data series obtained from the raw data shown in A.

Figure 6. Mean Approximate Entropy values for the raw and surrogate data of all the subjects. The perpendicular distance (in meters) of hand location from the straight line path to the target for a set of 240 trials on day one was used for analysis. The surrogate data were obtained using *Theiler's algorithm.* Approximate Entropy values were calculated for the raw and A0, A1 and A2 surrogate data. The figure shows significant differences at $p<0.001$ for comparisons between raw ApEn and ApEn for each of the surrogate data.

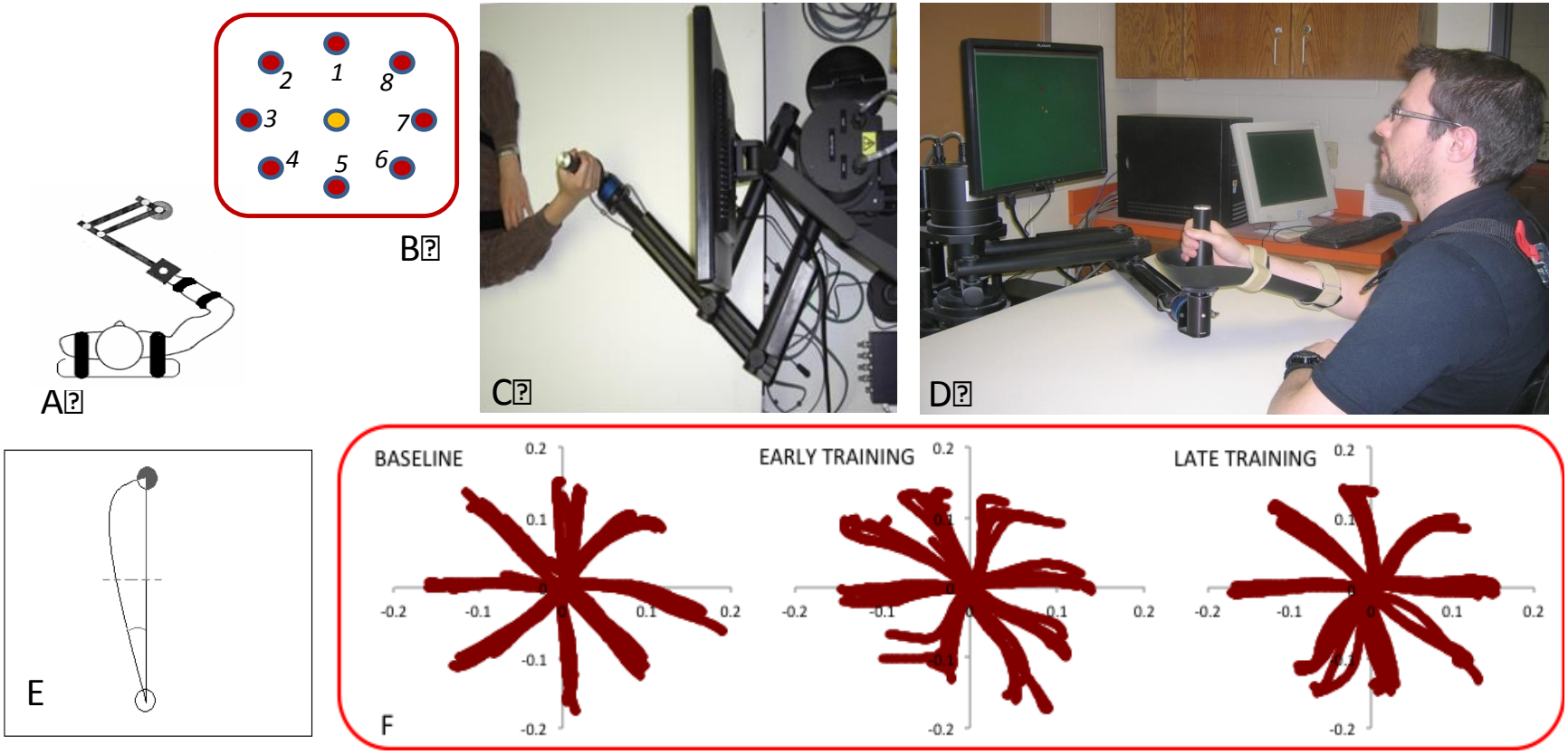
1
2
3
4
5
6
7
8
A
B
C
D
E
F
BASELINE
EARLY TRAINING
LATE TRAINING
0.2
0.1
-0.1
-0.2

Figure 1.

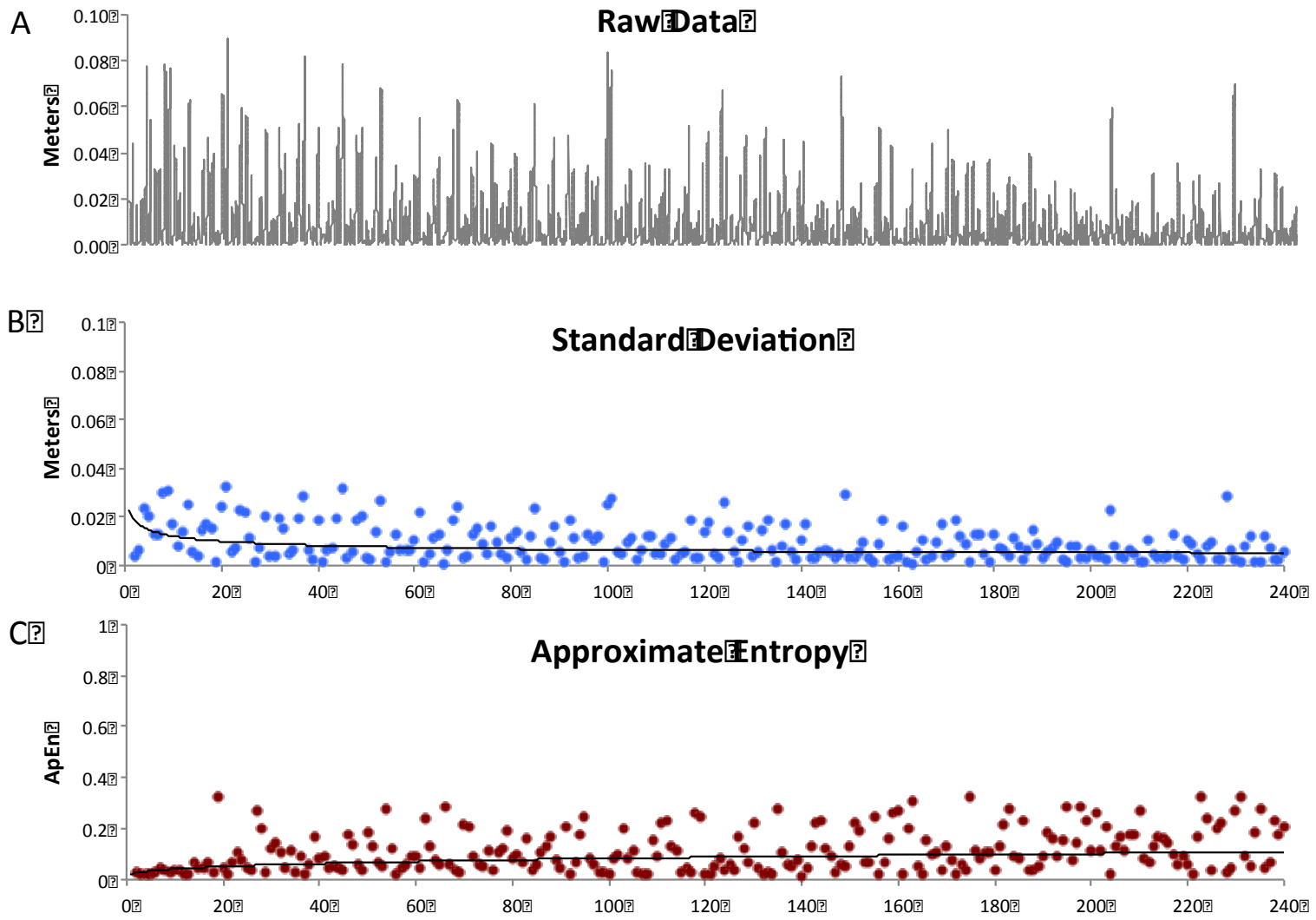
A
Raw Data
Meters
0.10
0.08
0.06
0.04
0.02
0.00
B
Standard Deviation
Meters
0.1
0.08
0.06
0.04
0.02
0
0
20
40
60
80
100
120
140
160
180
200
220
240
C
Approximate Entropy
ApEn
1
0.8
0.6
0.4
0.2
0
0
20
40
60
80
100
120
140
160
180
200
220
240

Figure 2.

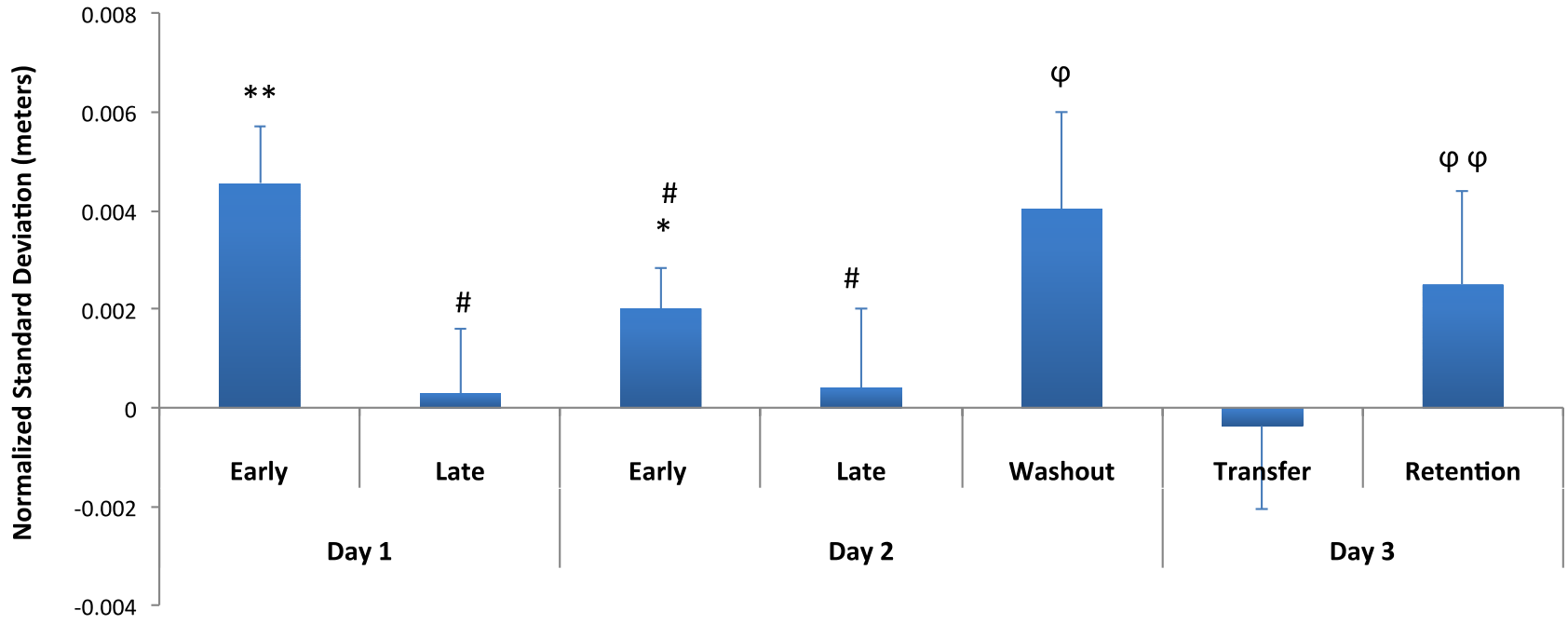
Normalized Standard Deviation (meters)
0.008
0.006
0.004
0.002
0
-0.002
-0.004
**
#
#
*
#
φ
φ φ
Early
Late
Early
Late
Washout
Transfer
Retention
Day 1
Day 2
Day 3

Figure 3.

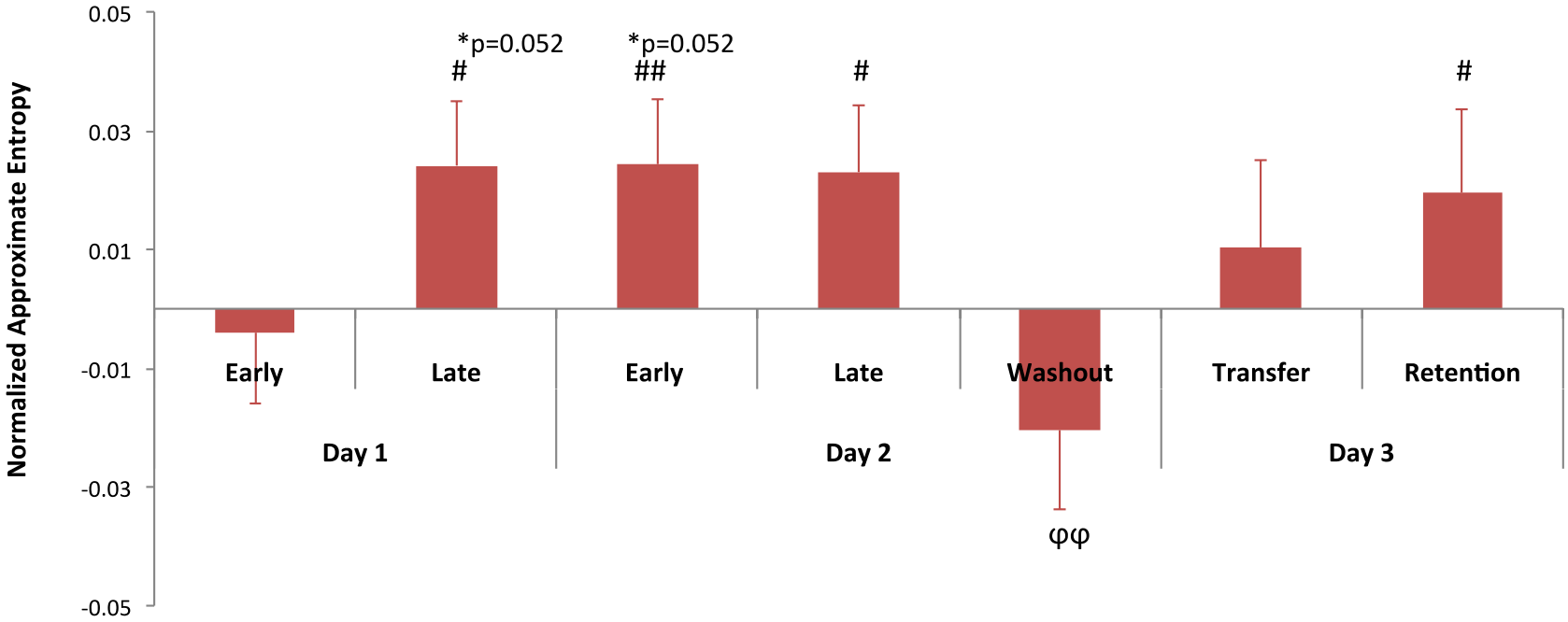
Normalized Approximate Entropy
0.05
0.03
0.01
-0.01
-0.03
-0.05
*p=0.052
#
*p=0.052
##
#
#
φφ
Early
Late
Early
Late
Washout
Transfer
Retention
Day 1
Day 2
Day 3

Figure 4.

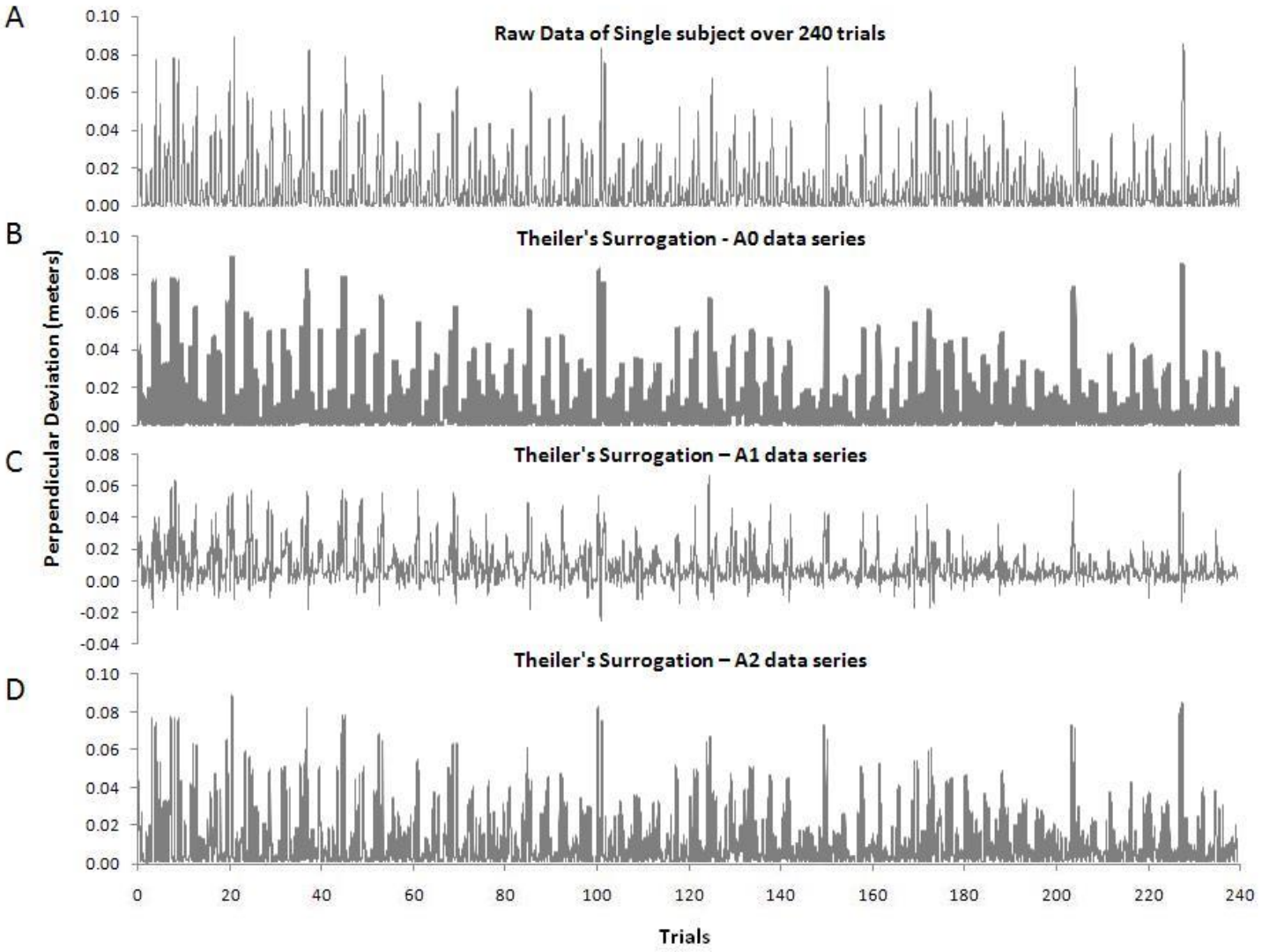
A
Raw Data of Single subject over 240 trials
B
Theiler's Surrogation - A0 data series
C
Theiler's Surrogation – A1 data series
D
Theiler's Surrogation – A2 data series
Perpendicular Deviation (meters)
0.10
0.08
0.06
0.04
0.02
0.00
-0.02
-0.04
0
20
40
60
80
100
120
140
160
180
200
220
240
Trials

Figure 5.

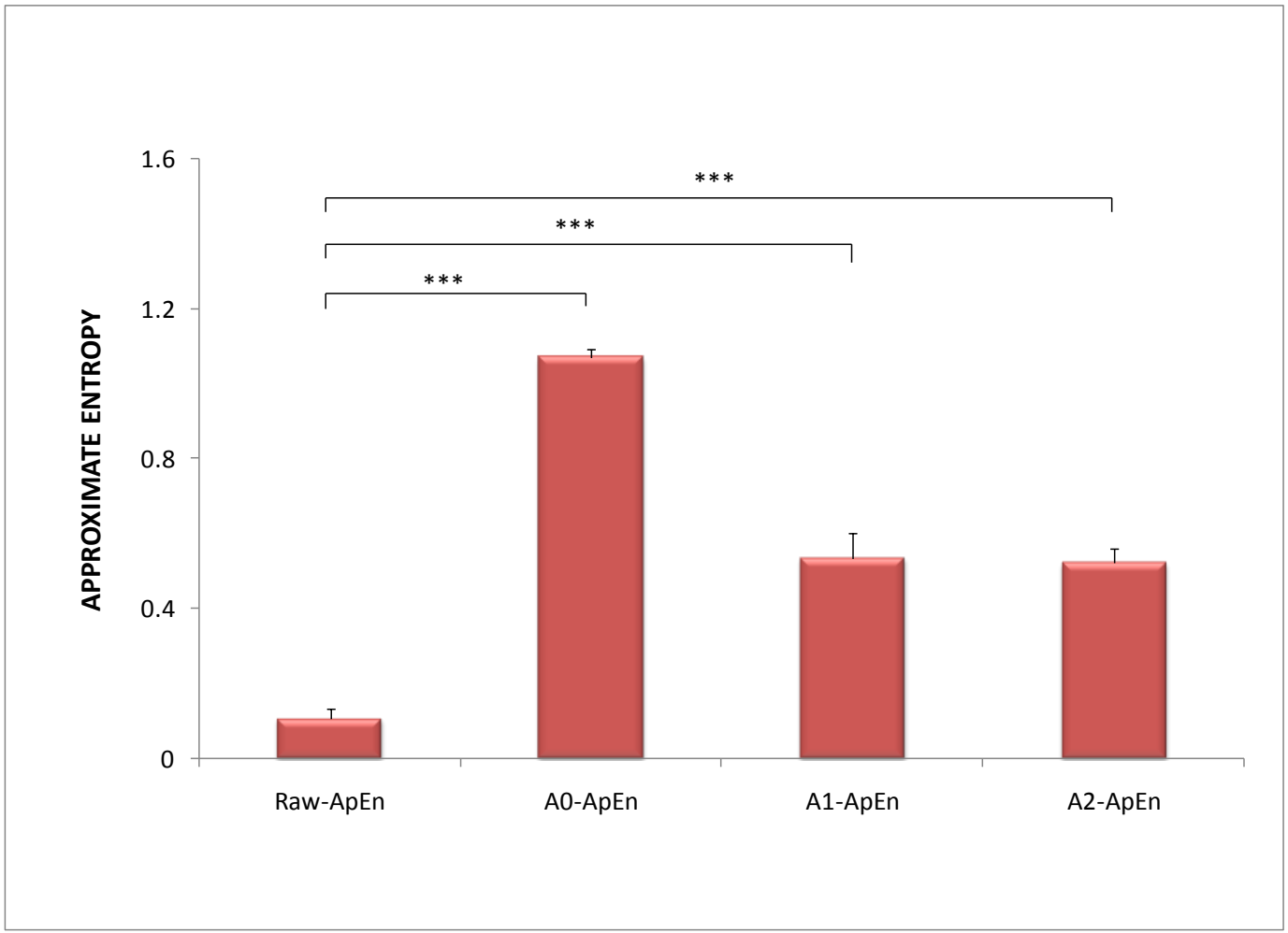
APPROXIMATE ENTROPY
1.6
1.2
0.8
0.4
0
***
***
***
Raw-ApEn
A0-ApEn
A1-ApEn
A2-ApEn

Figure 6.