REHABILITATION AND KINESIOLOGICAL ANALYSIS OF MOTOR CONTROL IN GRASP

by

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ABSTRACT OF THE DISSERTATION

Rehabilitation and Kinesiological Analysis of Motor Control in Grasp

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Rehabilitation of grasp following brain injury remains a challenge that is seldom completely successful. Current biofeedback protocols for fine motor rehabilitation are generally limited to single-muscle or single-joint movements, and their application to Activities of Daily Living (ADL) is constrained by the simplicity of motions feasible during training. Herein, a novel biofeedback device, termed Proprioception-Augmenting and Measurement Interface (PAMI) was used to train thumb-index opposition, a task relevant to ADL. PAMI uses a novel method to non-invasively measure muscle forces in the arm during grasp, using Surface Muscle Pressure (SMP).

The efficacy of PAMI training was assessed using a standard therapeutic test, the 9-hole peg test. In addition, the neural control features of grasp were examined using motor variance analysis. Features of the PAMI signal were extracted from recorded signals and compared to clarify the mechanisms by which PAMI aids rehabilitation. Variability analysis of recorded SMP signals measured the effect of PAMI biofeedback on the coordination of muscle activity in impaired and healthy persons. Training with the PAMI device was shown to be effective in the short-term improvement of fine motor function for brain injured participants ($p<.05$), and the kinesiological mechanisms for this change were explored in terms of coordinated muscle activity.

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Chapter 1 - Summary

The present work is a study of fine motor control and its restoration in cohorts of healthy and neurologically impaired subjects. A novel biofeedback device, the Proprioception-Augmenting and Measurement Interface (PAMI), guides participants as they repeatedly cycle between muscle activation and relaxation. PAMI biofeedback is a real-time representation of the upper extremity's activity, based on Surface Muscle Pressure (SMP) signals from pressure sensors on the subject's forearm. The efficacy of PAMI as a rehabilitative device is characterized using features of the SMP signals as well as a 9-Hole Peg Test as an assessment of fine motor function. The change in function from training with the PAMI device in impaired persons is contrasted with its effect on healthy control subjects, as well as to the improvement that follows standard repetitive training without the device. The Difference in Variance Index (dVI), a technique for the analysis of structure in motor variability, is applied to recordings from both healthy and impaired subjects in order to assess the role of changing coordination in fine motor improvement.

Hypothesis 1:

Restoration of fine motor control can be enhanced by the use of biofeedback from the Proprioception-Augmenting and Measurement Interface (PAMI) device to supplement proprioceptive deficit. Performance on standard functional tests will improve after training with feedback (WF) as compared with the no feedback (NF) condition.

Hypothesis 2:

The PAMI signal will reveal the successful motor control strategies in learning specific tasks. Signal features including onset slope, range, maximum value, duration, and jerk are expected to be greater during training with feedback (WF) than without (NF). It is expected that the difference between values will be indicative of the mechanism by which task-specific feedback enables improvement in motor function.

Hypothesis 3:

During repetitive thumb-index opposition, muscle contraction measured by the PAMI device will reveal the coordination of the motor control system for both the healthy and brain injured cohorts. A comparison between the WF and NF conditions is expected to reveal the increase of synergy in brain-injured subjects when using PAMI biofeedback. In this way, a change in the coordination pattern will be confirmed as the mechanism by which PAMI promotes rehabilitation.

Methods

Surface Muscle Pressure (SMP) sensors record the subject's muscle activity, and the instantaneous values from each of the SMP sensors are used to determine a location in a component space. Feedback is given as a scalar representation of the distance between the subject's current location in that space and a pre-set template location. The single-session efficacy of this rehabilitative tool is gauged via a comparison of subjects' performance on a standard therapeutic task, the Nine Hole Peg Test (9HPT) [Braun 2007, Oxford 2003], after training with and without feedback.

In addition to the 9HPT, which represents acute improvement of fine motor control, the features of PAMI feedback are extracted post-hoc as a measure of motor function. The slope, maximum value, range, duration, and jerk of the signal are expected to be different in the two training conditions. This would support the use of augmented feedback for subjects with diminished sensation, having shown whether repetitious movement alone (i.e., training without the PAMI device) produces the same activity as the with-feedback condition [Van Dijk 2005].

Variability of muscle activity during grasp can be measured in the context of the coordination. While there may be little variability in the scalar value represented by PAMI, it is possible that the individual sensors will vary from repetition to repetition in their relative values, reflecting the synergies that underlie control. By comparing variability using the dVI analysis to which the UCM hypothesis reduces [Latash 2002], the role of synergies in the improvement of motor function can be quantified. This comparison is conducted between the with- and without-feedback conditions for healthy and brain-injured subjects.

Results:

Training with PAMI biofeedback is shown herein to be significantly more effective in restoring fine motor function than standard repetitive training without the device. This is especially true for subjects with more significant initial impairment, for whom the average improvement on the 9HPT after training with the PAMI device is greater than for the entire impaired cohort. The significance of the difference between the effects of standard training and PAMI training is measured as $p<0.05$. In contrast, healthy control subjects do not experience significant changes in performance of the 9HPT as a result of training in either condition.

The features extracted from the PAMI signal for post-hoc analysis are, for the most part, significantly different between conditions for the impaired subjects. The duration and time above threshold are significantly greater when training with feedback, which suggests that motivation plays a role in improving motor function ($p<0.05$). However, the similarity of maximum values between training conditions, the decrease in the PAMI signal slope over a session, and the greater jerk value in PAMI training indicate that a change in strategy is occurring concordantly with improvement.

The mechanism by which motor function is altered during training for impaired subjects can be measured using the dVI value, where lesser values correspond to discoordination. Healthy control subjects are typically well-coordinated, resulting in an approximately constant value across time. In contrast, impaired subjects often yield dVI values marked by considerable discoordination during the early activation. The waveform that results can be quantified in terms of curvature, which is shown to be greater for standard repetitive training than for PAMI training. This reduction in curvature using PAMI suggests the utility of the device in restoring coordination in fine motor control, especially in early activation of thumb-index opposition.

Chapter 2 – Rehabilitation Strategies for Brain Injury

The present work is built on the fundamentals of rehabilitation science. A muscle activity sensing device, the Proprioception-Augmenting and Measurement Interface (PAMI) was developed. Biofeedback derived from registered signals was tested on a cohort of brain-injured subjects and a group of healthy controls. The recordings were analyzed post-hoc to observe the mechanism by which fine motor function is improved. The physiology underlying brain injury, for both stroke and traumatic brain injury survivors, allow a characterization of the typical dysfunction of users of the PAMI device. The literature detailing the neurological changes that are known to result from fine motor rehabilitation is also reviewed, to contextualize the later discussion of results. Current therapies for fine motor rehabilitation after brain injury will be detailed, including the opportunities for improvement. In this way, the following explains the motivation for the present work and possible explanations for its results.

Stroke and Traumatic Brain Injury

Etiology of Stroke:

Approximately 730,000 new or recurrent strokes are recorded each year in the United States [Winstein 2003, Byl 2003]. The two major forms of stroke include the occlusion of blood flow, such as by stenosis or clotting, and the interruption of blood flow due to arterial leakage or rupture [Mohr Stroke 1997]. At least 80% of cases are diagnosed as thrombotic [Feinberg 1996]. More generally, stroke injures the brain by denying blood to a portion of the nervous tissue. The resultant morbidity can impair central nervous function, including effects on motor skills, cognitive abilities, memory, and emotional control.

Improvements in emergency medicine and public awareness of symptoms have reduced the frequency with which stroke leads to death [Yang Stroke 2006]. Pharmacological intervention after the sudden onset of symptoms, such as the administration of thrombolytic drugs to break up clots, can minimize the extent of necrosis when administered properly [Lutsep 1999]. In this way, stroke is gradually becoming less prevalent as a cause of death.

As mortality rates due to stroke decrease, the number of survivors with impairments increases. The need to treat the effects of stroke extends beyond the emergency room, with stroke survivors experiencing lasting functional deficits due to changes in the central nervous system. The following is a review of research, culminating with the present work, on the effects of stroke on the motor control system. While these effects are neither local nor simple, studying the typical characteristics of stroke enables some degree of precision in treatment.

Stroke Recovery Timeline:

Immediately following a stroke, healing at a physiological level can be encouraged using a multi-pronged approach. Strategies for salvaging neural structures include drug management, rest, proper positioning of the body, and guided strategic movements [Byl 2003]. These treatments are most likely to occur in a hospital setting, since they are intended for use as soon as possible following a stroke. While the present work is intended to influence rehabilitation in the months and years following brain injury, rather than immediately thereafter, it is worthwhile to include a review of short-term treatment.

More than half of people for whom stroke has caused a brain injury experience some motor disability as a consequence [Winstein 2003]. For these individuals, the functional deficits can range from diminished fine motor control to complete hemiparesis on the side contralateral to the brain lesion. The specific nature of the impairment, for motor as well as psychological function, may depend on which hemisphere of the brain was injured.

Restoration of function commences as soon as circumstances allow, preferably within the first few days following the injury [Kwakkel 2004]. However, the brain's response to treatment over time is not constant. The most extensive and spontaneous improvements of function are known to occur in the first 30 to 90 days post-stroke [Byl 2003]. Thus, there is an emphasis on rehabilitation during these early days after brain injury. One practice that targets this acute time period is the employment of inpatient rehabilitation. While still hospitalized, stroke survivors can make use of physical, occupational, and speech therapy to begin healing [Jauch emedicine 2007].

It has been reported that 55% of stroke survivors with motor impairment experience persisting deficit after five years [Winstein 2003]. While the extent to which therapy in the acute period of recovery, including both rehabilitative practice and pharmacological treatment, can mitigate a prolonged effect is not certain, outpatient rehabilitation is generally recommended [Jauch emedicine 2007]. The period following the first few months after brain injury, named the chronic phase is a difficult period for restoring function. However, it is possible to induce improvement for chronic stroke patients, which is the basic assumption and overall goal of the present work. The remodeling and reorganization of neural structures can be encouraged, such as with goal-oriented learning, in patients with chronic stroke [Byl 2003].

Typical Effects due to Stroke:

The effects of stroke vary from individual to individual. The dependence of symptoms on the location of the lesion, the type of stroke, the extent of damage to brain tissue, and the timing and type of therapy immediately post-stroke, along with the non-uniformity of neural architecture between individuals, combine to confound attempts to predict the type and extent of impairment. Whether motor dysfunction will be hypertonic or hypotonic, spastic or ataxic, etc. cannot be precisely assessed without hands-on testing by a clinician.

Nevertheless, it is possible to make several generalizations about the relationship between lesion location and resultant impairment. Such broad estimates are of interest for the present work, for several reasons. First, that any inference that can be drawn to guide therapy is relevant for clinical or rehabilitative research. Second, the inclusion criteria of this study are designed based on the typical effects of stroke. Most importantly, the results presented herein are best explained in the context of the underlying injury and its stereotyped symptoms.

Stroke can produce changes in cognitive and emotional function in addition to motor deficits. Cognitive and emotional changes are not the focus of motor rehabilitation, and therefore they are beyond the scope of the present work, but their review is also worthwhile. The location of a lesion often plays a role in the cognitive deficits that follow stroke [de Haan 1995]. For example, right hemiparesis – that is, injury specific to the left hemisphere of the brain - often entails compulsive behavior, difficulty initiating and sequencing tasks, and increased distractibility. On the other hand, left hemiparesis is associated with marked irritability and the inability to comprehend abstract concepts [Byl 2003]. While these effects may be of interest to clinicians, it seems that they are not particularly pertinent to the stroke survivors themselves; their reported quality of life has little correlation to the type of stroke [de Haan 1995].

Many stroke survivors experience motor deficit in the chronic phase following injury. Three quarters of impaired patients regain enough function to ambulate. However, it is reported that as many as 75% continue to have diminished control of the upper extremity [Feys 1998]. The so-called "unaffected" extremities may also experience a decrease in coordination, impairing a stroke survivor's ability to use the ipsilesional limbs in Activities of Daily Living (ADL) [Sainburg 2006]. The contralateral side experiences decreased voluntary control, weakness, co-contractions of agonist and antagonist muscles, and abnormal synergies, in addition to which the ipsilateral limbs demonstrate weakness, discoordination, and decreased reaction speed [Byl 2003].

The psychological impact of motor impairment on stroke survivors is profound, perhaps extending beyond the simple decrease in ability to perform ADL. Participants in one survey had more aversion to hemiplegia than to confusion, aphasia, or even death [Solomon 1994]. This finding did not serve as guidance in the development of the present experiments; it did, however, serve as motivation.

To a considerable extent, the specific nature of persisting deficits in motor control may be a function of lesion location. For example, while right hemiparesis causes motor apraxia, left hemiparesis is more likely to interfere with visual and spatial perception [Byl 2003]. The deficits experienced by the ipsilesional limbs have been shown to depend on the location of the injury as well; a lesion in the non-dominant hemisphere will incur deficits in stability control of movement, while injury to the dominant hemisphere causes diminished velocity control [Sainburg 2006]. This disparity of dysfunction may prompt different approaches to rehabilitation.

Traumatic Brain Injury:

Traumatic Brain Injury (TBI) has an occurrence rate of 1.4 million incidents per year in America. Of the 40% whose trauma results in needs for services after hospitalization [Corrigan 2004], a significant portion of the population experiences motor deficit. Because of the wide variety of etiologies and symptoms of TBI, less is known about its typical effects than has been established for stroke. In some cases, for instance, abnormal kinematics can be attributed to impaired motor planning [Wilson 2007], while other subjects suffer from muscular spasticity [Gordon 2006].

While the specific effects of TBI are generally more diffuse than stroke, previous work has shown that therapies similar to rehabilitation after stroke can be effective in the restoration of function. For example, repetitive therapy, constraint induced therapy, and virtual reality biofeedback have all been employed in rehabilitation after TBI. For this reason, TBI subjects are included in the present study, although the analysis of their results will not go into the same depth as in the case of stroke subjects.

Knowledge of the typical effects of brain injury motivates research and innovation in rehabilitation engineering. The desire to improve the quality of life of brain injury survivors is ubiquitous among practitioners and academicians in the field. Increasing the specificity of rehabilitative protocols by tailoring them to patients' symptoms may be facilitated by experimentation. Previous research has shown that the variability in dysfunction complicates treatment, but that restoration of function is possible in the chronic period of stroke. The present work seeks, in part, to improve the efficacy of rehabilitation with a novel device that incorporates the flexibility of the SMP sensor modality unique to the author's group.

Neurophysiological Rehabilitation

Just as a review of brain injury etiology showed what concepts underlie the motivation for the present work, work done to characterize neurological changes following brain injury has played a role in its development. Unanswered questions about the nature of neural restructuring during rehabilitation pervade the literature. It is generally accepted that the vehicle for functional improvement in motor control after brain injury is neural plasticity, which entails a lasting change in the location and characteristics of activity in the brain. Less clear are the specific location and nature of that restructuring. For example, numerous papers report observing new activity in a variety of regions in the injured brain, as reviewed below. While the present work does not attempt to answer these questions, interpretation of the results will be better accomplished in the context of previous work.

Neuroplasticity:

Recent literature has been nearly unanimous in attributing the restoration of function to changed patterns of activity in the injured brain. As discussed above, in the chronic phase of recovery, remodeling and reorganization of brain tissue can be facilitated with goal-oriented learning [Byl 2003]. Note that this is distinct from simple physiological healing, which might entail the regeneration of damaged tissue and the resumption of normal activity. Instead, restoration of function is based on reorganization of the uninjured portions brain. While the exact nature of the relationship between brain restructuring and motor function improvement remains unclear, the reliance of rehabilitation on plasticity is almost without question [Liepert 1998].

Rehabilitative protocols seek to improve the quality of life of subjects from multiple angles, as mentioned earlier: cognitive therapy, encouragement of motor learning, acquisition of new skills, etc. It is often a team of practitioners that administer services to brain injured patients, coordinated to aim for some level of function independence [Kwakkel 2004]. The broad singularity of this goal invites the generally uniform methods outlined below, all of which have the promotion of central nervous system reorganization as their foundation [Byl 2003]. Recruitment patterns of sensorimotor cortex neurons change during training, reflecting the cortical reorganization that is the hallmark of plasticity. Consequently, the uninjured tissue of the brain experiences much greater activity than would be observed in a healthy brain [Liepert 1998].

Further credence is lent to the concept of neuroplasticity by observations of neural activity over extended training. The increase in neural activity in uninjured regions of the brain, reflecting the organizational changes that underlie the restoration of function, is not necessarily present over the entire course of training. On the contrary, it has been shown that cortical activity decreases after new skills are learned. It is at this point in rehabilitation of chronic stroke that automated processing of neural commands is observed to be enhanced [Pascual 1995].

The restructuring of the central nervous system during rehabilitation is not limited to any one hierarchical level of organization. Reorganization is possible in sensory and motor mapping at the cortical level, and also through a number of mechanisms at the neuronal level. The creation of new synapses can be responsible for functional change, but it is also possible for neuronal networks to be tuned differently over the course of changing by enforcing or inhibiting existing neural connections [Kwakkel 2004].

These findings indicate that neuroplasticity enables the return to normal function that is the ambition of rehabilitation science. Damaged tissue is unlikely to recover, thus requiring that its function be assumed by uninjured regions of the brain. Moreover, as learning becomes more solidly ingrained, the amplified activity in this healthy tissue decreases, which suggest a corresponding increase in efficiency, and thus sustainability. Plasticity is undoubtedly the basis for these changes in motor function, which drives the design of rehabilitative protocols, including the one presented herein.

The effect of neuroplasticity is expressed in a theory termed “vicariation of function” [Nudo 2001]. This theory hypothesizes that the function of damaged tissues is relocated to undamaged tissue. Whether the new locus of activity is cortical or subcortical, and whether the relative distance from the site of the injury is adjacent or remote, are open questions [Kwakkel 2004]. It is, however, possible to discuss generalized explanations of this neural reorganization, as follows.

Location of plasticity:

A review of the rehabilitation science literature does not reveal a consensus regarding the region of the brain that assumes the duties of damaged tissues in the brain. Even considering the wide variety of necrotic loci that can produce motor dysfunction, as described in detail above, it is noteworthy how disparate the reports of different mechanisms for the restoration of function by plasticity have been. A brief review of the literature is presented herein to suggest mechanisms for neural restructuring rather than to motivate some answer to this highly contended question.

Rehabilitative schemes based on mirroring call for the simultaneous activity of the affected and unaffected limbs. This technique is specifically designed to recruit healthy tissue into the coordination of movements, enforcing the synaptic connections of involved neurons. Mirroring with a task such as bilateral gripping seeks to increase primary motor cortex (M1) activation in the affected hemisphere via the corpus callosum [Staines 2001]. Anecdotally, during preliminary trials of the PAMI device, a number of stroke patients used mirroring while performing thumb-index opposition. While the instructions given to the subjects neither encouraged nor discouraged mirroring, it was a spontaneously elicited response to the effort of repetitive training. The natural inclination to mirror may be indicative of the potency of plasticity via the motor cortex.

Functional Magnetic Resonance Imaging studies on Constraint Induced Therapy users (discussed in more detail below, in Current Therapies) have provided detailed data on the spatial distribution of neural activity in the damaged brain over the course of rehabilitation. In this way, CI has been shown to promote activity in the ipsilateral (unaffected) hemisphere [Kopp 1999, Johansen-Berg 2002]. However, as is frequently the case in the literature, the location within the ipsilateral hemisphere is a subject of contention. It has been proposed that this adaptation favors M1 [Kopp 1999], but the dorsal premotor cortex (iPMd) has also been cited as the site of neuroplasticity [Johansen-Berg 2002].

Responses to the above studies have further elucidated their findings, although there remains no conclusive answer. For example, it has been shown that the pathway for lateralization of motor learning is unlikely to be the corpus callosum, as a subject with a lesion in the callosum was able to lateralize the learned dynamics of a reaching task [Criscimagna-Hemminger 2002]. It is consequently tempting to design a therapy capitalizing on adaptation in the iPMd, as variations on such a protocol could elucidate the mechanisms of lateralization in healthy subjects. However, the bilateral PMd connections that enable lateralization are not linked to distal movement [Johansen-Berg 2002]. The Criscimagna task involved only shoulder and elbow control, restricting distal activity that might require the corpus callosum.

Whether plasticity takes place in the motor, premotor, or sensory cortices, or some combination of the three, is an unresolved question of rehabilitation science. Work with animal studies and with fMRI on human subjects has explored possible mechanisms for neural restructuring, and a variety of conflicting conclusions have been drawn. The commonality among all such studies, which bears the most significance to the present work, is that training after brain injury elicits neuroplastic reorganization as it restores motor function.

The research presented herein analyzes motor control at the level of muscle pressure, and no attempt is made to register neural activity in the peripheral or central nervous systems. As such, there are no claims made about the specific locations of neural restructuring in the brain, nor about the mechanism for plasticity in neuronal circuitry. However, motor control literature includes numerous techniques for inferring the nature of the motor control system from minimally invasive recordings such as those used in the present work. Applying these techniques, described later (see Chapter 3), will yield insights into the changes of the motor control system. The above review of the plastic properties of the central nervous system serves to contextualize the results of motor control analysis.

Current Therapies

The state of rehabilitative science holds great promise for the many stroke survivors who continue to suffer motor impairment. Traditional therapies have been incrementally refined in focus and efficacy, approaching the task of restoring motor function using a combination of proven ideas and innovative advancements. Low-tech braces and high-tech biofeedback modalities alike are incorporated into the development of increasingly effective protocols. Nevertheless, there remains ample opportunity to improve upon existing therapies, which is the goal of the present work. The following summarizes current therapies in terms of their methodologies, their physiological effects, and the obstacles that persist.

Repetition

Rehabilitative protocols vary in approach, timing, and tasks, with no one method emerging as "best". In general, the "use it or lose it" dogma is pervasive, entailing activity in the affected limbs to facilitate cortical rearrangement at the neural level. At its most basic, this approach is comparable to exercise, inasmuch as practicing a task is expected to improve performance of that task. However simple the premise may seem, research has shown that the effect of repetitive training is complex.

Mapping the primary motor cortex in primates, Nudo found that the repetitive use of digits increases the cortical representation of those digits [Nudo 1996]. Extending this concept to the restoration of function, studies have shown that cortical re-differentiation in injured persons can be accomplished by repetitive training [Byl 2003]. While cortical plasticity and improved motor function are not proven to be linked by this finding, the ability of repetitive training to generate change in the injured brain suggests its potential for rehabilitation.

The implementation of repetition in the restoration of motor function is more involved than a simple instruction to perform a task over and over. A primary concern is that the training must be conducted under the supervision of a clinician or therapist. Additionally, desirable motor function should be rewarded, as opposed to being a reward in itself [Byl 2003, Merians 2002]. These considerations promote desirable neural restructuring with efficacy not afforded by unattended, open-loop repetitions.

A further question is whether more is better – that is, whether the improvement of function continues as the number of repetitions increase. Previous work suggests that this question can be answered in the affirmative; more is indeed better [Langhorne 1996, Kwakkel 1997]. This finding guided the development of the present work's experimental protocol. While subjects are instructed that they should report fatigue and are free to stop the trial, care is taken to include as many repetitions as possible.

Constraint Induced

A more recent development in rehabilitation science is the adoption of Constraint Induced therapy (CI). In CI, the application of an orthotic restraint to the unaffected limb is intended to force patients to use the affected limb [Miltner 1999, Levy 2000]. A comparative study found that targeted bilateral training may be more efficacious, especially in the proximal upper limb, but that CI yields better results for performing ADL [Lin 2009]. In other words, the frequency and complexity of tasks for which the impaired motor control system commands the affected limb during CI fits into the guidelines described above.

CI therapy has been applied to individuals with such physical impairments as stroke, TBI, and cerebral palsy [Kopp 1999, Taub 1999, Eliasson 2005]. MRI studies have suggested that its use promotes activity in the damaged motor and premotor cortices [Kopp1999, Johansen-Berg 2002], which provides a physiological explanation for its promising results [Miltner 1999, Levy 2000]. This method has considerable limitations, as discussed below. As an extreme interpretation of the “more is better” maxim, it demonstrates the potential for neural restructuring that accompanies the use of the affected limb in real-world tasks.

Biofeedback

Traditionally, patients are guided and motivated by an onlooking therapist during repetitive training. This puts a considerable burden on the therapist, whose time and attention must be dedicated to observing the practice and providing feedback about performance. Additionally, the detail with which feedback can be given is bound by the limits of the clinician's perception. A human observer, no matter how expert, cannot use their perception of the task to provide estimates of muscle activation or coordination as accurate as from devices that directly measure performance.

The need for repetitive training to be accompanied by attentive oversight and rewards for desirable activation, as described above, is analogous to the feedback portion of a control system. While healthy motor control incorporates visual, tactile, and proprioceptive feedback, brain injured individuals are often insensate to some extent in the affected limb. With the motor control system using reduced non-visual information, the resultant impairment can be viewed in light of the limited feedback available to the central nervous system. Biofeedback, which translates recorded features of task performance into a modality that is readily accessible to the impaired motor control system, supplements the limited information to which the impaired motor control system has access. The customization of feedback allows the individualization of rehabilitative protocols, which suits the wide variety of dysfunctions caused by brain injury [Merians 2002].

The terminology used to describe biofeedback classifies the various modalities according to the source of the information and the timing with which it is delivered to the subject. Knowledge of Results is the term used to describe feedback related to the nature of the result, meaning it is dependent directly on the movement goal. On the other hand, Knowledge of Performance is derived from aspects of the movement itself, irrespective of the goal [Schmidt and Lee 1999]. Another classification defines feedback as Inherent or Augmented. Inherent feedback uses successful completion of tasks as a rater of control during rehabilitation, while Augmented feedback measures hidden layers of control – such as electromyographic (EMG), kinetic, or kinematic recordings – to guide subjects during activity [Van Dijk 2005].

Using Augmented Feedback has been shown to improve normal function of complex tasks in the elderly, aged 60-82 [Swanson 1992]. Since many chronic stroke patients are of comparable age, this suggests the applicability of Augmented Feedback for restoring function for post-stroke rehabilitation. Additionally, Augmented Feedback has been similarly effective in motor learning in young adults [Lee 1990], based on which this feedback modality is expected to be effective for TBI patients.

One prevalent feedback modality is electromyographic (EMG). Because EMG measures neural signals across muscles, it provides an estimate of muscle activity to produce a form of Augmented Feedback. EMG visualization has been used to improve upper extremity function in patients with severe impairment [Crow 1989] or significant hemiparesis [Armagan 2003]. There are a number of EMG biofeedback devices that are popular among clinicians and patients [Popovic 2002, Armagan 2003, Rampa 2003].

However, the limitations of these devices, as described below, motivate the present work as an alternative.

Challenges

Great strides have been made in pursuit of restoring function to brain injured persons, but viewing these accomplishments comparatively reveals the room for improvement that remains. Tradeoffs exist in current technologies, in compromises such as between convenience and effectiveness, and between generalizability and performance. A review of these issues is pertinent to the present work, having served as a guide during the development of our novel device.

Of primary concern is the pervasive frustration that is reported by recipients of therapy. An adage from prosthetics that suits the field of rehabilitation reminds us that the fanciest, most expensive prosthesis is still useless if it never leaves the drawer. Rephrased to pertain to the restoration of fine motor function, the adage suggests that successful rehabilitative protocols are those that subjects are willing and able to use with great frequency, thus fulfilling the “more is better” maxim. Unfortunately, a problem that marks current schema is boredom [Byl 2003].

Repetitive training protocols for brain injured individuals in the chronic phase often include practice performed in the home, without the presence of a therapist. Because, as described above, repetitive training requires supervision and positive feedback, this home-care is encouraged to be accompanied by involvement of the user's family. Thus, a potential obstacle posed for repetitive training can be the family members' ability to dedicate time to supervising the practice. Constraint Induced therapy obviates the need for repetitive training by forcing the user to train the affected limb during daily life. In doing so, Constraint Induced therapy prevents boredom during in-home rehabilitation, but this benefit comes at the expense of user frustration. Using a limb that experiences motor dysfunction to perform ADL may prevent those activities entirely, hampering the quality of life of the brain injured individual. The resultant frustration reduces users' compliance with home-care instructions, decreasing the effectiveness of CI [Byl 2003].

EMG has major deficiencies as a rehabilitative interface for the disabled population. Not surprisingly, it is often difficult for persons with hemiplegia to reliably register residual muscle activity from their affected limbs; likewise, it is challenging for their providers. The considerable impairment of subjects for whom EMG-based feedback during repetitive training was effective demonstrates the limitations of EMG as a biofeedback modality [Crow 1989, Armagan 2003]. Moreover, feedback is generally restricted to the control of single muscles or joints [Huang 2006]. Although the EMG approach can adequately recognize binary volitions such as grasp/release [Farina 2004], it is otherwise limited in its applicability to rehabilitation of fine motor control [van Dijk 2005, Krebs 2003]. EMG can be frustrating and time consuming for the clinician as well. Its proper use depends on precise and fixed placements of sensors on the body, clean and dry conditions, low physical activity, and skin contact with electrode pastes, or invasive wires [Turker 1993]. For these reasons, the present work utilizes an alternate modality for registering muscle activity, which has been both simple and effective.

One final issue of note is related to the study of rehabilitation more than to its application. When trying to measure the efficacy of a rehabilitation protocol, it is preferable to control for external influences on the restoration of function. For example, many longitudinal studies will report, if not restrict, the amount and type of practice performed by subjects at their homes. Additionally, the role of mental practice, which is extremely difficult to monitor, may affect fine motor improvements independently of the prescribed therapeutic regimen [Byl 2003]. A number of case studies have avoided this complication by adding mental practice to their protocols, thus mitigating its unpredictable influence on results [Byl 2003, Page 2001]. The present study minimizes the effect of mental practice by looking only at improvement of function over a period of approximately thirty minutes.

The obstacles described above include a number of limitations that confound current technology; however, these tradeoffs also represent incremental improvements to rehabilitation science. Well-attended repetitive training facilitates motor learning using positive feedback, at the expense of the therapist's and family's time commitment. Constraint Induced therapy alleviates the pressure on the therapist and family, but users report dissatisfaction with the frustration it incurs. EMG and other biofeedback modalities supplement the limited sensory information available to brain injured subjects, although for limited movements and with extensive therapist involvement. These examples serve as lessons, providing opportunities to mimic or improve on the best aspects of current rehabilitative devices while attempting to avoid the pitfalls.

For survivors of stroke and traumatic brain injury, motor deficits are among a number of effects that can persist for months and years. The particular dysfunctions are highly variable between individuals, although their gross correlation to the location and type of brain injury imparts a degree of predictability. Restoring function is best accomplished soon after the injury, although it is possible to improve motor control after an extended period of impairment, such as in the chronic phase of stroke. To do so, rehabilitative protocols make use of the brain's capacity for neuroplasticity. Although the exact mechanisms of neural reorganization are not yet known with certainty, it is likely that over the course of therapy, the functions of the damaged tissue are transferred to uninjured regions of the brain. Current therapies, including repetitive training, CI therapy, and EMG biofeedback, attempt to promote restructuring with some combination of frequent use of the affected extremity, assessment of performance, and motivation. Each therapy, while proven to facilitate the restoration of function, includes some drawbacks that complicate their use in therapy. The present work introduces an alternate technology, which addresses some of the shortcomings of current therapies while promoting neuroplastic recovery of function for the brain injured population.

Chapter 3 – Motor Control Theories

The present work demonstrates that the PAMI device facilitates the restoration of fine motor function after brain injury. While this finding is significant in and of itself, it raises questions about the nature of the motor control improvement experienced by participating subjects. Having described the role of neuroplasticity in rehabilitation in the previous chapter, the observation of functional gains should be followed by a discussion of the motor control system in which plasticity takes place.

There are a variety of claims that have been put forth in the literature regarding the nature and location of neural reorganization during motor rehabilitation (see above). With such disparity among observations, it is clear that the issue remains unresolved, and the present work does not measure neural activity in a way that might shed light on questions of neuroplasticity. Instead, well established techniques are applied to recordings of muscle activity, with the intention of drawing inferences about the state of the motor control system before and after training.

Just as there is no consensus in rehabilitation science about the specifics of neuroplasticity after brain injury, the field of motion science is characterized by diverse explanations for motor control. Some of the more prevalent postulations, serving as possible explanations for healthy function and frameworks for rehabilitating impaired function, are reviewed herein. A fundamental aspect of motor control that is especially pertinent for the present work is the treatment of variability. The theories' explanation for variability is discussed below, and a number of statistical techniques for characterizing the role of variability in motor control are described.

Motor Variability

Movement, at every level of the motor hierarchy, is typified by limited consistency. Even consecutive performances of the same motor task, under exactly the same conditions, will not be identical. Instead, some degree of difference will persist, and repetitive performance of nearly any movement is properly described by its average trajectory and the distribution of repetitions about that mean. This can be attributed to any number of inescapable biological factors, including but not limited to the nonlinear dynamics of joints crossed by multiarticulated muscles, the probabilistic recruitment patterns of motor units, and the stochastic nature of neural signals. Indeed, motor variability can be considered inevitable. Unlike a mechatronic approach, however, in which the distribution about the mean can be compared to a tolerance, motion science places value on the nature of the distribution and its implications about the properties of the motor control system itself.

A wonderfully demonstrative example of the origins of motor variability and their importance for understanding control, is the act of touching one's index finger to one's nose. An audience, instructed accordingly, can easily observe the disparity between their neighbors' solutions to this seemingly simple problem. While this demonstration is a useful illustrative tool, the rich history of the study of the underlying phenomenon has spawned a number of precise and powerful analyses in motion science.

Redundancy vs. Abundance

In a seminal study of biomechanics, Nikolai Bernstein recorded experienced blacksmiths as they struck an anvil with a hammer. Having performed this movement, presumably, thousands of times per day for years, these participants were as expert at this task as possible. It was reasonable to expect that the variability of such a highly-practiced movement would have very low variability. Looking at the statistical outcomes of the location of the hammer-strike, Bernstein did, in fact, observe the low variability that was expected [Bernstein 1967, Latash 2008].

Of note, though, was the difference between variability at the end-effector, the hammer, and the variability of the kinematic variables that determined the hammer's location, the joints angles. While the hammer strike location was highly consistent, the joint angles were significantly more dissimilar from repetition to repetition. Despite the prodigious expertise of the participants in this experiment, their joint angles – and likely, the recruitment of their muscles, and even their neural impulses – were inconsistent [Bernstein 1967, Latash 2008].

This discrepancy was codified as the Principle of Redundancy. In the performance of a motor task, there is more than one solution available to the system; in fact, there may be a large, if not infinite, number of possibilities. The Principle of Redundancy affects motor control at every level of the system's hierarchy, and it may be responsible for much of the motor variability that characterizes natural movements. Such inconsistency could be said to confound whatever attempt at repeatability might be generated at the planning stage of movement. For this reason, Bernstein believed that the Redundancy problem is the central question of motor control [Latash 2008].

In contrast to this depiction of the multiple Degrees of Freedom (DoFs) as an obstacle for the motor control system, Bernstein's results suggest that the motor control system is able to perform motor tasks with flexibility. While the joint angles were subject to considerable variability, the location of the hammer strike was repeatable across trials, which fits the instructions given to the subjects. To decry the inconsistency of the component variables as an impediment to motor control is to presume an unlikely scheme for the motor control system, and worse, to ignore the marked stability of the performance of the hammer strike task.

Recently, Mark Latash published an alternate explanation for Bernstein's results [Latash 2008]. Rather than look at the inconsistency of component variables as a so-called Redundancy problem, Latash proposed that the motor control system takes advantage of this phenomenon. According to the Principle of Abundance, the motor control system generates so-called families of solutions to produce desired movements. Each solution is equally capable of generating the correct movement, and thus the task can be accomplished with consistency. Moreover, any disturbance to the performance, such as a mechanical perturbation or an unexpected physiological input, can switch the motor control system to another member of the solution family. In this way, the redundancy of a multi-DOF system is actually the key to resisting disturbance and stabilizing motor performance [Latash 2008].

Bernstein's exploration of movement asked, not simply how humans move, but how the brain controls those movements. His proposed answer, that the motor control system freezes DoFs to eliminate kinematic redundancy and thereby simplify motion, has since been refuted [Latash 2008]. The Principle of Abundance, which addresses the same kinematic phenomenon as Bernstein's Principle of Redundancy, paints the so-called redundant degrees of freedom as assets to the motor control system. According to

Abundance, the central nervous system generates movements according to families of solutions to the body's inverse dynamics, which lends flexibility and stability to its motor control. How this is accomplished remains a fundamental question of motion science [Latash 2007]. Although the present work does not seek to answer this important and complicated question, the results presented herein may add pieces to its puzzle by illustrating nuances of motor control and dysfunction.

Synergies

Latash's postulation of the Principle of Abundance suggests that the motor control system approaches the inverse kinematics or dynamics of the intended movement using equivalent task variables. While the solutions consist of disparate component variables, such as joint angles or muscle activations, the goal of the movement is achieved in each. The stability of movement afforded by the Principle of Abundance is the result of the coordination of activity according to whichever solution, or solutions, the motor control system uses. This coordination is commonly referred to in motion science literature as synergy [Latash 2007, Schoner 2007, Kargo 2008].

Before discussing the nature of synergies in motor control, it is imperative that the term is clarified. It is common to refer to synergy, or rather synergistic muscle activation, in rehabilitation science. However, these uses of the word are of negative context, inasmuch as synergistic activation involves the coactivation of agonist and antagonist muscles. This type of activity is indicative of a motor dysfunction, not of a purposeful pattern of muscle recruitment [Hesse 1996]. Any variant of the term “synergy” in the present work is intended to indicate the latter – i.e., a purposeful pattern – rather than the former.

The synergies that are of interest herein can be observed at the level of muscle activation. Multiple motor units, as component variables of the movement, covary during the performance of a task. The resultant muscle activations are coordinated accordingly, as are the joint rotations that follow, in the case of non-isometric movement. In this way, a single control signal from the CNS induces common, proportional activations in all of the components that are involved in the movement [Latash 2007].

The intuitive examples of movements that embody the Principle of Abundance, as described above, allow the assumption that movements are subject to coordination in terms of muscle activity. While we can, and in fact must, expect variability at every level of analysis, it is common for performance of a task to follow some observable trajectory that is consistent over multiple repetitions of that task. Analysis of that variability, and more specifically of its distribution, reveals the tendencies that underlie the production of movements. In this way, it is possible to observe the role of synergy in motor control, as the enactment of a control signal.

The analysis of movement variability is often conducted in a mathematical space where each dimension consists of one component variable of the studied movement. One example of such a space is the orientation of the eyes in ocular control [Latash 2007]; another is the angle of the joints of the upper extremity during reaching [Scholz 2000]. A property of synergies that is readily evident in component space is the sharing of task production among the components. Observing the distribution of movement variability in component space, its location corresponds to sharing [Latash 2007]. In other words, the dependence of the task on one of the components is inherent to the location. A possible explanation for the mechanism of sharing, in the case of motor unit space, is the size principle of motor unit recruitment. Since, according to the size principle, motor units are activated in the order of their size, from smallest to largest, the distribution of motor unit recruitment over many trials will be positioned accordingly [Latash 2007].

Another feature of motor control that can be inferred from distributions in component space of records from movement is the stabilization of the performance variable. Coordination of the muscle activations that produce the task performance is equivalent, in terms of statistics, to covariation in component space. Thus, the shape of the distribution bears information pertaining to the role of synergy in the movement. Note that the location and the shape of a cluster of movement repetitions in component space are generally independent. The eccentricity of the distribution is indicative of the stability, or conversely, the flexibility, of the motor function produced by the synergy [Latash 2007]. This concept and the methods by which it is tested are addressed more thoroughly in the explanation of Uncontrolled Manifold Hypothesis, below.

The physiology that might underlie synergies in motor control is not fully understood. There is however, empirical data that suggests the role of specific areas of the central nervous system in the coordination of muscle activity. Known as a nexus of coordination for many central nervous functions, the cerebellum has been identified as a potential location for synergies. The same study found that activity in the motor cortex is connected to coordinated neuromotor activity [Kargo 2008]. It may be that the organization and strength of inhibitory interneurons and Renshaw cells plays a role in causing the covariation that has been observed in so many tasks [Katz 19993]. While there does not seem to be consensus regarding the location of and neural basis for synergies in motor control, the coordination of muscle activation may be of importance for the restoration of fine motor function.

Synergies are not the only possible explanation for coordination in motor control, but they provide a fruitful context for the analysis of movement. Studying covariation in records from repetitive movements can yield insight into the sharing and stability afforded by the synergy being employed. Of interest to the field of rehabilitation engineering, as in the fine motor restoration protocol presented herein, is the interpretation of the change in coordination that accompanies a successful rehabilitative therapy. This analysis is made possible by the analytical methods that characterize synergies, and conclusions about the mechanisms of functional gain can be made in terms of the coordination of muscle activation by synergies.

Motor Primitives

An alternate proposal to explain the coordination of muscle activations is the use of motor primitives. Acting as the units from which movements are created, primitives are considered elements of motor control and are, to an extent, analogous to synergies. However, the two concepts have distinguishing properties, and their explanation in the literature frames them as mutually exclusive. This may or may not be the case, as will be explored in the following discussion.

At its most basic, the idea of motor primitives as the elements of control follows the precedent of well known behaviors. For example, just as sounds are the elements of words, and words are the elements of sentences, primitives are meant to be the subunits from which movements are generated [Flash 2005]. Since the speech center of the brain is, to some extent, spatially distinct from the motor cortex, it is tempting to infer that the covariation of muscle activation is not the result of motor cortical control; however, because the comparison between the elemental control of motion and speech is generally figurative, making an inference about the neurophysiology of motor primitives based on the analogy may be presumptive.

As is the case with synergies, motion science has not concluded with certainty what physiology underlies motor primitives. The basis for motor primitives may be bursts of neural activity in the premotor cortex [Kargo 2008]. The location of primitive generation may also be the motor cortex or the spinal cord [Kargo 2000, Kargo 2008], as was plausible for synergies. The neural representations of primitives and the mechanisms by which they are modified and combined are not yet known [Flash 2005]. With this in mind, the neurophysiology of coordinated motor control is given less attention in the present discussion than its effects on muscle activation in repetitive fine motor tasks and their implications for rehabilitation after brain injury.

When a brain injury affects the performance of motor tasks, the nature of the motor deficit can be analyzed by means of a comparison to healthy, age-matched control subjects. In one such study, evidence of motor primitives was found in the reaching trajectories of stroke victims. Healthy reach was determined to be approximately linear [Flash 2005]; that is, the gross behavior of a healthy person's reach trajectory is a straight line [Hogan 1984, Flash 1985, Adamovich 2001].

In contrast, and not surprisingly, the spatial paths of stroke victims' reaches were found to be non-uniform and non-linear. The kinematics of these reaching paths were composed of two or more elements, so that the velocity profiles of the movements were multi-modal. A defining characteristic of these velocity primitives was the consistent proportionality between the peak velocity of a primitive and its duration. This relationship is typical of motor primitives, and it serves as a qualitative answer to Bernstein's redundancy problem [Flash 2005]. Of additional note is that this comparison to healthy control subjects as a means of motor control analysis is used in the present work.

Two explanations of the role of primitives in motor learning have been proposed in the literature. One hypothesizes that cerebellum contributes to the regulation of movements by learning trajectory control [Spoelstra 2000]. The role of the cerebellum in activation of the motor cortex, as described above, supports the biological relevance of this postulation [Holdefer 2000]. A model that learns predictive feed forward control was developed [Spoelstra 2000]. It has been suggested that the slow conduction time of the peripheral nervous system necessitates that the coordination of motor control in the central nervous system is feed forward [Zatsiorsky 2004]. An inverse dynamical system, intended to model the cerebellar neuronal network [Spoelstra 2000], would produce motor primitives in a physiologically plausible way.

Another possibility for the involvement of primitives in motor learning puts the coordination of any movement in the framework of combined elements of movement. According to this proposal, learning might be accomplished in the CNS by combining the primitives that already exist [Flash 2005]. The simplicity of this concept lends to its feasibility as an answer to the redundancy problem. At an intuitive level, though, the combination of motor primitives to develop complex new movements seems insufficient to explain early developmental motor learning. Unless all motor behavior is learned from a very limited vocabulary of ingrained primitives, the logical extension of this idea is unsatisfactory. However, relaxing any restrictions on the exclusivity of Flash's hypothesis, it may be that both Flash's idea of combining motor primitives and Spoelstra's trainable feed forward model contribute to motor learning.

The similar definitions of synergies and motor primitives prompt comparisons of the two. However, great care has been taken in the literature to distinguish between these two concepts. For example, the elements that are the foundation of movement are composed of premotor bursts. Kargo and Giszter note that this descending command should cause muscle activation that is proportionate, and more importantly, synchronous [Kargo 2008]. This is a stark contrast to the principles of synergies, which are time-varying and can therefore be asynchronous [Bizzi 2007].

Empirical evidence has added support to claims of motor primitives as the basis of movement coordination. During frog hind limb wiping, the organization of premotor drive primitives is preserved, even when modified by the incorporation of proprioceptive feedback at the spinal level. However, the consistency is primarily found in burst duration, and not in timing or amplitude. From these results, Kargo and Giszter concluded that motor primitives, not synergies, are the fundamental units of motor control [Kargo 2008].

Previous work has also studied how the motor control system modifies the properties of primitives. During a reaching task, healthy volunteers were subjected to a force field that perturbed their upper extremity kinetics [Thoroughman 2005]. As subjects adapted to the novel condition, as evidenced by their straight hand paths, a time-series analysis was conducted on their movement errors. Results indicated that the movements were derived from a combination of tunable Gaussian curves, corresponding to the combination of primitives to coordinate the reaching movement. Furthermore, the analysis showed that the properties of the primitives, especially during their modification, resemble the tuning curves of Purkinje cells in the cerebellum [Thoroughman 2005]. This finding indicates a possible mechanism for the use of primitives in motor control and learning, and it further supports the claim that primitives are more likely as elements of control than synergies.

Motor primitives can be observed explicitly in terms of their relevance to Bernstein's redundancy problem. Work with reaching movements in octopi takes the idea of kinematic redundancy to its extreme. There are no joints in the completely flexible arms, which makes them “hyper redundant” [Sumbre 2006]. The invertebrate motor control system, while structurally and evolutionarily distant from that of primates, makes use of motor primitives [Flash 2005]. Expanding on this finding, studies dealing with the coordinate space of motor control find that octopi use a strategy that is, of necessity, distinct from human motor control. The octopus first stiffens its arms by means of muscle activation, effectively forming three joints. This stiffening is performed in a so-called “limb configuration space” [Sumbre 2005]. The movement is then completed in intrinsic coordinates [Sumbre 2006], which is comparable to human reach control [Hollerbach 1990].

This scheme reduces the degrees of freedom available for the task considerably, making control easier. While this may call to mind the “freezing DoFs” theory described above, it does not necessarily support that argument. The creation of joints, which is accomplished by the intersection of proximally- and distally- propagating waves of muscle activation, may be a motor primitive itself [Sumbre 2006]. The coordination of muscle activation in the hyper-redundant arm demonstrates the utility of motor primitives in simplifying a complex system using synchronous muscle activations, thus providing evidence from a non-primate model that suggests motor primitives instead of synergies.

These examples of empirical evidence in support of motor primitives as the elements at the foundation of movement coordination, as well as the above descriptions of synergies in the role of the elements of movement, are typical of the polemic in the motion science literature. Motor primitives and synergies are generally depicted as being mutually exclusive, and in the infrequent cases where both are mentioned in the same paper, the intention of the discussion is to advocate one rather than the other [Feldman 2006, Kargo 2008]. However, it may be that the distinction between motor primitives and synergies is more distinct in theory than practice, which would obfuscate the common attributes of the two hypothetical elements of control. For example, while motor primitives are strictly defined as synchronous and synergies can be time-varying [Kargo 2008], it may be possible that synergies are effectively synchronous in many cases. Furthermore, the consistent relationship between speed and duration in motor primitives fits the definition of synergies as well [Flash 2005, Latash 2007]. Since the present work does not record neural activity directly, the distinction between synergies and motor primitives is not treated strictly. However, the properties described above are considered in the discussion of the present work's experimental results, as the motor learning from training with the PAMI device can be considered the combining of primitives or synergies.

At a higher level of control - specifically the theoretical cortical activity in which coordinated activations in the form of synergies or primitives are generate - the properties of elements are reflected in the planning mechanisms. The following brief review will give additional background for a possible role of motor planning in the motor control analysis herein. Internal models fall under the umbrella of frameworks in which the central nervous system somehow solves the inverse dynamics necessary for a given movement. In contrast, the Equilibrium Point Hypothesis (EPH) hypothesizes that movement is the result of retuning of muscle spindle's “set points”, so that the stretch reflex is responsible for muscle activation [Zatsiorsky 2004, Latash 2008]. As was the case with the elements that enable coordination in motor control, these two approaches are framed as opposing one another [Feldman 2006], but share some common attributes [Spoelstra 2000].

Optimization reduces the complexity of motor control problems like redundancy by limiting the DoFs, and thus the variability, of a multidimensional movement. Its implementation follows a general algorithm that begins with the selection of a cost function. This cost function can be characterized in a number of ways, including mechanical, psychological, etc. The unique solution that maximizes or minimizes the cost function is then found, presumably by some component of the central nervous system [Mussa-Ivaldi 1991, Todorov 2004].

Kargo's above-described work, which measured parameters of motor primitives in an animal model, includes evidence that may suggest that internal models are more accurate a concept than EPH. The results indicated that the three premotor drive bursts that cause a frog hind leg wiping movement were not regulated according to any pairwise covariance. Furthermore, the three bursts were not uniform in their sensitivity to the phase of a feedback-inducing vibration. These findings imply that control is the coordination of single bursts [Kargo 2008], not the covariation of two or more bursts that would follow a modification to the equilibrium point.

The Equilibrium Point Hypothesis (EPH) was originally proposed in 1965 [Feldman 2006]. At the basis of EPH is the notion that the central nervous system coordinates movements without any knowledge of the kinematic or kinetic relationships at the cause. Predicting the state variables, such as muscle activations or joint angles, necessary to perform a task would require the motor control system to calculate muscle activation levels from an inverse dynamic model; this requirement is a general characteristic of internal models. Instead, the EPH predicts that the objects of control are parameters of the neuromechanical systems that the inverse dynamic models would characterize. Thus, rather than control a state variable – such as a joint angle – by predicting the parameters that would lead to it, the central nervous system alters the parameters themselves, and the state variable changes as a result [Latash 2008]. This difference is subtle at the semantic level, but the physiological explanation of the EPH is distinct from the state variable control of internal models.

The parameter that is the object of central nervous control according to EPH is the threshold of change in muscle length. By changing the threshold length of the muscle, termed λ in the literature, the motor control system can induce activation and a resultant force. This phenomenon is linked to the stretch reflex, inasmuch as a change in muscle length past its threshold will cause a contraction in opposition to the perturbation that stretched the muscle. In this way, changing the λ value of the muscle is essentially analogous to activating the stretch reflex [Feldman 2006].

Because of its computational simplicity, λ control is plausible not only at the level of individual muscles, but also of joints and limbs. Changing the set point via λ therefore causes activations of the agonist muscles whose λ values have been shortened, while the antagonist muscles are inhibited from activation during the lengthening during joint rotation by their longer λ values [Feldman 2009]. The muscle activity that results from a change in λ can be expected to covary, which is an essential characteristic of synergies. In other words, the role of coordination of movement by synergies can be traced back to the physiological explanation of EPH.

The role of λ control in muscle activation has been suggested empirically through illustrative examples. For example, passive oscillation of the elbow joint causes small EMG bursts that oppose the opposition. These bursts are similar before and after a large voluntary change in elbow angle [Ostry and Feldman 2003]. This implies that the λ values of motor neurons in resting state are close to their current length, and that a change in these values is associated with a voluntary change in muscle length [Feldman 2006]. Because EPH, like internal models, is an explanation of a very high level of motor control, it is a theory that is difficult to prove conclusively.

While internal models and EPH are usually framed as being opposing ideas, it should be noted that in some respects, the two are not dissimilar. For example, it has been noted that optimization is not incompatible with EPH, as the essential difference between the two concepts is one of semantics [Latash 2007]. Along those lines, consider the model developed by Spoelstra, described above, in which a neuronal network in the cerebellum generates the control signal for movement. Feedback pertaining to error, a primary control signal in EPH, trains the inverse model, allowing the system to learn [Spoelstra 2000]. In this way, the two are actually compatible. Moreover, equilibrium point trajectories have been described as being generated by neuronal computations [Latash 2007]. This may be the foundation of a fundamental overlap between the EPH and internal models.

The mechanisms underlying motor control are not fully understood. At a number of levels of the motor control hierarchy, hypotheses explaining the nature of movement generation have proven to be contentious. Nevertheless, some consensus of the basics of control has emerged, and this comparability informs the present work. Inverse models and EPH are fiercely contested in the literature, but their common treatment of motor variability as the result of a solution to the redundancy problem – or rather, as taking advantage of the Principle of Abundance – motivates the Hypothesis 3, above. Furthermore, while motor primitives and synergies are defined according to distinct features, there is little doubt that elements at the foundation of movements coordinate kinetic and kinematic activity to produce repeatable task performance. The methods that have been developed to explore this idea are modified for use in the present work, and their descriptions follow.

Structure of Variability

It is not sufficient to simply study the average performance of a motor task. The variability of repeated performances is information bearing as well. In fact, it can be considered as fundamental a measure as the average trajectory itself [Latash 2007]. Knowledge of the component space in which the movement is being performed allows variability to be associated with temporal and spatial relationships. The measured correlations can be reflective of the synergies employed by the motor control system, particularly in a time-locked movement [Scholz 2000].

A number of methods have been developed to reconcile statistical variability in observations of movement. Ranging from a simple comparison of variance to a randomization technique, these approaches resolve variability into a meaningful analytical rater of motor coordination. The following is a summary of some of the methods that have been used in the motion science literature. Note that these techniques are not ordered according to their relevance to the present work, but are instead introduced such that their interrelation is easily understood.

Uncontrolled Manifold Analysis

Variability can be associated with either detraction from repeatability or with the abundance available to the system. Looking only at the task variable, repeated performance may be seen to be highly invariant. However, the components, such as joint angles or muscle activation levels, that generate movement, are often much more variable than the task they produce (For a complete review, see above). Thus, the stability of a performance variable can allow insight into the pattern of elemental variables.

The fundamental principle of Uncontrolled Manifold (UCM) analysis is that the motor control system accounts for kinematic redundancy by orienting variability along a trajectory in component space that stabilizes performance of the task to which the system is attending. In coordinating muscle activity during movement, and thus answering Bernstein's redundancy problem, synergies increase movement reproducibility. The stable states that emerge in multiple repetitions of a task can be considered patterns of movement, and measuring their variability can be used to measure the stability imparted by the motor control system [Latash 2007]. UCM analysis hinges on the resolution of variability into that which does and that which does not stabilize the task variable. The Uncontrolled Manifold is the subspace of component space in which variability does not affect task performance, and thus is left uncontrolled by the motor control system.

To that end, UCM analysis is concerned with the structure of variability during repeated performance of a task. Specifically, the variance of components is numerically or analytically partitioned into the directions that do and do not affect the performance variable. The two directions are termed V_{ucm} and V_{orth}, corresponding to the directions that define the UCM and the space orthogonal to it, respectively. The contrast in distributions into these directions shows how coordination stabilizes performance, but also how flexible it allows performance to be [Latash 2007].

UCM analysis can be applied at a number of levels of the motor control hierarchy. Variables can be mechanical, such as forces, moments, angular displacements, etc. [Latash 2007], or electrophysiological, such as the amplitude of muscle activation [Krishnamoorthy 2003]. For this reason, the uses of UCM are diverse, including studies of finger force generation to characterizing whole-body coordination during gait [Latash 2001, Black 2007]. UCM can also be applied in cases where the task variable is known, or it can test hypothetical task variables to identify the target of control [Latash 2001, Scholz 2000].

A particularly illustrative example of UCM analysis with an unknown task variable is the control of pistol aiming. It is unclear, prima facie, how the motor control system ensures that the upper extremity orients a pistol such that it is pointed at a target. Possibilities for coordinating this movement include the orientation of the gun, its spatial position, and the position of the center of mass of the arm and gun. To determine which of these task variables the motor control system stabilizes during the movement, UCM analysis was conducted on the kinematics of the upper extremity with respect to each possible task variable. Through this analysis, Scholz determined that the motor control system coordinates joint rotations such that the orientation of the pistol is stabilized throughout the duration of the movement [Scholz 2000].

UCM analysis has also been used in work with a population with motor dysfunction. In one study, kinematic recordings of typically developed children between the ages of 8 and 10 during treadmill gait were compared to age-matched Down syndrome patients. By partitioning the data with respect to two hypothetical task variables, head location and center of mass location, the two groups' control strategies for ambulation were evidenced by their total variability and their task variable [Black 2007]. Earlier work performed a similar analysis on finger force production in adult subjects with and without Down syndrome [Latash 2002].

By performing multiple analyses over the course of repetitive training, it is possible to observe a change in synergies during motor learning. UCM analysis compares multiple repetitions of a task, but rather than use all recorded trials for one analysis, it is possible to separate records into epochs in order to compare conditions before, during, and after training. Previous work has found suggestions of the patterns of

UCM analysis that emerge during motor learning. Total variability increases as the system begins to adapt to new conditions, after which V_{ucm} decreases less than V_{orth} in concordance with the establishment of a new synergy [Yang 2007]. In an open kinematic chain, highly redundant, ballistic movement such as throwing a Frisbee, days of practice resulted in decreased total variability [Yang 2005]. Completely novel tasks, such as bimanual movements, are associated with a decrease in variability [Schoner 1992].

It has been proposed that learning may be the elaboration of new internal models, or the refinement of existing internal models [Wolpert 2001, Shadmehr 2004]. This does not immediately appear to agree with the increase in V_{ucm} after adaptation [Yang 2005, Yang 2007]. Refining existing internal models can be expected to decrease V_{ucm}. To explain the patterns of V_{ucm} and V_{orth}, we can look at the improvement of internal models. After the initial increase in variability due to novel conditions, stability will increase. Stabilizing a movement is not dependent on V_{ucm}, but rather it requires a decrease in V_{orth}. Thus, while V_{ucm} can be expected to decrease over the course of training [Yang 2005, Schoner 1992], learning is associated with a decrease in V_{orth} [Yang 2007].

Difference in Variance Index

It is also possible to compare the structure variability of the component variables and the task variable based only on their distributions, without resorting to the linear algebra inherent to UCM analysis. In principle, this approach is a simple version of the UCM method. The technique has garnered the informal nickname "Poor Man's UCM" as a result, although it is referred to in the literature as the Difference in Variance Index (dVI) [Latash 2002].

dVI has been used to compare synergies in motor control between populations in tasks where the units of the components and the task are the same. In such tasks, dVI can eliminate the need for partitioning variability into subspaces. In doing so, it bypasses the requirement of a forward model, which is partly responsible for the simplicity of the technique. The task variable is considered a simple combination of components in tasks that can be analyzed by dVI. For example, the variability in the sum of finger forces can be compared to the sum of the variabilities in the individual fingers during a force production task [Scholz 2003, Latash 2002].

As with UCM analysis, dVI has been used to compare synergies in control between healthy subjects and those with Down Syndrome. Results were similar, suggesting that subjects with Down Syndrome experience a deficit in coordination that interferes with the total force control, so that subjects did not make use of motor abundance as well as healthy subjects. Additionally, total force variability decreased with practice [Latash 2002]. For this reason, it is expected that dVI will be a potent tool for analysis of motor learning after brain injury in the present study.

Other Analysis Techniques

In addition to the above analyses, a number of techniques for the characterization of motor variability have been developed and used in the motion science. For a variety of reasons, such as similarity to UCM or insufficient utility in motor control analysis, these methods are not used in the present work. However, their description is worthwhile, if only to provide a perspective on the complexity of the motion science field. Note that this review is neither deep nor broad, and a number of approaches are not included, including entropy, dimensionality, or dynamical systems analysis.

The Covariance by Randomization (CR) method, developed by Shadmher, is one such technique for motor control analysis. As in the UCM method, a forward model relating component variables to the task variable is the basis of an assessment of variability in component space. If component variables are structured in component space in a way that stabilizes the task variable, this can be considered a reflection of coordination, such as by synergies. To test this hypothesis, recorded data are shuffled so that the order of component variables is randomized within each component.

In this way, the new task variable is calculated from a new grouping of disordered component variables, but the range and variance along each dimension of the component space are unchanged by the CR processing. The variance of the new task variable is then compared to recorded values to determine whether the component variables were generated under the coordination of a synergy [Muller 2003]. A review of this method has suggested that UCM and CR are fundamentally related [Schoner 2007].

A key difference between the UCM and CR approaches is that the component space in UCM analysis must have the same units. CR analysis, on the other hand, has been applied to throwing and drumming, both of which are dependent on both position and velocity. The use of a forward model to relate the component variables to the task variable, while common both to UCM and CR analyses, allows the latter to generate a direct, scalar comparator for motor analysis.

The Goal Equivalent Manifold (GEM) approach also shares traits with UCM analysis. For example, the manifold of GEM is calculated as a subspace of component space using a forward model that maps components to the task. Using this manifold, the coordination of activity to produce a repeatable task can be measured. A key difference, however, is that while UCM analysis is concerned with the orientation of the manifold, the GEM manifold is calculated as the set of all components that produce equivalent task behavior. Thus, the result of GEM analysis is an analytical solution, which is then used to assess the sensitivity of task performance to error in the components. This is similar to UCM analysis enough to obviate its use in the present work, but the concept is unique in that it yields a multidimensional rater of performance sensitivity [Cusumano 2006].

Another analysis tool makes use of the fact that the overall amount of variability is also information bearing; performance tightly clustered about the mean can be thought of as precise, and vice versa [Latash 2007]. The Variance Ratio is a two-way statistic that measures variability in multiple signals, providing a rater of the precision of repeated movements. Its values range over the spectrum between identical repetitions and random noise. It has been applied to the motor control analysis of gait, and it has also served as a comparator for SMP and EMG [Hwang 2003, Yungher 2009]. Using Variance Ratio to assess the variability of repeated motor performance can be productive, but it may not yield as much information about motor control as a model-based technique like UCM or dVI.

Several other explanations of variance in motor control employ similar techniques. One attributes trajectory selection to a terminal variance-minimization scheme. While this has been supported by experimental evidence from saccadic eye movements and reaching tasks, it has not been tested on redundant motor systems [Harris 1998]. Another postulation, “minimal intervention”, uses feedback optimization between effector and target as well as among control signal variances. The latter are used as representations of the effort involved in the performance of the task. This method is actually compatible with UCM analysis, although it is more computationally complex [Todorov 2002]. In addition, it introduces questions regarding the incompatibility of feedback loops with biologically relevant time delays. As noted above, however, work by Spoelstra incorporated feedback as a learning tool for an optimized neural network [Spoelstra 2000].

The wide range of techniques available in motion science are evidence of the effort that has gone into answering questions about the nature of motor control. Experiments may be designed to generate data that, when processed with such tools, yields insight into aspects of the motor control system. The present work was designed with this capacity in mind, and the analysis of movement variability herein is expected to contribute to knowledge of the mechanisms by which fine motor function is improved after brain injury. The process of selecting the methods of data analysis was chosen with respect to precedents from the literature and to the features and limitations described above.

Chapter 4 – PAMI Development and Use

The Proprioception-Augmenting and Measurement Interface (PAMI) was developed with a dual intention: to restore function to brain injured individuals experiencing motor dysfunction, and to enable inference into the properties of the motor control system during rehabilitation after brain injury. The former falls into the category of rehabilitation science, and it is both motivated and informed by reports on the efficacy of current technology. The latter is a question of motor control analysis, therefore performed using established techniques on recorded data.

The following is a description of the background for the research presented herein. The development of the PAMI device is recounted, highlighting the support in the literature of aspects of its design and previous experiments performed in our lab that guided the process. The demonstration of PAMI's efficacy in the restoration of function is outlined, and the selection of specific methods, such as inclusion criteria, is described. The features that are extracted and compared post-hoc are explained as well. Finally, the techniques for analyzing data from the perspective of motor control are discussed. In this way, justification for the present work's methods is detailed below.

Proprioception Augmenting and Measurement Interface (PAMI)

The name of the device that is introduced herein was selected to encompass its capabilities. Its feedback provides information to the insensate user that is not available via normal, afferent neural activity; hence, whatever residual proprioceptive signals are incorporated into motor control are supplemented by PAMI visual feedback. The records of muscle activity that are converted to feedback in real-time are also stored for post-hoc evaluation. Because of their utility in motion analysis, these measurements are another important function of the device.

PAMI was developed to fulfill these purposes, which is reflected in specific aspects of its design. The hardware is based on a muscle activity measurement modality unique to our group, and previous versions of the device have been used in a wide variety of projects. The software was designed to fit the particular needs of the brain injured population for whom PAMI is intended, although it is also the product of iterative improvements on previous work in our group. A number of studies have used the device for populations or protocols distinct from the present research, suggesting the hypotheses set out above. The device is shown in use in Figure 1.

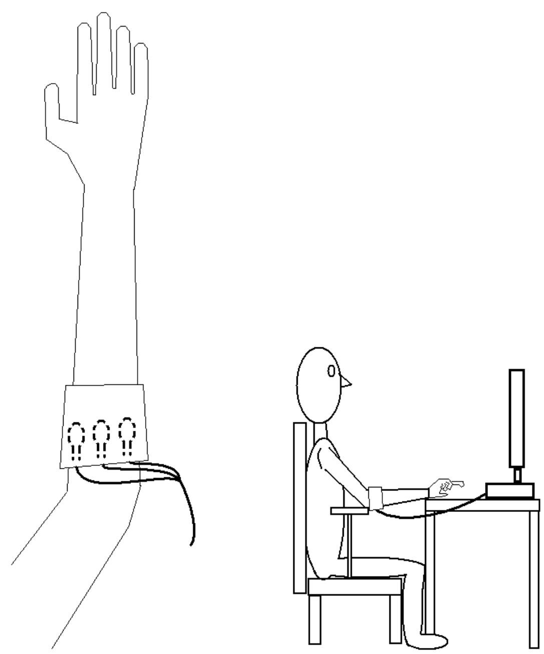

Figure 1 – The PAMI device. Worn on an upper limb as in typical use (left), and shown during training (right). Note the distribution of sensors about the forearm, and the support of the elbow and wrist during training.

Surface Muscle Pressure

A technology unique to the RU Rehabilitation Laboratory group, called Surface Muscle Pressure (SMP), has been in use for a number of years in diverse applications relating both to rehabilitation science and motion analysis. SMP registers muscle activity in the extremities by measuring the pressure they exert in the radial direction. While SMP is comparable to EMG in many ways, its use entails certain features that are distinct from myoelectric recording. In this way, SMP is ideal to serve as the hardware of PAMI.

SMP works on the principle that as limb muscles contract, the radial force pattern in the limb changes, which can be measured as positive or negative pressure changes at the surface. The SMP sensors register signals that can be generated by both near and distant muscles, including muscles that are either deep or superficial. Studies in both the upper extremity [Kim 2007, Wininger 2008] and the lower extremity [Yungher 2009] have used an array of SMP sensors to register whole-limb muscle activity.

It is possible to target specific muscles using SMP for limited applications. For example, Morris used a pair of SMP sensors to record voluntary activation of the thumb extensor muscle in children with CP [Morris 2008] and Shain compared the flexor digitoris longis SMP signal to grip force [Shain 2009]. In both of these cases, targeting the muscles of interest was accomplished by palpating for anatomical landmarks, which suggests the difficulty this procedure. Additionally, the measured muscles were selected in part due to their ease of identification with palpation, and no attempt was made to distinguish between those muscles and others, neither agonists nor antagonists. Targeting of individual muscles is limited to studies that are constrained in scope to simple movements with predictable kinematics and one major agonist. It should be noted that a similar limitation characterizes rehabilitation using EMG biofeedback (see Chapter 2)

In addition to its spatial amalgamation of information, SMP signals are temporally smooth as well. Previous work has shown that the conformational changes in muscle shape and consequent pressure distribution throughout the limb are low-frequency processes that yield highly reproducible waveforms for specific motions. Using the Variance Ratio of measurements from gait as an example, where 0 signifies identical waveforms across repetitions and 1is the result of completely random signals, SMP values consistently generated values less than 0.1 [Yungher 2009]. SMP values from forearm muscles were remarkably well correlated to grasp force, in a whole-wave comparison, when subjects varied grasp force according to a slow, sinusoidal cue [Kim 2007].

In contrast, EMG values are considerably more noisy. Variance Ratios of EMG signals during gait are substantially greater than those of SMP records, the former usually exceeding the latter by at least an order of magnitude [Yungher 2009, Hwang 2003]. This disparity, which is visible in an individual subject's ambulation at three different speeds in Figure 2, can be attributed to the nature of the electrical signal that generates mechanical activity. The neural processes that underlie muscle activation are transient and stochastic, which explains their highly variable EMG recordings [Granata 2005].

In addition to the smoothness inherent to SMP signals, they also compares favorably to EMG in terms of sensor donning. Onset timing of the *vastis lateralis and medialis* muscles in a healthy leg during gait has been shown to be highly dependent on EMG electrode position [Wong 2006]. SMP outputs, in contrast, are relatively unaffected by variations in placement on the muscle, due to the spatial summation described above.

An array of surface EMG sensors for

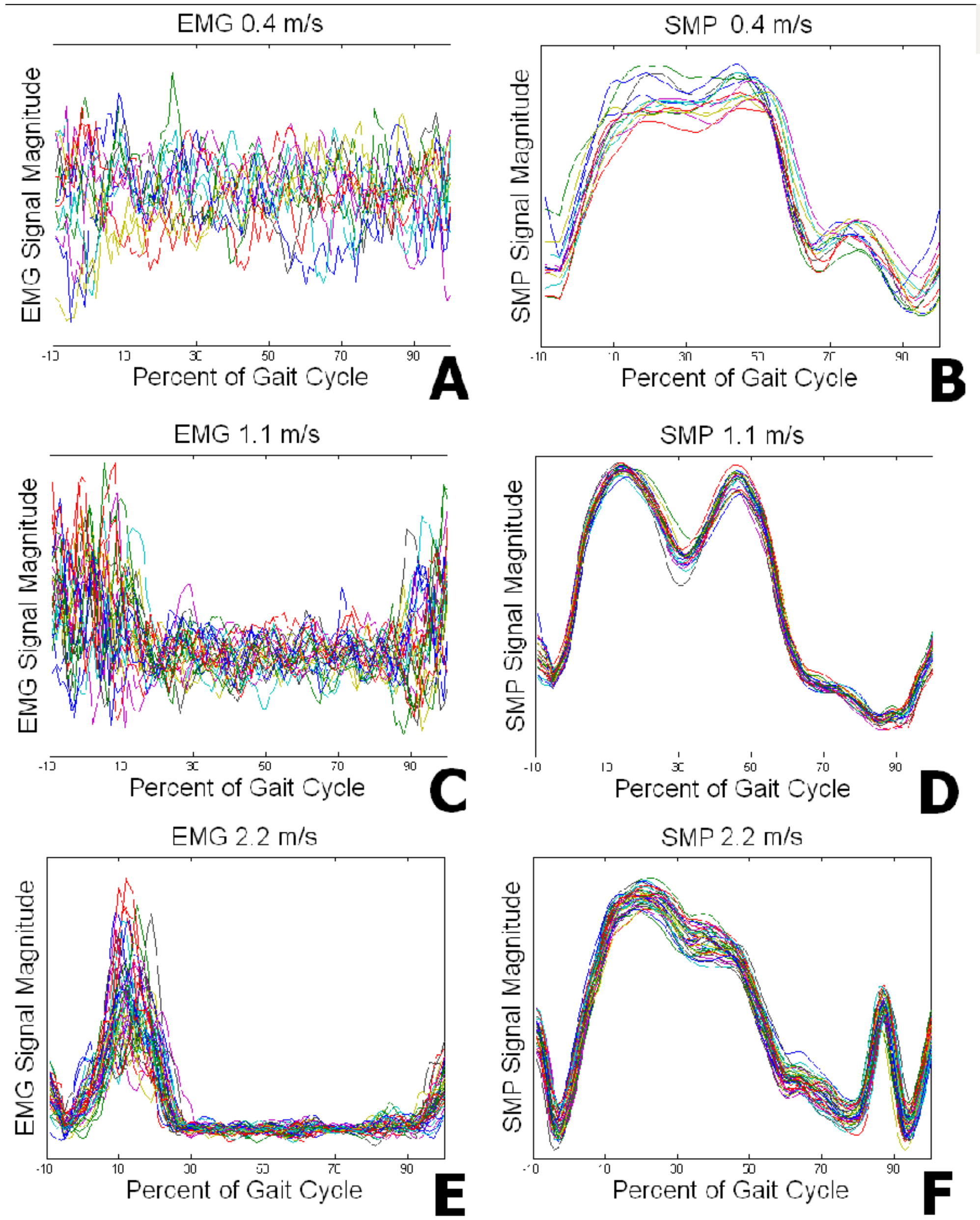

Figure 2 – Superimposed recordings during successive strides for a representative unimpaired subject during gait. EMG (left) and SMP (right) traces are shown for 13 strides at 0.4 m/s (A, B); for 24 strides at 1.1 m/s (C, D); for 39 strides at 2.2 m/s (E, F).

EMG biofeedback must be applied with care in order to register useful records of muscle activation. On the other hand, an SMP array can be donned quickly and easily, since signals will register both near and distant muscle activations regardless of placement.

Another contrast between the EMG and SMP modalities can be found in the processing required to make records useful. In order to be used in real-time, EMG signals must be demeaned, rectified, and smoothed in a process termed “enveloping” [Hodges 1996]. Since SMP signals are naturally smoother, none of the above processes are necessary in the applications for which the technology has been used as yet, with the exception of a comparison to EMG in which the two modalities were processed identically for the sake of comparability [Yungher 2009]. The lack of a standard method for smoothing EMG may complicate post-hoc analysis and confound comparison to previous studies. Moreover, the computational requirements of EMG processing, especially the tendency of smoothing to induce delay, makes EMG difficult to use for real-time applications such as biofeedback.

While EMG and SMP register muscle activity with similar fidelity to important temporal landmarks, the differences in their use are significant. Donning and doffing sensor arrays is easier and faster for SMP than for EMG, which is advantageous both for the practitioner and the user. EMG output is buried in noise, which requires that the signals be heavily processed before use. In contrast, SMP records are smooth and consistent from trial to trial. The calculation of PAMI feedback, which is described below, must be based on low-frequency signals that are consistent across repetitions if the feedback value is to be relevant to the restoration of function. At best, the use of EMG technology with the PAMI device would be marked by a frustrating lag between action and feedback. For this reason, SMP was the technology that was chosen for use in the present work.

PAMI Feedback

The design of the PAMI software was geared towards generating clear, useful biofeedback that would facilitate restoration of function after biofeedback. This task was accomplished using lessons from the literature, as outlined above (see Chapter 1), as guidance. Previous work from our group, involving SMP but otherwise unrelated to rehabilitation science, was also incorporated into the development process. The result is a biofeedback modality that provide advantages compared to existing rehabilitative technology.

SMP was originally developed as a control source for control of a prosthetic hand [Phillips 2005]. While it was originally processed using a linear adaptive filter, the project was revisited using pattern recognition techniques to increase the applicability and the robustness of the controller. In this application, SMP measurements are used for prosthesis control using principles of pattern recognition [Yungher in preparation].

Using the voltage across each SMP sensor as a dimension in feature space, repeated performance of a variety of grasp types generates clouds of data. In one version of the scheme, each repetition generates one data point; another, more physiologically relevant method creates data points from 250ms windows of SMP signals, which minimizes the lag between volition and action such that it is virtually imperceptible [Englehardt 2003]. Among the techniques of pattern recognition that were applied to grasp data was the Nearest Neighbor method. An unlabeled data point is classified according to the label of the data point nearest to it in the feature space, which is found according to the minimal Euclidean distance between points.

The fundamental concept of Nearest Neighbor pattern recognition, the on-line calculation of the distance in feature space between generated values and known, labeled values, was adapted from the realm of prosthesis control for use in rehabilitation science. PAMI biofeedback is simply the distance in feature space between the real-time SMP values, termed Performance, and a previously recorded value. Rather than comparing the Performance to clouds of data, only one comparison is made, to a single point recorded during calibration. This known point in feature space is dubbed the Target.

As described above, the amplitude of each SMP sensor constitutes one dimension of the feature space. The dimensionality of the feature space is limited only by hardware considerations; as many sensors as can be incorporated into the PAMI device can be added to the feature space. Using the Euclidean distance between Performance and Target acts as a reduction of dimensionality. Euclidean distance is the square root of the sum of the squares of the differences in each dimension, calculated using

$$\text{Dist} = \sqrt{\sum_{n} (\text{Target}_{\text{i}} - \text{Performance}_{\text{i}})^2} \qquad \text{EQ 1}$$

where n is the number of sensors. In this way, the feedback generated from multiple sensors is a scalar value.

Using a scalar value for biofeedback can be advantageous for a number of reasons. A one-dimensional value such as the distance between Performance and Target is easily represented as a visual modality. We chose to display this distance as the level of fluid in a Tank in the Labview Virtual Interface [*National Instruments Corporation, Austin, TX, USA*] that the user sees, such that minimizing the distance between

Performance and Target is shown as maximizing the height, or “fullness”, of the Tank. A screenshot of the display from the Virtual Interface is shown in Figure 3. This visual configuration was chosen to make the incorporation of PAMI biofeedback into motor control as intuitive as possible, as is discussed below.

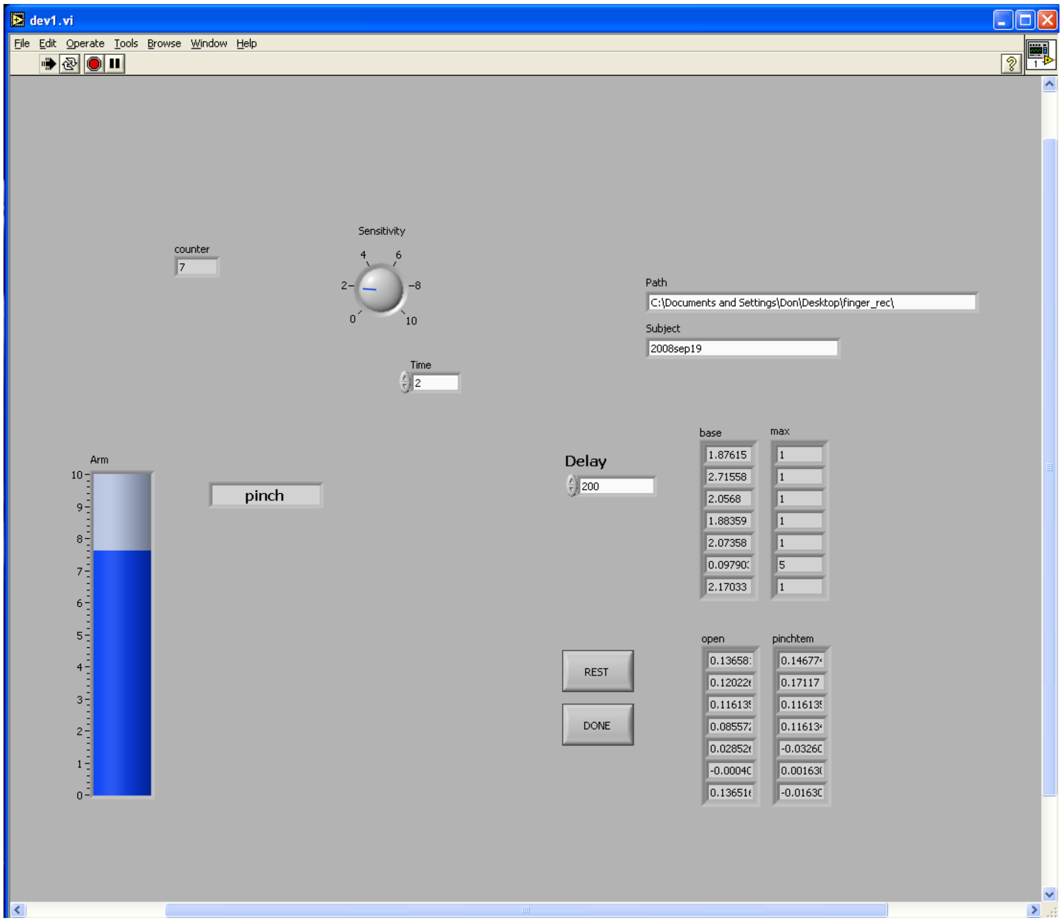

Figure 3 - Screenshot of PAMI Software Display during training with feedback. Note the tank on the left, which shows the PAMI value in real time.

The smooth waveforms generated by SMP fit very well into this feedback design. It is also likely that a higher-frequency measurement modality such as EMG would not work for PAMI biofeedback. The noisy signal from each EMG signal would vary widely in feature space, making the distance between Performance and Target in an EMG-based feature space a very noisy signal. The range and variance of the biofeedback signal would probably be much greater with EMG than with SMP, making the use of EMG for this novel biofeedback modality considerably more difficult for users.

The nature of PAMI biofeedback allows for a specific advantage that addresses a number of shortcomings of existing therapeutic devices. For example, the repetitive task performed by the user can operate with any configuration of the hand. Since the Target in SMP space is essentially a signature of that hand posture, specific muscles do not need to be identified and measured by the device. Thus, as the biofeedback value signifies the distance in feature space from between Performance and Target, the user is informed about the performance of the task. No attempt is made to give more detailed feedback about the nature of performance; it is assumed that the PAMI biofeedback is sufficient to promote neural reorganization. This assumption is tested as part of Hypothesis 1, inasmuch as improvement of motor function using PAMI biofeedback is contingent on the efficacy of the feedback modality.

The utility of SMP for a wide variety of hand postures and movements has been demonstrated previously. Applied in pattern recognition for prosthesis control, in which the goal is to successfully discriminate between grasp types, the SMP amplitudes during a grasp were found to be highly separable. Looking at whole-wave mean values, six distinct hand postures were separated with accuracy as high as 97% [Yungher 2007]. This suggests that replacing the clusters of data that define each grasp type with a single point would result in comparable distribution. In turn, this separation in feature space implies that the distance between Performance and Target is representative of the correctness of muscle activation during repetitive performance of a fine motor task.

To translate this implicit utility to real-world application, the protocol for use of the PAMI device was designed around setting the Target value. Under the supervision of a clinician, the subject performs one repetition of the task that will be the focus of the repetitive training. As described above, the SMP values recorded during this activation become the location of the Target in feature space. The clinician's involvement ensures that the biofeedback promotes goal-oriented learning [Byl 2003]. In this way, the calibration stage of PAMI use is the key to the device's flexibility.

The robustness of PAMI biofeedback in its applicability to complex hand postures stands in contrast to the limited utility of EMG biofeedback. As described above (see Chapter 2), training with EMG is generally restricted to the control of single muscles or joints [Huang 2006]. The feedback is often shown as activation values from agonists and/or antagonists during such rotations, but the intuitiveness of the feedback display decreases with each additional muscle. Binary volitions such as grasp/release can be identified using EMG sensors [Farina 2004], but generally, fine motor control restoration with EMG is constrained to simple movements [van Dijk 2005, Krebs 2003].

This type of feedback is Augmented, according to the distinction detailed previously (see Chapter 2). Registering muscle activity during a fine motor control task facilitates feedback about the “hidden layers of control” [Van Dijk 2005]. Additionally, using SMP recordings allows for feedback to fall in the category of Knowledge of Performance, also described above, because PAMI feedback operates in real-time, guiding activity on-line rather than following it. Designing PAMI to give Augmented feedback fitting the Knowledge of Performance characterization promotes the restoration of motor function and substantiates the “Proprioception-Augmenting” naming of the device.

Preliminary Studies

A number of studies that have been performed in recent years have used the PAMI device with some success. While the present work demonstrates with statistical significance that the device promotes the restoration of motor function, previous research suggested the likelihood of this outcome. Brain injured individuals whose impairment excluded them from the cohort of subjects in this thesis work were able to use PAMI in alternate ways. In some cases, their adaptation of the technology to their needs was surprising and informative.

One volunteer agreed to participate in a preliminary study of PAMI, which was performed during the development process. Approximately twice a week for eight weeks, this subject performed a repetitive pinching task with PAMI biofeedback displayed on a computer monitor. No attempt was made to gauge his motor function or its change over the course of training. Additionally, since the software had recently been programmed, there were a number of changes made to it from week to week. Data generated during training were only captured during one of the sessions, and their analysis was exploratory rather than thorough.

Despite the lack of consistency in training and the complete lack of independent functional testing, the subject reported an improvement in fine motor control. His ability to perform thumb-finger opposition increased with the index finger, he began training with the middle finger, and again moved on to the ring finger thereafter. This result encouraged the use of PAMI in a more rigorous clinical study to assess its applicability to fine motor rehabilitation.

During the preliminary work in collaboration with physical therapists at JFK-Johnson Rehabilitation Institute, PAMI was also used to restore function for a small number of persons experiencing significant impairment. The functional deficits displayed by these participants did not meet the inclusion criteria of the present work; their movements were characterized by considerable spasticity and the inability to release muscle tone. They were unable to perform the repetitive task due to its periodic relaxation requirement, and while they were not tested immediately before or after training with PAMI, it is unlikely that they would have been able to complete the Nine Hole Peg Test.

The physical therapist administering the training modified the protocol in response to these subjects' abilities. Rather than perform a repetitive action, subjects were instead instructed to maintain a specific hand posture, and to use the PAMI biofeedback as guidance. The therapist positioned the subject's hand in a posture that required activation of non-spastic muscles, so that coactivation of the antagonists would decrease the feedback value. Anecdotal reports from this type of work suggested that participants were able to improve the sustained hold of hand posture over the course of training.

The above work is preliminary and anecdotal, and with the exception of the work with CP, it is entirely qualitative. However, the experience gained from these efforts was instrumental in the development of the experimental protocol of the present work. The potential of PAMI for long term use, for a variety of motor impairments, and for a range of degrees of impairment has been suggested by participants' reports. Perhaps the most encouraging result was participants' frequent eagerness to continue use of the PAMI device in the future. It was with these reports in mind that the experimental protocol was defined.

Restoration of Function

Assessing the efficacy of the PAMI device is a key to the present work. The device is intended to guide the restoration of fine motor function after brain injury, so the assessment of its use is based on a measure of subjects' fine motor control. Recall that Hypothesis 1 states,

> “Restoration of fine motor control can be enhanced by the use of biofeedback from the Proprioception-Augmenting and Measurement Interface (PAMI) device to supplement proprioceptive deficit. Performance on standard functional tests will improve after training with feedback (WF) as compared with the no feedback (NF) condition.”

The selection of a standard functional test for this hypothesis was based on a literature review and coordination with collaborating therapists, as was the choice of how many repetitions subjects are instructed to perform. Inclusion criteria were also developed in conjunction with clinicians' input. The details of the experimental protocol are explained in Chapter 5, but the rationale for their development is as follows.

Repetitive Training

In accordance with Hypothesis 1, the experiment is designed to promote the improvement of motor function in brain-injured participants. Instructions to perform periodic activity, interspersed with periods of relaxation, are concomitant with repetitive training. The selection of specific aspects of the training protocol followed examples from previous studies, and was intended to mitigate uncertainty in conclusions about the efficacy of PAMI.

At its most basic, the study consists of subjects undergoing repetitive training with PAMI biofeedback. To measure the efficacy of training with PAMI, performance on the 9HPT, a fine motor function assessment, is timed before and after the training period. In this way, the change in time to completion of the 9HPT is indicative of the change in fine motor function. However, it is possible that any training would be beneficial for brain injured subjects, regardless of feedback, and repetitive training has long been used successfully [Byl 2003]. To control for this possibility, subjects participate in two training epochs – one with feedback from the PAMI device (WF), and one without (NF). Results from each condition are compared, both to each other and to baseline. It is expected that performance on the 9HPT will improve more after WF training than after NF.

Another possible influence on conclusions about the PAMI device's efficacy could be the order of training epochs. The potential for artificially favorable performance in the WF condition could arise from a number of sources. For example, as a subject performs more repetitions, her subsequent fatigue might unduly increase her time to completion of the 9HPT. In this case, having subjects train with feedback first, followed by the NF condition, could generate misleading conclusions. On the other hand, it is possible that fine motor control improves for a subject after an initial warm-up period, in which case the second training epoch would be associated with a bigger improvement in 9HPT performance, regardless of biofeedback. In light of this possibility, as well as the similarly time-dependent artefactual effects of cognition, it is necessary to develop the experimental protocol to mitigate the effect of order.

The simplest solution was to divide the cohort of subjects into two groups. One group trained in the WF condition first, followed by the NF condition (WF-->NF); the other group trained in the opposite order (NF-->WF). It was also possible to divide the groups into a control group, which trained only in the NF condition, and an experimental group, which trained with feedback; however, this setup would not allow within-subject comparisons, and it would yield substantially less information for use in testing Hypotheses 2 and 3. Subjects were randomly assigned to one training-order group or the other. It is likely that both groups will demonstrate more improvement after WF training than after NF; however, the groups' results are analyzed separately in case training order has any effect.

Peg Test

It is expected that fine motor function will be temporarily restored by a single session of training with the PAMI device. An independent measure of this change in function is used in parallel to training, by intermittently testing the user with a representative task. Since training in the present study is conducted via a specific motion, opposition of the thumb and index finger, the test was selected with the purpose of gauging that pinching movement.

The Nine Hole Peg Test (9HPT), a standard motor control test [Braun 2007, Grice 2003], is the test that was selected to assess changes in fine motor control. Using only the affected hand, subjects place pegs into a peg board and then remove them, one by one and as quickly as possible. The reliability of the total time to completion as a metric of function has been shown previously [Grice 2003]. Subjects perform the 9HPT three times during the course of treatment: before treatment begins, halfway through the treatment period, and at the end of the study.

The 9HPT, which is commonly known as the Purdue Pegboard Test, was developed as a dexterity test in 1948 [Tiffin 1948]. Normative values have been published to characterize performance among specific populations, including both adults [Grice 2003] and children [Smith 2000]. The rating of subjects' initial performance on the 9HPT with respect to norms is reported, as are the results from other motor function tests performed by participating physical therapists. However, analysis for Hypothesis 1, as well as Hypothesis 2, is based primarily on the change in 9HPT performance on a within-subject basis. That is, what is of the most interest is the effect of training on the time to completion of the 9HPT, rather than its effect with respect to normative values.

The 9HPT was not the only option available as a test of fine motor control. For example, it would have been possible to use the Wolf Motor Function Test. However, the Wolf test is a series of tasks that necessitate and measure movement in the upper extremity joints. Its protocol includes movements ranging from simple to more complex, including elbow and shoulder activity [Winstein 2003]. The level of control over all upper extremity joints that the Wolf test gauges is not compatible with the subjects' training.

Therefore, the Wolf Motor Function Test is eschewed in favor of the 9HPT. Its simplicity reduces the influence of elbow and joint control on results, and the manual dexterity needed to complete the task is closely related to the fine motor function trained by thumb-index opposition. The baseline 9HPT serves as a final inclusion criteria, ensuring that subjects in the present study have only moderate dysfunction and are capable of improvement in an short-term training protocol.

The PAMI device was designed with the intention of restoring fine motor function after brain injury. Its efficacy is tested using a cohort of participants, whose motor dysfunctions are the result of stroke or traumatic brain injury. In light of results from preliminary studies and a review of conclusions from the rehabilitation science literature, the characteristics of the present work have been designed to assess the effect of training with PAMI feedback on fine motor performance. The inclusion criteria, control conditions, and representative test were all chosen in this manner. Results pertaining to the PAMI device's ability to restore motor function are therefore expected to be accurate and representative.

Features of Improving Activity

If the PAMI device works as expected, then performance on the 9HPT will improve after training with feedback. The motor control processes that govern the performance of the test will have been altered, which will be evident in its contrast to the NF condition. While this change is not expected to be plastic due to the limited volume of practice, it is likely that the short-term improvement in performance of the 9HPT will be indicative of a short-term change of some kind in the sensorimotor regions of the brain.

The changed coordination of neural activity will be expressed not only in the 9HPT performance, but also in performance of the rehabilitative task on which subjects are trained. In principle, it is the motor learning that occurs during training that spills over into control during the 9HPT. Therefore, the change in function during training is likely to be more pronounced than during the 9HPT

Post-Hoc Analysis.

Observing subjects' changes in fine motor function is primarily accomplished by the 9HPT, as is explored via Hypothesis 1. In addition to this independent measure of function, it may be possible to assess changes in the motor control system using the PAMI device itself. Recall that Hypothesis 2 states,

> "The PAMI signal will reveal the successful motor control strategies in learning specific tasks. Signal features such as onset slope, range, maximum value, and duration are expected to be greater during training with feedback (WF) than without (NF). It is expected that the difference between values will be indicative of the mechanism by which task-specific feedback enables improvement in motor function."

To accomplish this comparison between conditions, the individual SMP sensor recordings and the resultant PAMI signal are written to a file on the computer, then saved for post-hoc analysis. Features are extracted from collected data, and the difference between the WF and NF conditions is compared across subjects.

It would be difficult to draw conclusions about fine motor rehabilitation using a within-subject analysis of PAMI data. While there are likely to be differences between the WF and NF conditions for each subject, these values cannot be associated with an improvement, or a decline in motor function, with any certainty. For example, it is impossible to predict whether a decrease in the time from onset to peak is indicative of improved muscle coordination or of a ballistic co-contraction due to fatigue. It is informative to examine the trends across subjects with respect to the experimental conditions.

Features

The purpose of this analysis is to explore the mechanism by which PAMI facilitates rehabilitation. Features for extraction in post-hoc analysis are therefore selected with the goal of estimating the functionality underlying performance during training. For example, the slope of the signal between onset and peak can be considered analogous to the angular velocity of joints in other studies. It therefore provides a first approximation of the control system's efficiency during the rehabilitative task [Camilleri 2007]. Additionally, the maximum value of the signal serves as an indicator of the subject's ability to repetitively perform the pinch.

Assuming that the subject is able to relax the agonist muscles, which is a component of the inclusion criteria described above, the minimum value of the PAMI signal is of interest when characterizing the mechanisms of rehabilitation with PAMI. The range is examined, rather than just the minimum value, because the range puts the minimum value into context. If the subject co-contracts or has difficulty reducing tone, the range will be relatively low, and the high minimum value will indicate poor performance; on the other hand, if the subject has trouble contracting, the minimum value will appear promisingly low, while the range will again be low. Because the range value indicates decreased function in both cases, it should be a useful rater of performance.

The duration of the signals serve as a measure of the connection between intention and muscle function. Cognitive desire to perform the pinch task may translate to coordinated muscle activation, as measured by slope, maximum, and range. However, the duration of this coordination will reflect consistent muscle activity, which could be a mechanism by which rehabilitation is enabled by PAMI.

Two measures of duration are used as features in post-hoc analysis. One estimates the time between the peak of the signal and the cessation of activity based on the time at which the PAMI feedback value decreases below a threshold. The other measure of duration is the total time that the signal is above threshold; this measure accounts for the possibility that the subject might temporarily decrease the coordination of muscle activity, while still gaining the benefit of the additional periods of high PAMI value activity. While the former assesses the ability to produce a sustained performance, the latter is a measure of the total time of coordinated performance. The two are likely to be correlated in many cases, but they are generated by independent aspects of activity.

Another feature that is extracted in post-hoc analysis is the jerk of the PAMI signal. The third derivative of the PAMI signal is calculated for the entire wave and integrated to yield a scalar value. The result acts as an estimate of the energy in the signal [Flash 1985], which has been used extensively as a rater of movement smoothness in rehabilitation. Previous work has suggested that jerk is not as quintessential a measure as its widespread use has implied [Wininger 2008]. Nevertheless, as a first approximation of the smoothness of pinching, it is likely that jerk will be a sufficient feature.

A key component of the present work explores the mechanism by which function is restored by training with the PAMI device. Findings related to the efficacy of the device in improving fine motor skills are supplemented well by work with Hypothesis 2. To apply PAMI in real-world settings, results that have bearing on the mode of change in performance can be leveraged into fine-tuning rehabilitative protocols. It will be difficult to draw inferences about structure in the central nervous system from an analysis of changes in the PAMI signal, because the features are essentially constructs of cognitive and mechanical aspects of muscle activity in addition to underlying motor control. Exceptions to this limitation include aspects of the early activation, such as range and slope, as well as jerk. Discussion of results of this analysis should be instructive about the capabilities of the PAMI device and its use in rehabilitation.

Muscle Coordination

Like any motor control task, prehensile tasks such as thumb-index opposition are subject to the Redundancy Problem [Bernstein 1967, Latash 2008]. In other words, while there may be little variability in the "performance variable" – in this case, the scalar value represented by PAMI – it is possible for the constituent variables – each individual sensor – to vary from repetition in their relative values. The present work analyzes the distribution of variability in the repetitive training task that subjects perform. In doing so, the synergistic coordination of muscle activity can be elucidated. Moreover, a comparison of healthy and impaired subjects can be performed in terms of variability structuring, as well as an analysis of the change in this structure after training with the PAMI device.

The expectation that coordination can be measured indirectly by comparing consistency in muscle activity has been established in the literature of motor control. Herein, the third hypothesis, which states:

> "During repetitive thumb-index opposition, muscle contraction measured by the PAMI device will reveal the coordination of the motor control system for both the healthy and brain injured cohorts. A comparison between the WF and NF conditions is expected to reveal the increase of synergy in brain-injured subjects when using PAMI biofeedback. In this way, change in the coordination pattern will be confirmed as the mechanism by which PAMI promotes rehabilitation."

is tested in this manner. The quantitative analysis of this hypothesis further allows insights into the relative importance of the temporal features of coordination.

Synergy

The motor control system coordinates muscle activation in a consistent manner. Despite the many degrees of freedom available at any level of motor control – nerve, muscle, joint, etc. - the general characteristics of movement are grossly similar from repetition to repetition. To explain this phenomenon, kinesiologists look to subunits of movement that underlie coordinated activity. As muscles activate according to a subunit-specific pattern, their covariation yields invariance at the task level.

The names given to these subunits vary between studies, and in some cases the differences between approaches are fundamental rather than terminological. Therefore, much care is given in this review to differentiating between the concepts that have been proposed in the literature. In particular, two possible explanations for coordinated muscle activity are relevant to the discussion of patterns in the PAMI recordings: Synergy and Motor Primitives.

The variability analyses conducted on recorded SMP signals and the PAMI feedback value are predicated on the notion that coordination of muscle activation can be represented by statistical comparisons. Previous work has suggested this concept, using different terminology with different details to propose grossly similar ideas. A more thorough review of this body of work is detailed above, in Chapter 3. Briefly, synergies and motor primitives have both been proposed as the so-called language of the motor control system.

The distinction between the synergies and motor primitives is primarily a question of timing. While motor primitives do not necessarily call for simultaneous activation of muscles, synergies involve synchronization of neural signals [Kargo 2008]. The present study does not try to answer the question of which model is correct. Moreover, the analysis performed on SMP and PAMI records does not necessitate the assumption of one over the other. While the data analysis methods used herein were developed based on synergies in motor control [Scholz and Schoner review paper], there does not seem to be a contradiction between synergies and motor primitives that would prevent the application of these methods, which have been used successfully to characterize a wide variety of movements [Scholz 1999, Krishnamoorthy 2003, Black 2007]. For the remainder of the discussion in the present work, the term synergy will be used to describe the coactivation of muscles, bearing in mind that this is not the only possible explanation of the motor control system's coordination of neuromuscular activity.

The nature of motor dysfunction after brain injury is of interest for analysis of data from training with the PAMI device. Improvement in performance on the 9HPT should be associated with a change in the motor control system, due to the central nervous system's plasticity (see Chapter 2). Characterizing the patterns that underlie that change in function will be informative from the perspective of motion analysis. The synergies that are employed by healthy and brain-injured individuals in thumb-index opposition can be compared to elucidate the systemic change that results from injury. Additionally, the mechanism by which training with PAMI biofeedback induces fine motor improvement, specifically its effect on synergies, will be suggested by this post-hoc analysis of variability.

Variability Analysis

Covariations in neuromuscular activity are often reflected in records of motor control. Properly designed experiments using sufficient instrumentation can be subjected to variability analysis to elucidate aspects of the hidden layers of control. Herein, the properties of fine motor control are analyzed with respect to the synergies that coordinate muscle activation during thumb-index opposition. While the design of the experimental protocol used in training of fine motor control was primarily intended for restoration of function after brain injury, it was recognized early during preliminary testing that the records could be used for variability analysis as well. The method used in the present work, the Difference of Variance Index, is a simplification of the common Uncontrolled Manifold analysis.

Previous work with UCM analysis has compared the structuring of variability before, during, and after adaptation to a force field during reaching [Yang 2007], but this work was not designed to address any deficit in motor function nor brain injury of any kind. Similarly, UCM analysis has been used to study the movement patterns of stroke victims, but no attempt was made to restore function during that study [Reisman 2003]. In this way, analysis of coordination presented herein extends motion analysis by applying the UCM in a unique experiment.

A consideration when applying UCM analysis is that as an analysis technique, it is heavily model based. Studying the partitioning of variability is predicated on knowledge of the orientation of the Uncontrolled Manifold, and accordingly, the orientation of the space orthogonal to it. The process of deriving this orientation involves calculating the rate of change of the task variable with respect to each component as a Jacobian matrix. Without a forward model relating the components to the task, it is difficult to resolve the variability properly. One alternate method is to apply principal component analysis to component variables in order to decorrelate them [Krishnamoorthy 2003]. The present work forgoes this method in favor of a more straightforward approach that was a stepping-stone in the development of UCM analysis.

In certain cases, it is possible to compare the variability of the component variables and the task variable directly. This approach, referred to in the literature as the Difference in Variance Index (dVI) [Latash 2002], has informally been given the short-hand nickname of “Poor Man's UCM”, due to its simplicity. However, it has been used as a powerful tool in the exploration of synergies in motor control. For tasks where the units of the components and the task are the same, this method can obviate the need for partitioning variability into subspaces, and in doing so, it eliminates the requirement of a forward model.

This procedural bypass is predicated on the simple combination of components into the task variable; for example, the variability in the sum of finger forces can be compared to the sum of the variabilities in the individual fingers during a force production task [Scholz 2003, Latash 2002]. Because the SMP sensors and the PAMI biofeedback value are recorded in the same units and are directly related, the dVI method is used as an alternate to UCM analysis in the present work.

The analysis of motor variability has been approached using a variety of methods, many of which were considered for the present work. The tradeoffs between simplicity and utility in these methods are substantial, prompting an emphasis on the potential of the statistical techniques to allow inferences about the nature of synergies in the thumb-index opposition task used herein. Selecting the Difference of Variance Index for analysis of recorded PAMI data follows these guidelines, based on the precedent in the literature demonstrating its efficacy in motor control studies [Latash 2002]. The use of this method is expected to yield insight into the mechanism of functional gain during short-term rehabilitation, similar to the approach of Hypothesis 2, above. Moreover, dVI analysis should allow a comparison between the coordination of healthy and brain-injured fine motor control in a unique task.

The present work extends the fields of rehabilitation engineering and motion science by contributing to ongoing questions using established techniques in a unique context. The PAMI device was developed by means of collaboration with clinicians, revision of prototypes, and preliminary testing with the brain injured subjects for whose use the device is intended. The experimental protocol for testing the device adopts findings the literature about the effect of motor rehabilitation at the neurophysiological level, as well as reflecting the lessons learned from early work with PAMI prototypes. Post-hoc data analysis is conducted using a variety of well-established methods, so that conclusions can be drawn rigorously based on quantitative comparisons . Testing the hypotheses expressed above thus combines established methods with the novel PAMI device in a way that should aid both brain injured users and kinesiologists.

Chapter 5 - Methods

Participants

A total of 12 volunteers suffering from chronic motor dysfunction from brain injury participated in the present work. Recruitment was conducted by collaborating Physical Therapists who were familiar with the participants and their capabilities. Care was taken to prevent any influence of this knowledge on the assignment of subjects to experimental groups. All subjects were patients in outpatient care at the JFK-Johnson Center for Brain Injury, with one exception as detailed below.

Inclusion criterion dictated that the participants suffered chronic hemiparesis due to brain injury from stroke or TBI. Thus, the brain injury must have occurred at least six months prior to participation in the experiment, and subjects experiencing conditions such as brain cancer were excluded.

Subjects must have moderate spasticity as a result of the brain injury, as well as the ability to release tone in agonist muscles. This ability was assessed beforehand by collaborating PTs, in addition to which the 9HPT served as a litmus test. The degree of spasticity and the ability to release tone were both necessary for the repetitious activation and relaxation of the experimental protocol. In addition, the inclusion criteria require sufficient cognitive function to assure subjects' comprehension of instructions. The ability to complete the 9HPT, being contingent on participants motor and cognitive function, supplemented the clinical assessments independently of PAMI use and was a requirement for inclusion. Handedness was not a category for exclusion, nor was the location of the brain lesion.

Informed consent was obtained from each subject after he or she was given a detailed explanation of the nature of the experiment. The study was approved by the IRB of Rutgers University and the JFK-Johnson Rehabilitation Institute.

Of the 15 total brain-injured volunteers that were recruited, 14 were undergoing outpatient care at JFK-Johnson Rehabilitation Hospital, where the experimentation was conducted. They had been previously assessed by physical therapists working in collaboration, and their motor and cognitive function levels met the inclusion criteria. One volunteer, who was 4 years post-injury and was not receiving therapeutic care at the time of testing, could not perform the 9HPT. As such, his data was excluded from analysis. Similarly, two JFK-Johnson patients who had volunteered did not meet the criteria and were excluded.

The subjects who met the inclusion criteria are detailed in Table 1. The assessments of motor function were performed by the PT. All other information was reported by the participant. This experimental group consisted of both stroke (n=4) and TBI (n=8) victims. Eight were male, although gender was not considered an experimental variable. Their mean age was 39.8, with a range of 48 years.

In addition to the experimental group, twelve healthy subjects participated as a cohort of control subjects. The control group was approximately age-matched to the experimental group, with a mean age of 46.4 years and a range of 42. None were aware of any neurological or biomechanical impairment in either upper extremity. Control subjects were not excluded based on handedness.

Materials

PAMI Hardware

The human-machine interface of the PAMI hardware is a sleeve that is worn about the user's forearm. Five SMP sensors are attached to the sleeve, which are connected to a Personal Computer by means of an Analog-Digital conversion chip. The same device was used for all subjects.

The design of the SMP sensors uses Force Sensitive Resistors (FSRs) to gauge the radial pressure exerted by active muscles [*Interlink Electronics*, Carpinteria, California, USA]. The resistance of an FSR varies in inverse proportion to the pressure being exerted on its surface. This relationship was found to be approximately linear in the range of 0-20 Hz at physiologically relevant forces [Yungher 2009]. Each FSR is connected in series with a fixed resistor of 10 kΩ, all of which are arranged in parallel (Figure 4).

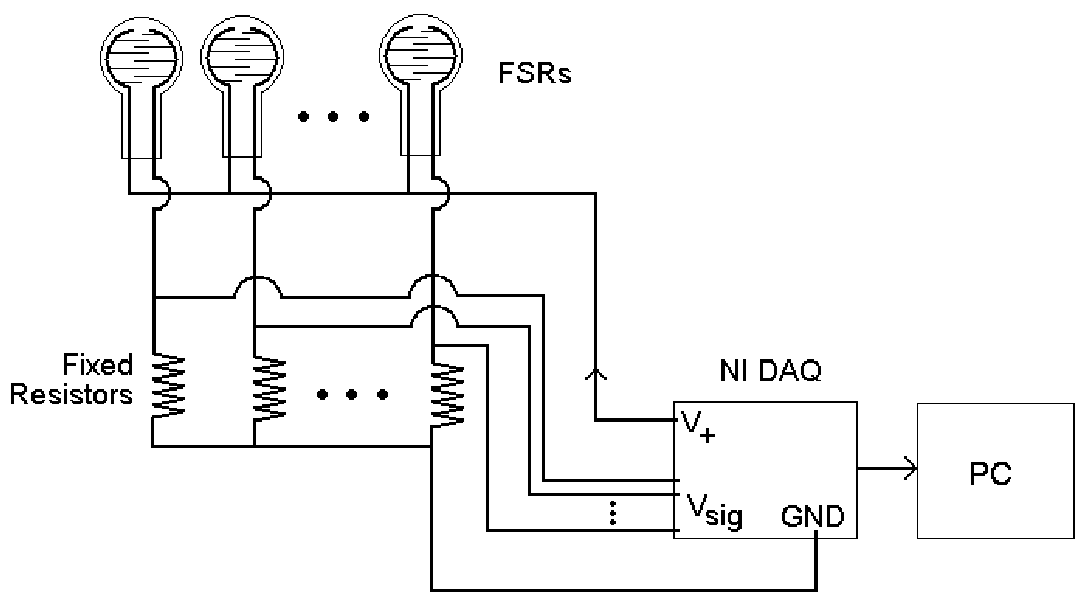

Figure 4 – Circuit Diagram of SMP hardware. Each Force Sensitive Resistor (FSR) is connected to a fixed resistor in series, creating an array of half-bridges in parallel. Voltages across the FSRs are digitized by the National Instruments DAQmx board and sent to the PC for display and recording.

The FSRs were modified for use as SMP sensors by attaching material to both sides of the resistor. Thus, each sensor was Embedded between a thin layer of soft fabric and a hard plastic backing. A strip of Velcro was glued to the plastic backing in order to attach the SMP sensors to the sleeve.

The sleeve was based on a standard therapeutic cuff. A long piece of Velcro at one end could be looped through a plastic D-ring at the other, so that the tightness of the sleeve could be customized for each user. The surface that contacted the skin was covered in a soft, comfortable material to which the Velcro surfaces could adhere.

The voltages recorded from each SMP sensor's half-bridge (Figure 4) were captured using a DAQmx board [National Instruments]. This digitization took place at 25 Hz, which has been shown to be adequate for registering muscle activity with fidelity to higher-frequency EMG signals [Yungher 2009]. The resultant myokinetic signal has been shown to be suitable for recording muscle activations in both the upper and lower extremities [Yungher 2009, Wininger 2008].

Donning the sensorized cuff provided a baseline static pressure with a uniform, comfortable fit while allowing for detection of local positive as well as negative pressure changes. The non-permanent attachment of the FSRs to the cuff allows the device to be customized to each user. However, while care is given to uniformly distribute the sensors about the forearm, it is not necessary to target specific locations. SMP signals are naturally low frequency, and the FSRs register muscle shape changes from both near and distant muscles. Additionally, normalization mitigates the variability that could result from imprecise FSR location.

Testing at the JFK-Johnson Center for Brain Injury was conducted using a PC with a 1 MHz processor. The PC used for data collection at Rutgers University had a 2.8

GHz processor. The location of each subject's testing is listed in Table 1.

Subjects	Cohort	Baseline (sec)	Injury	Post-Injury (yrs)	Affected Side	Handed-ness	Age (yrs)	Gen-der	Test Loc
1	WF→NF	36.41	Stroke	1.5	L	R	62	M	JFK
2	NF→WF	58.94	TBI	1.5	L	R	38	M	JFK
3	WF→NF	144.6	TBI	24	R	R	33	F	JFK
4	WF→NF	47.50	Stroke	1.25	R	R	56	M	JFK
5	NF→WF	138.38	TBI	27	L	R	45	F	JFK
6	NF→WF	95.25	TBI	1.0	R	R	25	M	JFK
7	NF→WF	263	Stroke	1.0	L	R	38	F	JFK
9	WF→NF	30.59	Stroke	0.5	L	R	69	M	JFK
10	WF→NF	81.59	TBI	1.2	R	R	25	M	JFK
11	NF→WF	52.15	TBI	0.75	R	L	24	M	JFK
13	WF→NF	28.66	TBI	1.3	L	L	37	F	JFK
15	NF→WF	43.25	TBI	2	R	L	21	M	JFK
Controls						Handed-ness			
1	WF→NF	20.2	--	--		R	61	M	RU
2	NF→WF	15.78	--	--		R	28	F	JFK
3	WF→NF	18.44	--	--		L	51	F	JFK
4	NF→WF	18.97	--	--		R	29	M	RU
5	NF→WF	19.17	--	--		L	25	F	RU
6	WF→NF	19.0	--	--		R	67	F	RU
7	NF→WF	25.56	--	--		R	58	M	RU

Table 1 - Subject Demographics – Important characteristics of impaired subjects (top) and healthy controls (bottom). Injury details are not germane to control demographics.

PAMI Software

PAMI biofeedback is generated based on a comparison between real-time SMP values and those recorded as a template for desirable activity. The software that was created for this purpose completed three tasks: (1) calibration, (2) template setting, and (3) training. All of these on-line processes were accomplished using Labview [*National Instruments Corporation, Austin, TX, USA*].

Calibration was accomplished by recording SMP values during quiet rest. Subjects were instructed to relax the affected hand, and care was taken to promote a static posture. The calibration therefore recorded baseline values that were obtained during rest in the geometric configuration that would be used during training. Maximum voluntary contractions were not recorded, because it was possible that such activation might induce undesirable fatigue.

Template setting immediately followed calibration. Subjects were instructed to continue resting while the “relax” state was captured. For approximately two seconds, the SMP values were measured, and the records from the final 200 ms were averaged to generate a template value for each sensor. While this template was of less importance to the experimental protocol than that of the “pinch” state, the addition of visual feedback during resting seemed to encourage resting rather than sustained activity. Thus, limited attention was paid to the similarity between the recorded resting template and the state of a relaxed hand during training.

Following the capture of the “relax” state template, subjects were instructed to “pinch”, producing a thumb-index opposition. Again, the pinch lasted for two seconds, and SMP records of the final 200 ms were averaged to generate the template. If the subject's pinching movement was not deemed appropriate by the supervising clinician, then the template setting for thumb-index opposition was repeated. More attention was paid to the posture of the hand for this process than for the resting template, in order to emphasize the role of muscle activation in generating feedback.

Training commenced immediately following the template setting process. Subjects were shown instructions that read “PINCH” and “REST”, which the supervisor stated aloud in addition. The switch between the two instructions was timed by a metronome coded into the Labview program. Prior to experimentation, the metronome was tuned to approximately 0.25 Hz.

Biofeedback is generated as a scalar value, although it incorporates the multidimensional information from all five SMP sensors. As mentioned above (see Chapter 4), the SMP sensors each constitute one dimension of a sensor space. The pinch template, which has the same dimensionality as the sensor space, is a static point whose location was defined during template setting. The real-time SMP values define a point in the sensor space that is time-variant and dependent on muscle activation.

To resolve the real-time and template SMP values into information about performance, their locations are compared using a simple spatial metric. The Euclidean distance between the real-time and template points is calculated as

$$\text{Dist} = \sqrt{\sum_{n} (\text{Target}_i - \text{Performance}_i)^2} \qquad \text{EQ 1}$$

where n is the number of sensors and Target and Performance are the SMP sensor values that define the ideal muscle activation and the real-time activation, respectively.

The Euclidean distance decreases as the real-time SMP approaches the template. To increase the intuitive utility of the PAMI device, the actual feedback value is calculated as the distance subtracted from 10. This gives the appearance that a lower Euclidean distance, corresponding to the improved performance of the thumb-index opposition relative to the template, will increase the feedback.

The Labview software facilitates the generation of feedback with built in applications. The Tank function, which takes a scalar value as an input, is visible to the user as an empty space that becomes fuller as the input increases. A screenshot of the Tank as it is used in the PAMI software is shown in Figure 3.

Nine Hole Peg Test

The 9HPT was administered using standard pegs and peg board. Testing conducted at JFK-Johnson and Rutgers University used identical materials [Sammons Preston, Bolingbrook, IL, USA]. Nine holes are evenly distributed on the peg board in a square 3x3 configuration, 2.5 inches per side. Nine wooden pegs of diameter corresponding to the holes on the board, 1.25 inches long, are arrayed on a flat, non-slip surface on the same side of the peg board as the affected hand. The subject is seated so that the board and pegs are directly in front of the subject's centerline and within comfortable reach. This setup is illustrated in Figure 5, which includes a photograph of a 9HPT and a sketch of its use by a participant.

Subjects were instructed to fill the board peg-by-peg, then to remove pegs one at a time. They were instructed to complete this test as quickly as possible, and using only the affected hand. Additionally, they were encouraged to ignore whatever pegs may be accidentally dropped or thrown, because the supervisor would ensure that enough pegs were available that the test could be completed without pursuing lost pegs. In this way, the time to completion of the 9HPT reflected only time spent manipulating the pegs.

Timing was measured by the experimenter using a stopwatch. Reminders of the instructions were given as necessary during the test. Finally, in the interest of within- and between-subject comparability, identical instructions were given before each 9HPT for each subject.

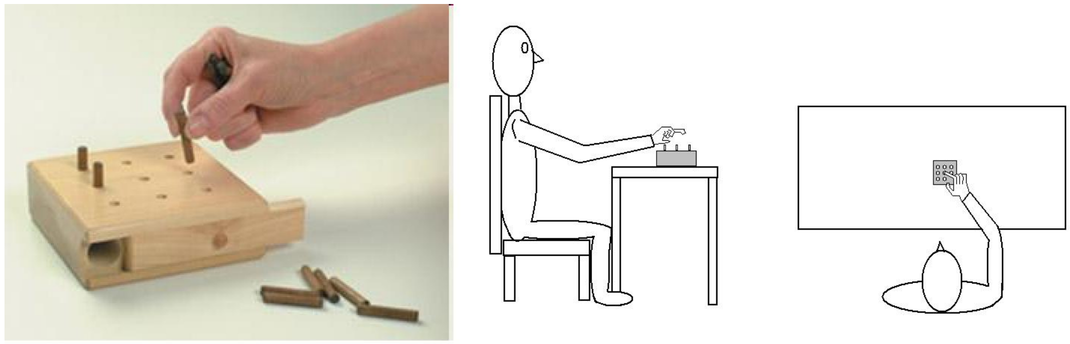

Figure 5 – Nine Hole Peg Test (left) and sketch of left-hemiparetic subject setup, profile (right) and top (far right) view.

Experimental Protocol

Experimental Conditions

There were two experimental conditions pertaining to biofeedback, selected to rigorously assess the PAMI device's efficacy. In the With Feedback (WF) condition, visual feedback is given as described above. In the No Feedback (NF) condition, the subject is instructed to either Pinch or Rest according to the metronome and spoken cues, but no visual feedback is given. Pinching was described as the opposition of the thumb and index fingers and demonstrated before training began.

Participants were randomly assigned to two groups, which determined the order that feedback conditions were used in training. One group (WF-NF) had PAMI biofeedback in the first training session and no feedback during the second session. The NF-WF group was trained in the opposite order. The same random grouping was used for the control subjects.

Subjects' fine motor function was assessed by the Nine Hole Peg Test (9HPT), which was performed three times during the study. The first 9HPT was conducted as a pre-training baseline, and the second and third 9HPT were performed after the first and second training conditions, respectively. The experimental conditions and tests are summarized in Table 2.

	WF-NF		NF-WF	
9HPT 1	baseline test		baseline	
1st condition	PAMI visual feedback	(WF)	timing only, no feedback	(NF)
9HPT 2	post-WF test		post-NF test	
2nd condition	timing only, no feedback	(NF)	PAMI visual feedback	(WF)
9HPT 3	post-NF test		post-WF test	

Impaired	n=6	n=6
Control	n=3	n=4

Table 2 – Training and Testing Conditions for the two Experimental Groups.

Training

The fine motor training through which participants were guided was designed to mimic standard rehabilitative protocols. Subjects alternated between pinching and resting, and each iteration lasted approximately four seconds. The supervision of a clinician ensured that subjects were following instructions as closely as possible.

Each session included approximately thirty repetitions per condition. Two mandatory rest periods divided the thirty repetitions into sets of ten. The durations of the rest periods were customized to the needs of participants, which had the aim of minimizing fatigue. This was supplemented by occasional questions about the subject's comfort and fatigue.

Since the same timing, cues, and software were used for the NF and WF conditions, the only physical difference between the conditions was the visibility of the feedback Tank. This had the potential to effect a difference in attention by encouraging focus during WF training, which was mitigated by occasional reminders to pinch “as well as possible” throughout the entire session. Additionally, during both training conditions, the tendency of some subjects to activate their muscles maximally was counteracted by attention and spoken reminders from the supervisor.

Data Processing

Nine Hole Peg Test

Changes in performance on the 9HPT are the basis of comparison in Hypothesis 1, which expresses the expectation that use of PAMI biofeedback will yield more functional improvement that training without feedback. Thus, results from the 9HPT were compared within subjects as the difference between each instance and the time to completion of the preceding instance.

The use of two experimental groups of impaired subjects was intended to mitigate the effects of artifacts such as fatigue or cognition. To gauge this robustness, 9HPT times are compared within experimental groups. With six subjects per group, a general dissimilarity between conditions for both groups should be sufficient to support the claim that results reflect improvement due to training with the PAMI biofeedback.

It is then possible to combine the two brain injured groups into one cohort for analysis. This will allow a statistical approach to the difference between experimental conditions. As before, the comparison is based on the difference in 9HPT time by training condition.

Finally, the inclusion criteria were narrowed in post hoc processing. Excluding participants whose baseline 9HPT exceeds an arbitrary minimum allows the analysis of only those subjects whose impairment is between moderate and severe. In this way, it is possible to draw inferences about the efficacy of the device for users with more severe hemiparesis. The arbitrary limit used herein is 50 seconds.

PAMI Biofeedback Timing

While Hypothesis 1 gauges motor function using only the independent rater provided by the 9HPT, Hypotheses II and III make use of the PAMI biofeedback signal itself in their assessments of the restoration of function. These analyses, described below, are heavily reliant on temporal landmarks of muscle activity. To identify these landmarks, the first step of the post-hoc analysis is to process the biofeedback recording in search of specific features.

The onset of muscle activity is defined as the time at which the PAMI signal exceeds a threshold based on its range. The threshold is calculated using

$$0.05 \times [\max(P)-\min(P)] \qquad \text{EQ 2}$$

where max(P) and min(P) are the maximum and minimum values, respectively, of the PAMI signal for that repetition. This technique has been used in a variety of motor control studies [Wininger 2008, Yang 2007].

Another important temporal landmark of muscle activity is the point at which the "best" pinch is attained. In other words, as the biofeedback signal approaches its maximum, it is an indication that the system has entered a rough steady-state in which the current muscle activation is as similar to the proper template as will be achieved on that repetition. While slight improvements may be possible using the incorporation of cognitive processes, the point of peak PAMI signal – as opposed to the maximum value – is a temporal representation of the end of the initial grasping movement.

In an effort to mitigate bias in the identification of temporal landmarks, the processes for defining onset and peak are designed to be as automated as possible. For onset identification, the process is fully automatic; the first instance of threshold crossing is defined as the onset. On the other hand, the identification of the peak is defined by a semi-automatic process. Repetition by repetition, the region in which the peak appears to exist is identified by the researcher, after which the peak is defined as the time of the maximum PAMI value in that region.

Feature Change

With the demonstration of the potential of the PAMI device to restore fine motor function after brain injury, the next step is to assess the mechanism by which the biofeedback changes the motor activity. The possibilities for a modality of functional change include temporal, kinematic, and kinetic changes. Based on these possibilities, the following scalar features are extracted from the PAMI biofeedback record of each repetition: (1) slope, (2) maximum, (3) range, (4) duration, (5) time above threshold, and (6) jerk, as in Figure 6.

(1) Slope

The slope of the PAMI signal is calculated using an indirect method that is intended to minimize the influence of noise on the derivation. First, for each repetition, the signal is z-normalized, so that its minimum is set to 0 and its amplitude is set to the

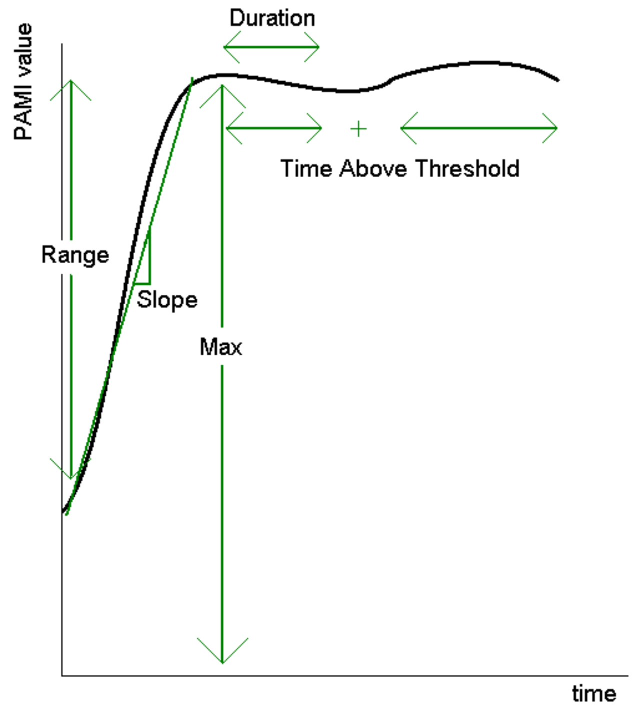

Figure 6 – Features of the PAMI Signal, demonstrated on an idealized PAMI waveform. Note that jerk is not shown.

inverse of the standard deviation of the signal maxima across all repetitions. The slope is then estimated at each point between onset and cessation using a 3rd order spline, with the equation

$$f'(t) \approx \frac{-f(t+2)+8f(t+1)-8f(t-1)+f(t-2)}{12} \qquad \text{EQ 3}$$

where t is the data point at which slope is being approximated. When the slopes have been estimated for each data point, the mean across data points is calculated, yielding a scalar value for the slope for that repetition.

This process is computationally intensive and may not provide any more accurate an estimate of slope than a simpler approach could. However, since this feature extraction is performed entirely post-hoc, the cautious use of splines is the chosen slope estimation method in the present work.

(2) Maximum

Higher values of the PAMI biofeedback correspond to better proximity to the target value in sensor space, which is the result of the subtraction of the instantaneous distance between real-time and template SMP values from a constant. Thus, higher values may be assumed to be beneficial to rehabilitation. For this reason, the maximum value near the peak of each repetition is computed numerically using MATLAB.

(3) Range

The value of the PAMI signal at the beginning of each repetition serves as an indirect measurement of the ability of the subject to relax the muscles used during pinching. Lower values of the signal correspond to increased relaxation, although it is also possible that activation of antagonist muscles may decrease the PAMI signal without necessarily indicating relaxation. Conversely, a high maximum value may be the result of continued activation from the previous repetition. The range is therefore calculated as

$$\max(PAMI) - \min(PAMI) \qquad \text{EQ 4}$$

(4) Duration

Duration is defined here as the length of time during which the subject is actively reproducing the template value set during calibration. Specifically, onset of duration is defined as the time when the PAMI signal exceeds 80% of the range, and cessation is when the signal drops below 80%. The first instance of sub-threshold PAMI signal is deemed the cessation of activity, regardless of any subsequent supra-threshold activity during that repetition.

(5) Time Above Threshold

In contrast to the duration feature, above, the time above threshold accounts for activity across the entire repetition. It is calculated as the total number of data points at which the PAMI signal is greater than the threshold, set at 80% of the range as above. Thus, time above threshold measures the quantized instances of measurement, rather than the analogous amount of time.

(6) Jerk

Jerk is a measure of the energetics of an activity. It has been used in a variety of motor control studies, including reaching [Flash 1985, Hogan 1984, Wininger 2008]. Jerk is calculated using the method of Flash and Hogan, with the equation

$$\text{Jerk} = \frac{1}{T}\int_0^T \frac{d^3}{dt^3}(PAMI)dt \qquad \text{EQ 5}$$

where the third derivative of the PAMI signal (technically, this is known as jerk, although for the purpose of clarity, herein it is not) is approximated using a third order spline, and T is the temporal length of the PAMI signal.

The features of the PAMI signal are compared across the seven most impaired subjects. In this way, the changes in the PAMI signal that correspond to improved motor function, if the analysis of 9HPT times supports this correspondence, are identified. This analysis extends to the trends that emerge across training sets.

The six features that were extracted for the present analysis represent characteristics of early activation as well as whole-wave metrics. Slope, duration, and time above threshold are based on temporal features of the thumb-index opposition. The maximum and range are calculated regardless of their timing. Jerk is essentially a kinetic variable, and its scalar value represents the energy of the entire repetition [Flash 1985].

The extracted features are compared across the group of most impaired subjects. The feature set derived from each repetition are grouped, allowing a statistical analysis using the one-tailed t-test. Since processing only compares the difference between the WF feature mean with that of NF training, the units of the different features have no consequence in the analysis.

In addition to the whole-set analysis, the features are also compared in terms of their change between sets. Divided into the repetitions performed between rest periods, the extracted values are averaged within the sets. Thus, the WF and NF features can be compared within each set, as well as in terms of their change over the course of training. The t-test is used in the within-set analysis. In all cases, the t-test is performed using the Microsoft Excel function “ttest”.

Difference of Variance Index

The dVI method is performed according to the methods of Latash [Latash 2002]. Time normalized records from both SMP and PAMI are truncated at the length of the shortest repetition, so that all repetitions are of the same length. The variance of each SMP sensor is then calculated across trials at each data point within sets, corresponding to the repetitions before, between, and after the mandatory rest periods. The variance of the PAMI signal is derived in the same way.

To determine the Difference of Variance Index (dVI), the sum of variances across all measurements at a certain point in time is calculated. Since all components in the present work are SMP sensors, this summation of their measurement variances does not involve multiple units and is therefore valid. In the case of the PAMI signal, there is only one component, and it is also in the same units. The dVI is then defined as the difference between the variance of the SMP sensors and that of the PAMI signal, which is then normalized to the former value, as

$$\mathrm{dVI} = \frac{\sum_j \mathrm{var}(SMP_j)/N - \mathrm{var}(PAMI)}{\sum_j \mathrm{var}(SMP_j)/N} \qquad \text{EQ 6}$$

where $\mathrm{var}(SMP_j)$ is the variance of the j SMP sensors across repetitions, N is the number of SMP sensors, and var(PAMI) is the variance of the PAMI value across repetitions. The dVI value has an upper bound of 1 and an undefined negative bound.

When the dVI value is maximal, the variance of the SMP sensors far exceeds that of the PAMI signal. This indicates that the muscle activations are coordinated by a strong synergy to produce a stable grasp. Conversely, a decrease in the dVI value suggests an increase in the VI of the PAMI signal, which is suggestive of a weakening of the synergy by which thumb-index opposition is controlled [Latash 2002].

The dVI is calculated for every time point of each subject, which done separately for the three sets. This process is repeated for the NF and WF conditions. Features are then extracted from the dVI waveforms:

- Minimum: the minimum dVI value during the first 50% of the initial pinch
- Peak: the value of the dVI waveform at 100% of the initial pinch
- Maximum: the maximum dVI value from the entire waveform
- Steady-State: the average dVI value from 151% to 200% of the initial pinch time, where it is assumed that the user has reached a steady state of muscle activation.
- Curvature: the difference between the Maximum and the Minimum of the waveform

All features are shown on an idealized dVI waveform in Figure 7. The time domain, set here as a percentage of the initial pinch, is defined according to the timing of the peak

PAMI value. These values were determined semi-automatically for the feature extraction from the PAMI signal of each repetition.

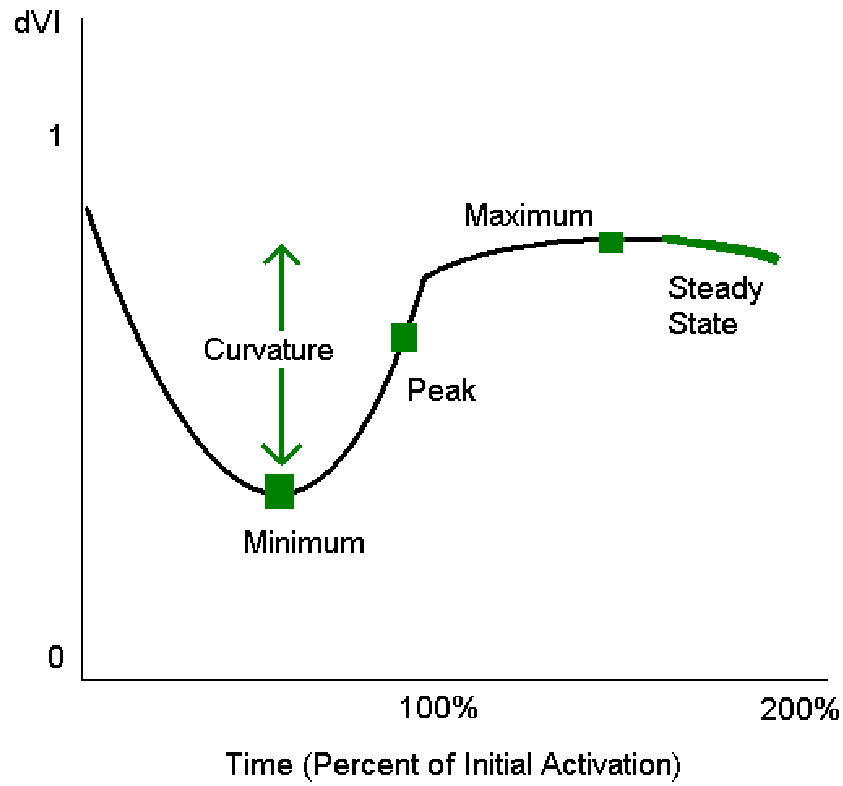

Figure 7 – Features extracted from the dVI values, demonstrated on an idealized dVI waveform.

Statistical Analysis

To accurately describe the difference between 9HPT results following NF and WF training, the times to completion are compared by using the Wilcoxon Signed-Rank Test. In all cases, the null hypothesis of these tests is the expectation that the two experimental conditions yielded identical times on the 9HPT. Since the number of subjects is relatively small, it is unlikely that the values are normally distributed. Furthermore, knowing that participants experienced a range of impairment severity, the multiple administrations of the 9HPT for a given subject can be characterized as capturing repeated measurements from one sample. These two factors suggest that the Wilcoxon Signed-Rank Test is the most valid statistical analysis for the present work [McDonald 2009].

Analysis is performed using a freely available utility from the Handbook of Biological Statistics [McDonald 2009]. The program was encoded as an Excel worksheet. The 9HPT comparisons, defined above as the difference between each test administration and the previous instance, are listed on the worksheet. Using a lookup table, the program returns the range of p-values that bound the significance of the difference between conditions.

Features of the PAMI signal are compared using one-tailed t-tests. Two types of tests are performed. The comparison between the WF and NF condition within cohorts (impaired and control) is performed across repetitions using a paired t-test, with a null hypothesis stating that the two conditions produce identical changes in the PAMI features for impaired subjects. Testing the difference between control and impaired subjects' PAMI features within experimental conditions uses an unpaired t-test, and the null hypothesis is the same as above.

For the dVI feature comparison, values are compared between the NF and WF conditions of the impaired subjects across sets. As with the 9HPT, the statistical significances of the comparisons were determined using the Wilcoxon Signed Rank test . This comparison was performed both between the training conditions and across the three sets. The null hypothesis for this comparison was that there is no difference between NF and WF training on the coordination as measured by the dVI.

Chapter 6 - Results

Restoration of Function with Biofeedback:

Hypothesis 1:

> Restoration of fine motor control can be enhanced by the use of biofeedback from the Proprioception-Augmenting and Measurement Interface (PAMI) device to supplement proprioceptive deficit. Performance on standard functional tests will improve after training with feedback (WF) as compared with the no feedback (NF) condition.

To assess the efficacy of training with the PAMI device, a 9HPT was administered to subjects before and after each training session. The change in the time to completion of the 9HPT is compared between experimental conditions (WF and NF), with a decrease in time indicating an acute increase in fine motor function. This comparison is performed within the experimental groups (WF-->NF and NF-->WF) as well as across the entire cohort of subjects. The Wilcoxon Signed Rank Test, a non-parametric test for paired samples, is then used to assess the significance of the difference between the WF and NF effects. All results are reported in Table 3.

Impaired	WF-->NF			
	Subject	Baseline	after WF	after NF
	1	36.41	36.37	33.31
	3	144.6	57.89	75
	4	47.5	42.16	44.94
	9	30.6	33.22	31.41
	10	81.59	54.78	56.25
	13	28.66	28.84	28.75
	NF-->WF			
	Subject	Baseline	after NF	after WF
	2	58.94	70.09	57
	5	138.38	121.03	105.49
	6	95.25	92.78	95.59
	7	263	340	173
	11	52.15	50.49	48.31
	15	43.25	38.99	38.81

Control	WF-->NF			
	Control	Baseline	after WF	after NF
	1	20.2	19.67	19.05
	3	18.44	20.22	18.72
	6	19	19.512	18.7
	NF-->WF			
	Control	Baseline	after NF	after WF
	2	15.78	15.71	15.78
	4	18.97	19.282	18.8
	5	19.17	20.22	18.12
	7	25.56	26.48	24.98

Table 3 – Hypothesis 1 Results – 9HPT times to completion before and after training for impaired subjects (left) and healthy controls (right). All results reported in seconds.

By Training Order

Subjects were randomly assigned to experimental groups, WF-NF and NF-WF, which determined the order of training sessions. The changes in 9HPT time to completion for the two experimental groups are shown in Figure 8. The results are normalized to the subjects' baseline time, so that all results are reported as percentages (mean ± S.E.).

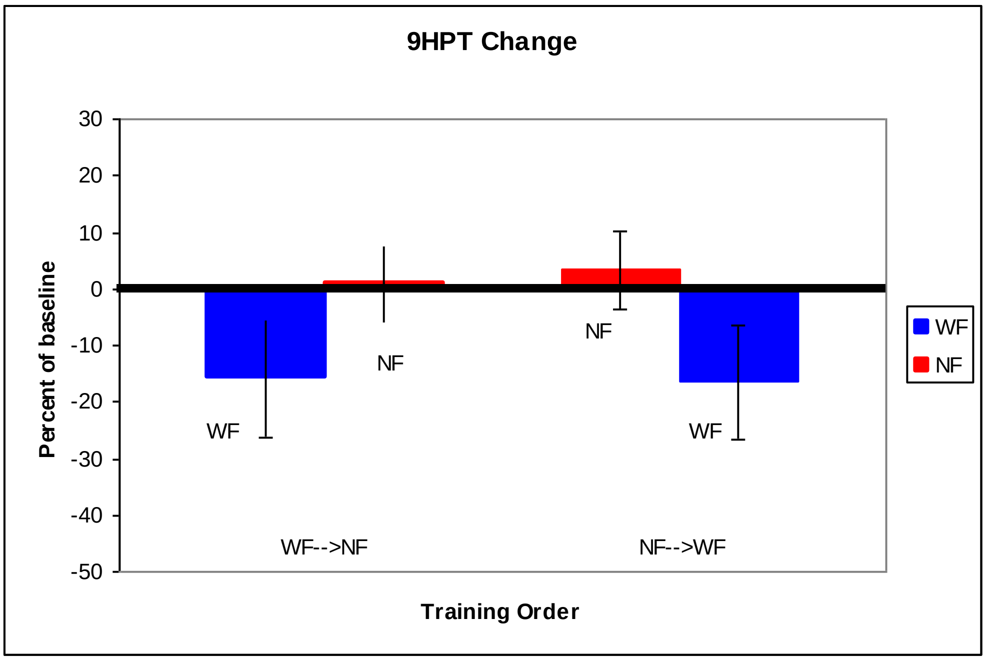

Figure 8 – 9HPT Times by Training Order – Change in times to completion of the 9HPT (Mean ± S.E.) for impaired subjects during the first and second training epochs. Training with PAMI biofeedback (blue) results in decreases in 9HPT time, while training without feedback. Represents all brain-injured subjects (n=12).

The WF-NF group, which trained with PAMI biofeedback first, changed their time to completion of the 9HPT with an average decrease of 15.8% ± 10.6 % after the WF period. Their change in 9HPT performance from NF training was an increase of 0.81% ± 3.05%.

The NF-WF group, in which the first training session did not involve the PAMI biofeedback, had an improvement of 16.43% ± 10.1% after WF training. Without feedback, the NF session had a 3.34% ± 6.98% change in time to completion.

Entire Cohort

Having demonstrated above that the order of training does not have a noticeable effect on the restoration of function with PAMI training, the analysis can be extended to the entire cohort of brain injured subjects. After a session of training with PAMI biofeedback (WF), the average change of 9HPT time to completion across all subjects was a decrease of 16.1% ± 6.98%. In contrast, a session of training without feedback (NF) yielded an average change that increased the 9HPT time by 2.07% ±3.61 %. This result fits the expectation that training with PAMI biofeedback can improve fine motor function better than training without feedback, as is shown in Figure 9.

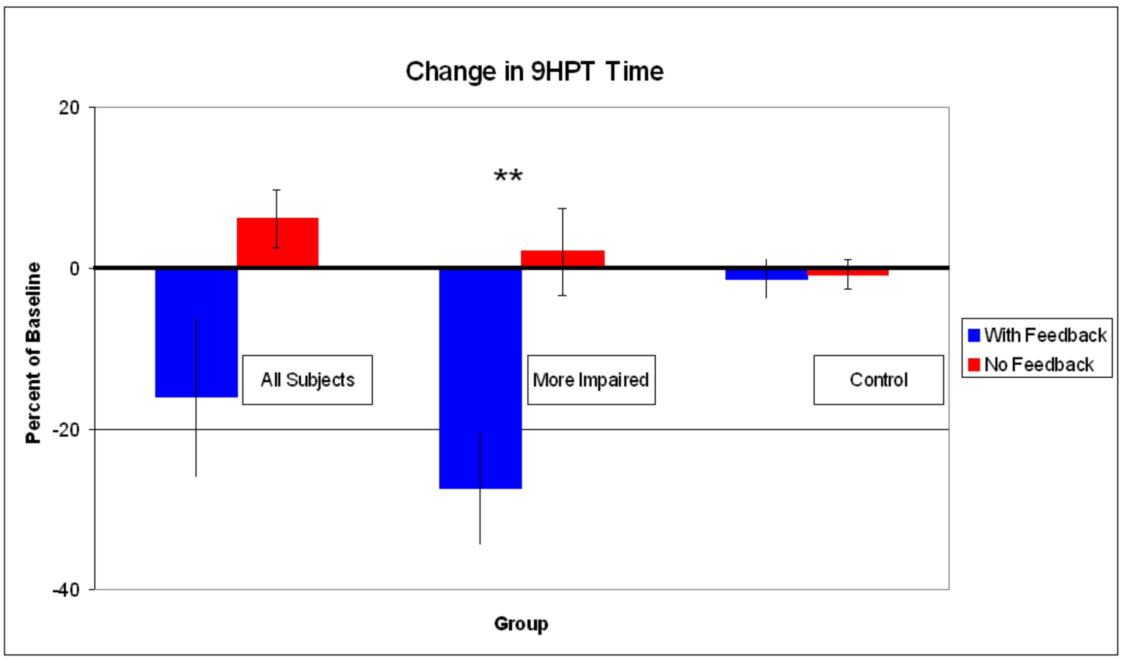

Figure 9 – 9HPT Times by Cohort – Change in times to completion of the 9HPT (Mean ± S.E.) for the entire population of impaired subjects (left), the 7 more severely impaired subjects (center), and the healthy controls (right) after WF (blue) and NF (red) training. Note that training with PAMI feedback improves 9HPT performance in brain-injured population ($p<0.05$ for most impaired), but does not yield a significant change for healthy subjects.

Tightened Inclusion Criteria

By imparting a minimum time for the baseline 9HPT time, the inclusion criteria are restricted to a subset of the participants. The minimum of 50 seconds to complete the 9HPT resulted in a cohort of 7 subjects, of whom two were from the WF-NF group. All seven subjects were analyzed in the same group, based on the above demonstration that the order of training has a negligible effect on results.

The more severely impaired subjects decreased their 9HPT time by 27.3% ± 9.93%. This value corresponds to a greater decrease than was registered from the entire cohort of participants. Training without feedback (NF) generated a 9HPT time increase of 6.22% ± 5.48%, which is comparable to the results of experimentation with no minimum baseline. Training order is thus shown to have minimal effect for the 7 most impaired subjects.

Results from the cohort of more severely impaired subjects are compared to the results from the entire population of brain injured participants in Figure 9. Assuming no effect from training order, training with the PAMI device yielded an improvement of 27.3% ± 9.93%. In contrast with the 2.07% ± 3.61% decline in function after NF training, this is a statistically significant improvement ($p<0.05$).

Another approach to characterizing the relationship between fine motor improvement and initial impairment is to generate a plot in which the percent change on the 9HPT is the ordinate and the baseline 9HPT time is the abscissa. Results from the present work are presented on such a coordinate system in Figure 10. The r^2 value of the lines of best fit for the WF and NF conditions are 0.64 and 0.01, respectively, indicating the measurable trend of improvement in the WF condition with increased impairment.

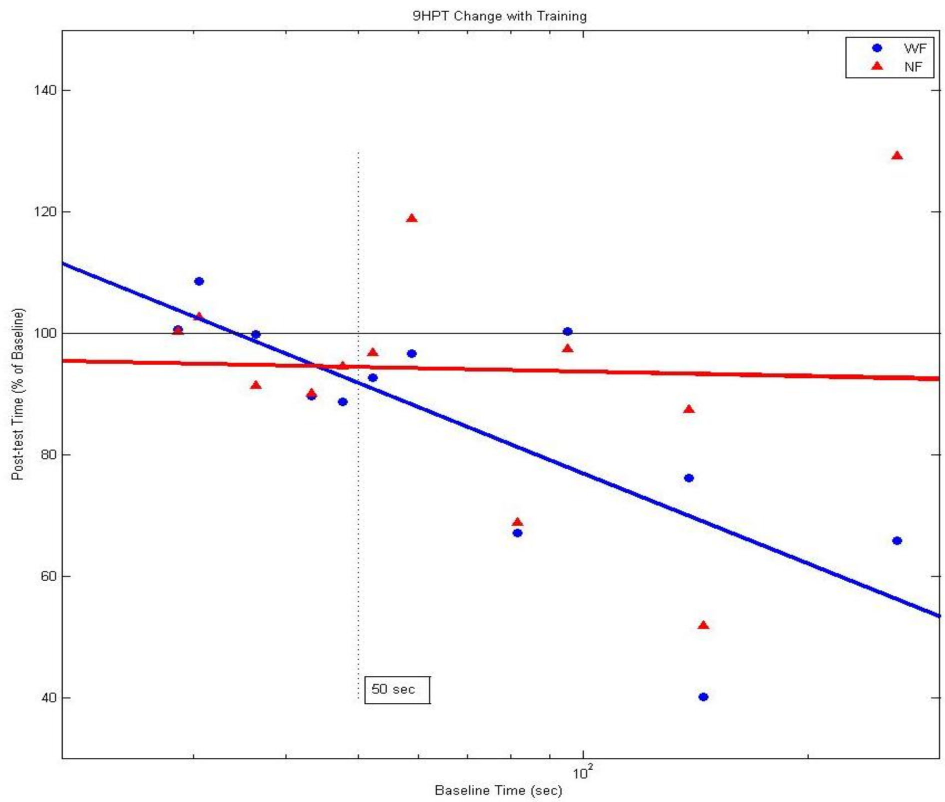

Figure 10 – 9HPT Improvement vs. log(Baseline) – Impaired subjects' changes (n=12) on 9HPT performance after training with (blue circles) and without (red diamonds) with lines of best fit. r^2 values for WF (blue line) and NF are 0.64 (red line) and 0.01, respectively. Semilog plot optimizes the fit of trend lines.

Healthy Control Subjects

The control subjects, whose motor control systems were not known to be impaired, did not demonstrate a change in 9HPT performance. Across all control subjects, the average change after the WF session was -1.31% ± 2.47 %, and the NF session had a -0.74 % ± 1.8 % change. Separating the subjects into WF-NF and NF-WF groups does not change results significantly; the most considerable change in 9HPT performance was a decrease of 5.16 % ± 1.53 % after the NF condition for the WF-NF group. Results for all control subjects are shown in Figure 9.

Features of Improving Activity

Hypothesis 2:

> The PAMI signal will reveal the successful motor control strategies in learning specific tasks. Signal features such as onset slope, range, maximum value, and duration are expected to be greater during training with feedback (WF) than without (NF). It is expected that the difference between values will be indicative of the mechanism by which task-specific feedback enables improvement in motor function.

An array of features from the PAMI signal are extracted in post-hoc analysis. The change of each feature over the course of training may yield insight into the mechanism of fine motor improvement during training with PAMI biofeedback. Extracting the features is performed for both the WF and the NF conditions, so that each feature's change with the PAMI biofeedback can be compared to the effect of traditional repetitive training.

The average PAMI feature changes for the 7 most impaired subjects are shown in Figure 11. Significance is shown using asterisks, where $p<0.1$ is indicated by one asterisk and $p<0.05$ has two. Results show that some features of the PAMI biofeedback waveform were significantly different when subjects trained with feedback as compared to the NF condition. The signal range, onset slope, duration, time above threshold, and jerk were all observed to be different between conditions, although some were greater in WF training and some were lower.

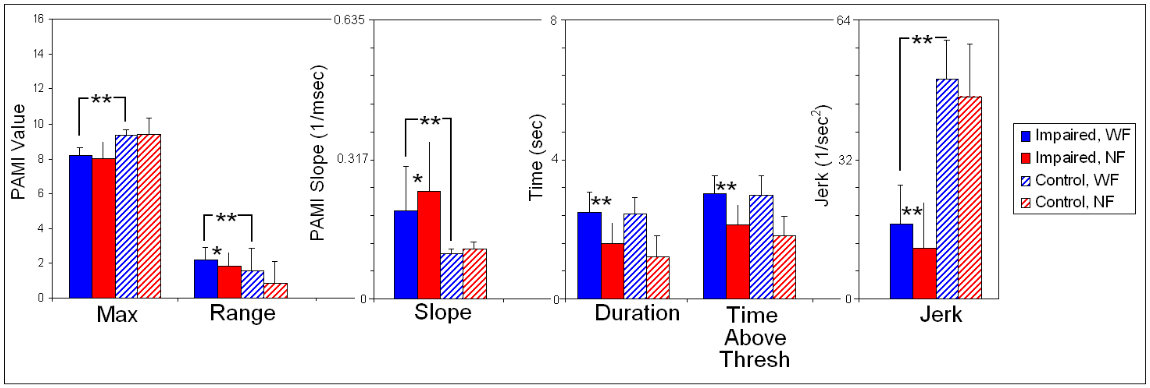

Figure 11 – PAMI Features by Condition – Features extracted from PAMI waveforms during WF (blue) and NF (red) training (Mean ± S.E.). Significance of comparison between WF and NF training for impaired subjects (n=7) shown between error bars; comparison between impaired (n=7) and control subjects (n=7) in WF training shown in brackets.

Max	Impaired	Control	Significance by Condition
WF	8.17 ± 1.22	9.36 ± 0.79	**
NF	8.05 ± 2.51	9.39 ± 2.5	**
Significance within Cohort			

Range	Impaired	Control	
WF	2.17 ± 1.96	1.56 ± 3.42	**
NF	1.82 ± 2.09	0.86 ± 3.27	**
Significance within Cohort	*	**	

Slope	Impaired	Control	
WF	5.04 ± 6.89	2.55 ± 0.89	**
NF	6.16 ± 9.17	2.87 ± 1.14	**
Significance within Cohort	*		

Duration	Impaired	Control	
WF	4.95 ± 3.1	4.89 ± 2.48	
NF	3.20 ± 3.11	2.45 ± 3.20	**
Significance within Cohort	**	**	

Time Above Thresh	Impaired	Control	
WF	6.08 ± 2.6	5.94 ± 2.97	
NF	4.25 ± 3.04	3.66 ± 2.90	**
Significance within Cohort	**	**	

Jerk	Impaired	Control	
WF	4.27 ± 5.98	12.6 ± 5.90	**
NF	2.92 ± 6.97	11.6 ± 7.97	**
Significance within Cohort	**	*	

Table 4 – Features of PAMI Signal – Values for WF and NF training (Mean ± St.Dev.) for impaired and control subjects. Significance is shown as * for $p<0.1$ and ** for $p<0.05$

Further analysis of the PAMI signal features compared the changes of the waveform over training. The result of this analysis is shown in Figure 12, and all data are reported in Table 4. The significant differences between WF and NF conditions are shown via asterisks as above, and the comparison of features from the first and third sets for each training condition is shown in the same way.

Similarly to the results of the all-repetition analysis shown in Figure 11, the WF condition yields mean, duration, and time above threshold values that exceed those of the NF condition in all three sets. Neither Duration nor Time Above Threshold change significantly between the first and third sets (Figure 12).

In the WF condition, both the maximum and the range values decreased significantly over the course of training. The maximum value decreased significantly in the NF condition as well, but the range value did not change in a noteworthy way. As a result, while the range value was significantly greater in WF training than in NF during the first set ($p<0.1$), the opposite was true in the third set. For the control subjects, there was no significant change across sets, and while the maximum values were approximately equivalent, the range in the WF training exceeded that of the NF condition.

Analysis of the PAMI signal slope in the impaired subjects revealed a decrease across sets in both the WF and NF conditions. In the third set, the slope in the WF condition was significantly less than that of NF training. The Slope values of the control subjects did not change significantly, and their values were exceeded by those of the impaired subjects across sets.

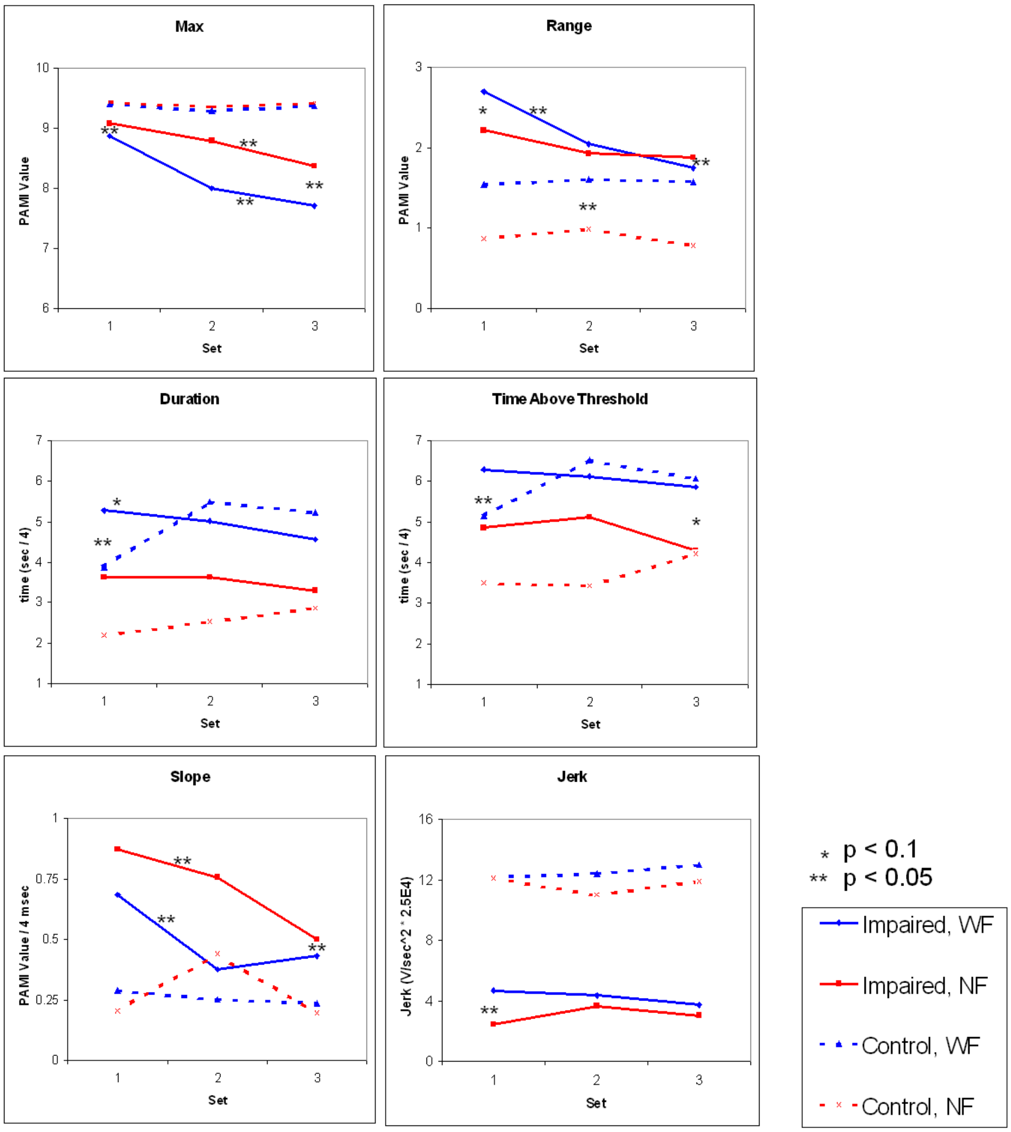

Figure 12 – PAMI Features by Sets – Features extracted within each of 3 training sets (abscissa, indicating training epoch) for impaired (solid) and control (dashed) subjects during WF (blue) and NF (red) training.

The jerk of the PAMI waveform, measured as the time integral of the third time derivative of the PAMI signal, did not change significantly across trials for the impaired subjects. In the first set, the mean jerk of the WF waveforms exceeded that of NF training ($p<0.1$), although the remainder of the sets did not have a significant difference. The jerk values of the control subjects did not change significantly, nor was there a difference between values within any set.

Coordination of Muscle Activation:

Hypothesis 3:

> During repetitive thumb-index opposition, muscle contraction measured by the PAMI device will reveal the coordination of the motor control system for both the healthy and brain injured cohorts. A comparison between the WF and NF conditions is expected to reveal the increase of synergy in brain-injured subjects when using PAMI biofeedback. In this way, change in the coordination pattern will be confirmed as the mechanism by which PAMI promotes rehabilitation.

Another analysis of the mechanism of changing motor function uses the Difference of Variance Index (dVI) to compare muscle activation patterns. Coordination is calculated as a function of the variance of muscle activations across trials, which are measured using the SMP values. Using Equation 6, the dVI values ranging from 1 (perfect coordination) to negative infinity (maximal discoordination). Analysis was performed within sets in order to assess the changes in coordination that are associated with the training conditions.

Typical dVI waveforms are shown in Figure 13. While some impaired subjects had dVI traces that were characterized by a unimodal decrease during the early period of activity, as in Figure 13B, others were visually similar to the control subjects' constant value as in Figure 13A. None of the features of the dVI waveform were correlated to baseline performance or improvement of the 9HPT.

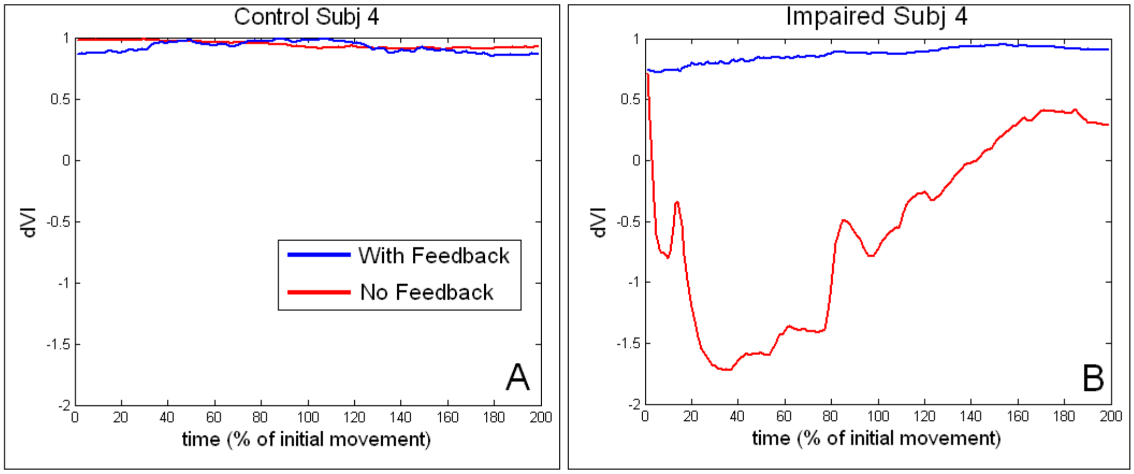

Figure 13 – Typical dVI Waveforms – Difference of Variance Index for a representative subject from the control (A, left) and impaired (B, right) cohorts, respectively. Note the consistently high value for controls, as well as the considerable curvature during early NF condition for impaired subjects.

Analysis of the dVI features between conditions is performed across all subjects. The values are compared as paired sources between conditions, and as independent sources of data for the comparisons of early and late training sets. The steady state value of the dVI signal was shown to decrease significantly ($p<0.1$), although no other significant differences were found.

For most of the features – specifically, the early, peak, maximum, and steady state dVI values – the difference between the NF and WF training conditions was negligible. This was the case both for the impaired subjects and the control subjects, as is shown in Figure 14. Another trend was the disparity between the mean dVI values for the healthy controls and those of the impaired subjects. The dVI value was generally greater for control subjects across the entirety of the signal, indicating that impaired subjects had worse coordination.

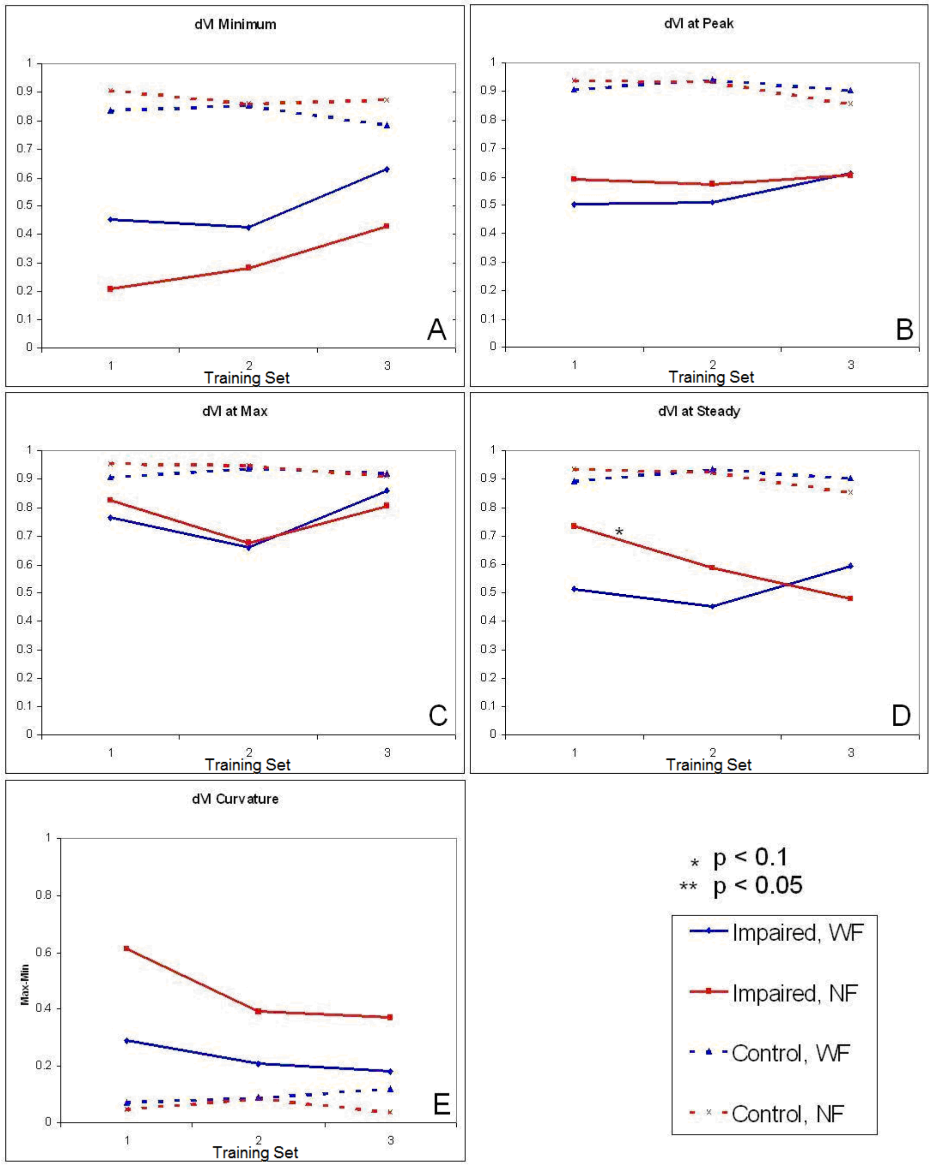

Figure 14 – dVI Features by Sets – Features extracted within each of 3 training sets for impaired (solid) and control (dashed) subjects during WF (blue) and NF (red) training. Note lesser curvature in WF training for impaired subjects, indicating greater coordination during PAMI training.

The curvature, measured as the difference between the maximum and minimum of the dVI waveform for each subject, did not exhibit the similarity between the NF and WF conditions that was typical of the other features. Instead, NF training had greater curvature than WF training across all sets. The decrease of curvature, evident visually in

Figure 14 for both training conditions, was not statistically significant. However, in the third set, curvature in the WF training condition was appreciably more similar to that of the control subjects than that of NF training.

Chapter 7 – Discussion: Validity of Methods

Thumb-Index Opposition

The PAMI device provided real-time feedback during a repetitive grasping task. While it could have been possible to choose any of a number of grasps or activations of the external muscles of the hand, the training task that was used for the present work was thumb-index opposition. The prehensile "pinch" allows for haptic feedback in partially insensate individuals while foregoing the need for an object to manipulate.

Thumb index opposition is critical to Activities of Daily Living and is common in the motor control literature. For example, thumb-index opposition has been a mechanism for mapping brain function [Carey 2006], and pattern recognition has been used to characterize its muscle activation. It has also been used as a measure of the effect of a rehabilitative intervention [Prochazka 1997].

Choosing a repetitive training scheme followed suggestions from the literature that repetition with biofeedback is an effective method for rehabilitation. As discussed above (see Chapter 2), it has been shown that improvement in motor function can be expected to increase according to the amount of training; in other words, that more is better [Langhorne 1996, Kwakkel 1997]. Furthermore, the effects of repetitive training can be magnified by coupling training with biofeedback. This follows the finding that the most effective training paradigms are highly attended and rewarded [Merians 2002].

Number of Repetitions

Approximately 30 repetitions of the thumb-index opposition were performed in each training condition, split evenly into three sets by resting periods of approximately one minute. This number of repetitions was sufficient to facilitate the restoration of fine motor function during training with PAMI biofeedback. However, without feedback, thirty repetitions were not likely to improve performance, even in the most impaired subjects.

The number of repetitions that subjects were asked to produce was primarily motivated by lessons learned in preliminary testing. Many of the more impaired subjects reported fatigue from excessive training, and thirty repetitions was the compromise that balanced fine motor impairment with subjects' needs. Because training without feedback did not produce even short-term gains in function after thirty repetitions, it is possible that additional training time might have facilitated some improvement. The total number of 60 seemed to be the best compromise possible between avoiding fatigue while fulfilling the “more is better” axiom [Langhorne 1996, Kwakkel 1997]. While some studies have used more repetitions during training, as many as 200 [Hesse 2005], there are a number of examples in the literature in which sessions used 30 to 60 repetitions [Teixeira-Salmela 1999, Volpe 2000].

The disparity between training conditions and its dependence on the amount of training can be found in previous work. Using biofeedback to train stroke patients' arm movements generated an immediate reduction in kinematic variability, which was evident in the first two to three repetitions of each trial [Thaut 2002]. Many studies report that subjects prefer feedback to standard training [Huang 2006, Byl 2003]. It is in the effects of long term therapy, totaling as much as 15 hours of training, that the line between standard and feedback-based therapy is blurred [Desrosiers 2005]. In this light, the thirty repetitions are both adequate to highlight the utility of PAMI biofeedback and encouraging for facilitating long-term recovery of function.

Number of subjects

Twelve brain-injured subjects participated in the present study, as well as seven control subjects. The number of control subjects matched the cohort of more impaired subjects, which were determined by adding a minimum time to completion on the 9HPT. Thus, the comparisons between impaired and control subjects' features of muscle activation are performed for seven subjects in each group.

Effort was made during subject recruitment to maximize the population of participants. All available patients at JFK-Johnson were screened, and the therapists on staff at JFK-Johnson were involved in the recruitment process. The resulting number of participants was the largest possible.

Statistical analysis indicates that the number of subjects was sufficient for making claims from the experimental results above, with power of greater than 80% (see Chapter 6). Some of the differences of PAMI features between training conditions were statistically significant. The difference between training with the PAMI device and standard repetitive training yielded a certainty of $p<0.05$ and a power greater than 0.95 using the Wilcoxon Signed Rank test.

Previous studies used 12 or fewer subjects. While some studies are designed to incorporate hundreds of brain injured subjects [Granger 1979], many are able to assess the efficacy of an intervention using approximately as many subjects as are involved herein [Prochazka 1997, Alon 2007]. Moreover, some studies have used as few as three subjects, although these studies were generally designed as demonstration-of-concept case studies [Luo 2005, Szturm 2008]

Impairment Types

The population of participants in the present study included both Traumatic Brain Injury and stroke survivors. For the purpose of analyzing trends across the entire cohort, the diversity of subjects requires the concomitant assumption that the two brain injuries can be treated identically. There have been precedents for this approach, in which both TBI and stroke were the cause of brain injury in a cohort of impaired subjects [Platz 2001, Bode 2002]. Moreover, the assessment of the efficacy of the PAMI device as a tool for restoring motor function yields similar results when the cohort is separated by injury type. It is thus shown that the device is useful both for stroke and TBI patients, which was the intention of its development.

In assessing the mechanism of changing motor function using the device, the subject's impairment type and level are possible significant variables. It is known that a number of specific impairments can be typical of TBI [Wilson 2007, Gordon 2006] and stroke [Sainburg 2006, Byl 2003] (see Chapter 2). However, for the present work, it is the restoration of function after brain injury that is of primary interest.

Realism of NF condition

Subjects trained in both an experimental condition, in which PAMI biofeedback was shown on the computer monitor, and a control condition, in which there was no biofeedback. The latter condition was included to contrast the effect of standard repetitive training with that of PAMI training. In this way, subjects were able to serve as their own controls, allowing a direct comparison of paired data.

The NF condition is representative of a typical rehabilitative protocol, in which a subject is instructed to repetitively perform a task in order to restore fine motor function. The tasks performed outside of the present study can include other ADL, while herein the only training involved thumb-index opposition. This allowed as direct a relationship between training and the 9HPT as possible.

The protocol of training in the NF condition was designed in collaboration with occupational therapists at JFK-Johnson. It is similar to the control condition in a number of studies comparing new rehabilitative methods to standard training [Alon 2007, Michaelson 2004]. Therefore, it can be expected that training without the PAMI device is representative of standard therapeutic training, and that the greater improvement when training with the device is indicative of its advantage over training without feedback.

Study Design

Participants in the present study were given two training sessions, one with feedback and one without, totaling approximately 16 minutes of training. The entire process of demonstration, testing, and training took no more than 30 minutes. By limiting the amount of training to a short period of time in a single day, the study effectively eliminates the potential of long-term changes from PAMI training. Thus, the improvement recorded using the 9HPT after PAMI training is unlikely to persist, although no further measurements were taken following the third 9HPT.

The short term nature of the present work allows insight into the immediate effects of training on the motor control system, as detailed below (see Chapter 7). This type of study has been performed before, specifically targeting the acute effects of rehabilitative protocols rather than assessing functional gains over the course of weeks [Michaelsen 2004]. Further assessment of the PAMI device will necessitate long term studies.

Block-Randomization

Brain-injured participants were subdivided into two experimental groups that differed only in the order in which training conditions were presented (WF→NF and NF→WF). Subjects were randomly assigned to one of the two groups. Although they were not kept blind to the design of the study, they were not informed of the expectations of their results on the 9HPT or muscle activation patterns.

Within the two groups, it could be expected that the severity of impairment would affect the potential of each subject for improvement [Fasoli 2005]. This is confirmed by the approximately linear relationship between improvement on the 9HPT and the initial time to completion, as in Figure 10. For this reason, the cohort of brain injured subjects was reduced to include the most impaired subjects using their baseline 9HPT time, chosen arbitrarily and without bias. This is comparable to the block-randomized paradigm used previously, although it was performed post-hoc [Alon 2007].

Chapter 8 – Discussion: Implications

Restoration of Function with Biofeedback

Hypothesis 1 tested the positive effect of PAMI training on the motor control system in impaired subjects. The improvement of fine motor function due to training can be quantified using an independent rater, the 9HPT, which allows a comparison to repetitive training without biofeedback. This comparison was tested using the Wilcoxon Signed Rank Test to determine the statistical significance of the improvement associated with the PAMI device. Results from 9HPT testing showed that subjects decrease their time to completion of the 9HPT to a greater extent after training with the PAMI biofeedback (WF) than after the no-feedback condition (NF) ($p<0.05$).

Referring to Figure 9, the general trends of subjects' fine motor function can be observed for each training condition. On average, the WF condition yielded a decrease in the time to completion of the 9HPT, which indicates an improvement in fine motor function. In contrast, training in the NF condition yielded no improvement – in fact, the mean difference was actually a slight increase in 9HPT time.

The improvement from training with the PAMI device and the lack of effect from NF training are essentially independent of the order in which the training conditions are presented. The parallel between WF training effects for the WF-NF group and the NF-WF group can be seen in Figure 8, as is the case between the NF training effects. For this reason, the possibility of a confounding effect from fatigue, cognition, or other artefactual influences as listed above (see Chapter 4) can be dismissed as unsubstantial.

Across the entire cohort of subjects, the mean effect of training in the WF condition was a decrease in 9HPT time to completion of 16.1% ± 24.2%. The change after training without feedback was an increase of 2.07% ± 12.5%. This indicates that training with the PAMI device has a positive effect on fine motor function in impaired individuals, especially as compared to the control condition. These results are shown in Figure 9. The relatively large standard deviations suggest that this may not be a statistically significant difference, which prompts further analysis of the results. Similarly, training with EMG-based biofeedback has yielded beneficial results from case studies, but statistically significant differences between standard and biofeedback training conditions are unusual [Huang 2006, Glanz 1997].

Analyzing the efficacy of training with the PAMI device, or of any rehabilitative scheme, is complicated by the range of impairment that can be the result of brain injury. Ideally, the entire population of subjects would be characterized by similar degrees of fine motor function, which would allow the assumption of normal distribution of results about the recorded means. The non-uniformity within the cohort of brain injured subjects was unavoidable in the present work, and therefore any statistical analysis based on the assumption of a normal distribution would be inaccurate.

The inclusion criteria of the present study were chosen to maximize the comparability of the participants in order to minimize this effect. However, the baseline times to completion of the 9HPT across all subjects ranged from 28 seconds to 263 seconds. The corresponding span of impairments prompted the adoption of further assumptions to characterize the data for analysis.

By appending an additional limitation to the inclusion criteria, such that subjects had a minimum baseline 9HPT time, the analysis was restricted to the more severe end of the spectrum of impairments. The threshold for this inclusion criterion was set arbitrarily at 50 seconds, which was observed to be a naturally occurring cutoff between those subjects whom the repetitive training affected and those for whom the protocol was ineffective. Analysis was repeated for both the limited cohort and the entire cohort.

While the assumption of a further inclusion criterion necessitates the exclusion of subjects with less severe effects of brain injury, it should not be interpreted as an assertion that less-impaired individuals receive no benefit from the brief exposure to the PAMI device. Instead, it indicates the potential of the training protocol described above for use with more severely impaired subjects. The efficacy of the PAMI biofeedback with an alternate training method for subjects with baseline 9HPT times less than 50 seconds should not be dismissed here, because the protocol may not be appropriate for this group.

The mean 9HPT time to completion for the limited cohort are shown in Figure 9. This analysis was performed across both groups, using the assumption that training order has minimal influence on the efficacy of training as was demonstrated above. The mean difference in the effect of training between the WF and NF conditions is more than 20%, and the change from the NF condition is approximately a 6% increase in 9HPT time. This further demonstrates the effectiveness of training with the PAMI device for the restoration of fine motor function. Furthermore, as compared with the results of the entire cohort of participants, also shown in Figure 9, these results indicate that the training protocol used in the present work is primarily effective for more severely impaired individuals. All of these results are reported in Table 3.

A further demonstration of the relationship between the efficacy of the PAMI device and the subjects' impairment as measured by their baseline 9HPT times is shown in Figure 10. Across the continuum of subjects' impairments, there is an approximately log-linear proportionality between the percent change of 9HPT time from baseline due to training with the PAMI biofeedback and the initial baseline time. In other words, the greater the initial impairment, the more significant the effect of training with the PAMI device. in contrast, the NF condition produced very little effect. The relatively small slope (Figure 10) indicates that the NF condition's efficacy has very little dependence on the subjects' degree of impairment, although the positive slope suggests that more severely impaired subjects are not well served by simple repetitive training.

A statistical analysis of the changes in 9HPT time reveals the significance of the difference between the training conditions. Based on the relatively small sample size (N<40), the analysis was done with the Wilcoxon Signed Rank Sum test. In addition to its non-parametric approach, the Wilcoxon Signed Rank Sum test assumes that paired data come from the same source, as is the case with the subjects' 9HPT times in the present work. This test of statistical significance is applied to the data from both the entire cohort of subjects and the group defined by a minimum baseline 9HPT time. For both analyses, participants are not separated by training order.

For the entire cohort of subjects, the Wilcoxon Signed Rank Test did not reach significance, as is reported in Table 4. While the mean of the 9HPT changes in the WF condition was a considerable 16.3% decrease, there may have been enough impact from the less impaired subjects to decrease the degree of certainty. Similar influences from the less severely impaired participants may have increased the variance in the NF condition. This possibility is further suggested by a qualitative analysis of the distributions of Figure 10.

To test the possibility that the less impaired subjects introduced uncertainty into the hypothesis that training with the PAMI device yields an increase in fine motor function, the cutoff based on a baseline 9HPT time of 50 seconds reduces the subject pool to the 7 more severely impaired subjects. The Wilcoxon Signed Rank Test results in a p value <0.05 for this population. For the more impaired subjects, the difference between the effects of training and without the PAMI biofeedback is statistically significant. This shows that the expectation of a significant improvement in fine motor rehabilitation via the PAMI device, is met in experimentation with more severely impaired individuals.

Features of Improving Activity

The improvement in times to completion of the 9HPT after training with WF training is strong evidence of a change, if only temporary, in the properties of motor control. By extracting features from the PAMI signal waveform, the underlying cause of fine motor restoration can begin to be explored.

A variety of features were selected for the present work, ranging from the straightforward duration of activation to the energetic approximation from signal jerk (see Chapter 5). The results for this analysis included both a comparison across all repetitions and an observation of the trends by training set (see Chapter 6).

Looking first at the results across all repetitions (Figure 11), the contrast between healthy control subjects and impaired subjects is clear. All features, except duration and time above threshold for healthy subjects, differ from those of the brain injured ($p<0.05$). In terms of the jerk feature, this difference is surprising, because the greater jerk for control subjects indicates that healthy prehension is less smooth than that of the impaired motor control system. Similarly, the control subjects' slope was significantly lower than the impaired subjects', suggesting that the healthy prehension begins less rapidly. The comparison for the other features is more easily explained as intuitive evidence of unimpaired motor control.

The analysis of the PAMI signal features from impaired subjects yields intriguing differences between WF and NF training. Since the seven most impaired subjects included in the feature analysis were significantly improved after training with PAMI feedback, the correlation between feedback condition and feature values is telling. Most features were significantly greater in WF training than in NF, although the opposite was true for the slope feature. Again, this is somewhat surprising for the jerk feature; however, knowing that healthy subjects' jerk was greater than that of the impaired subjects, this appears to be indicative of decreased impairment.

The difference between the maximum at peak of the PAMI signal from WF and NF training is not statistically significant. While this does not necessarily indicate that they are similar, it is unexpected. The availability of feedback should facilitate the improvement of that feedback. However, this does not seem to be the case for impaired subjects.

Interpretation of the duration and time above threshold values is relatively straightforward. The longer the duration, the more time the muscles are activated in the proper pattern. Assuming that subjects are attempting to maximize the PAMI value by repeating the target pinch, the duration and time above threshold values could indicate that the availability of visual feedback aids in that effort.

However intuitive the possibility of using the knowledge of the feedback value to maximize the feedback value may be, this inference must be modified by the maximum at peak values. The decrease in maxima, shown in Figure 12A, suggests that the muscle activations are actually less accurate after training. Thus, the duration, time above threshold, and maximum at peak values indicate that motivation plays an important role in fine motor rehabilitation. The use of motivation from task-oriented feedback has been demonstrated in the rehabilitation science literature [Byl 2003]. By adhering to the principles outlined in previous work, the PAMI device can be said to improve fine motor function by serving as a visual reminder of the goal of training.

Motivation is likely not the only mechanism by which PAMI biofeedback facilitates motor restoration. This can be seen from the changes in slope and jerk with training. The slope of the PAMI signal is greater during NF training than in the WF condition. When observed by set, the NF slope decreases significantly, while the WF slope does not. This implies that a lower PAMI signal slope, reflecting a slower rate of approach to the target muscle activations in sensor space, is of benefit to fine motor improvement.

Similarly, the jerk values imply that smoothness of the PAMI signal is not associated with healthy fine motor control. The gap between the jerk in the two experimental conditions decreases during the training process, although neither condition changes significantly (Figure 12D). While no inferences about the properties of the motor control system can be drawn directly from this result, it does suggest that the WF condition and the NF condition produce energetically different muscle activations.

The potential of PAMI biofeedback to influence the operation of the motor control system is the result of the information it makes available to the user. Augmented feedback's use of the state variables – in the case of the PAMI device, the muscle activations measured by SMP – provides meaningful information to the motor control system about the real-time product of its activations [Swanson 1992, Van Dijk 2005]. It is therefore not surprising that there may be a change in the motor strategy. The slope of the PAMI signal is suggestive of the nature of that change. Thus, while the analysis of PAMI features cannot draw strong inferences about motor planning, it prompts the use of the Difference of Variance Index for that purpose.

Coordination of Muscle Activation

Herein it has been demonstrated that the PAMI device does work, and that it does so in a way that is different than traditional repetitive therapy; how the device restores motor function has not yet been discussed. Hypothesis 3 states the expectation that the structure of variability in records from the PAMI device elucidates the mechanism by which fine motor control is restored.

Results from this analysis did not yield significant differences that would pinpoint changes in the motor control schema employed in thumb-finger opposition. Nevertheless, inferences can be drawn with regards to the changing recruitment of muscle activity over the course of training as they relate to the Difference of Variance Index (dVI). Moreover, the temporal features in the dVI waveform may suggest the role of deeper layers of fine motor control in rehabilitation with the PAMI device. These characteristics are shown to be different for control and impaired subjects. Moreover, differences can be identified between training conditions for the impaired subjects, indicating the possibility of learned coordination in the restoration of fine motor function.

The dVI is, in essence, the measure to which Uncontrolled Manifold Analysis reduces for direct biomechanical variables [Latash 2002, Scholz personal communication]. Rather than resolve variance into subspaces of a movement's multidimensional records, the similarity of units in the Task and Component spaces lets the dVI approach directly compare their variances. Generally, more positive values correspond to a strong synergy underlying the control, while lower values indicate discoordination in the recruitment of muscles.

The poor coordination of impaired subjects is evident in all features of the dVI waveform. A distinguishing feature of the dVI records from impaired subjects' training sessions is their waveform morphologies. The average waveform, shown in Figure 13 (right), is characterized by a lower dVI value preceding 100% of activation, followed by a sharp increase. The dVI record is approximately unchanging following this sharp increase, suggesting that after the initial pinching movement, the motor control system reaches a steady state.

In contrast, healthy control subjects are better coordinated in their thumb-finger oppositions. Their typical waveforms had very little curvature, indicating that their muscle activations were well coordinated throughout each repetition (Figure 13, left). In the first set, the dVI values from healthy subjects are consistently greater than those of impaired subjects, reinforcing the suggestion that the brain injured population experiences discoordination. There are no significant changes between the first and third sets' values, which shows that WF training does not necessarily reduce discoordination in all subjects.

This trend of increasing coordination within an activity has been shown to emerge from repetitive fine motor training. In a finger force production task for subjects with Down syndrome, the early phase of a total force increase was marked by error-amplifying discoordination, as defined using UCM analysis. The middle and late phases of the ramp had greater coordination [Scholz 2003]. This pattern is comparable to the waveform of the dVI trace up to 100% of the initial pinch. In another study, control subjects had much better coordination throughout a finger force task than did impaired subjects, with minimal discoordination during early activation [Latash 2002].

In contrast, healthy control subjects are better coordinated in their thumb-finger oppositions. Their typical waveforms had very little curvature, indicating that their muscle activations were well coordinated throughout each repetition. The difference between control and impaired subjects' typical behavior can be seen in Figure 13.

Because each training condition included approximately 30 repetitions divided evenly by two rests, the recorded signals can be partitioned into three sets. Each set, containing approximately 10 repetitions, bears sufficient data to perform the dVI analysis within the set. In this way, any trends in the dVI trace over the course of a training session can be observed. This analysis results in the extracted feature values plotted in Figure 14.

The poor coordination experienced by impaired subjects relative to that of healthy controls is evident in all features of the dVI waveform. In the first set, the dVI values from healthy subjects are consistently greater than those of impaired subjects, reinforcing the suggestion that the brain injured population experiences discoordination. There are no significant changes between the first and third sets' values, which shows that WF training does not necessarily reduce discoordination in all subjects.

The only exception to the lack of significant changes across training is found in the steady state values from training without PAMI biofeedback. As Figure 14D shows, on average there is a decrease in the dVI value in the late stages of activity. This result suggests that while the WF condition does not significantly improve coordination, it may prevent the decrease in coordination that is typical of NF training. It may be through this mechanism of continued coordination that the Duration and Time Above Threshold features of the PAMI signal are greater during WF training.

Another noteworthy set of dVI features is the Curvature value that is extracted from the minimum and maximum dVI value of each subject, as in Figure 14E. Although this trend is not strictly significant, there seems to be a typical decrease in waveform Curvature for the impaired subjects over the course of training. Moreover, the Curvature starts and ends lower in WF training than in the NF condition; in the third set, the impaired subjects' Curvature in WF training is more similar to the control subjects' values than to the impaired subjects' NF value.

The difference in trends between Curvature and the features from which it is derived, Maximum and Minimum, may be of some importance for the present analysis. While neither the Maximum nor the Minimum of impaired subjects' dVI waveforms approaches the corresponding values of the control subjects, the gap between them does. This suggests that coordinating muscle activation could be important for restoring motor function.

Latash's application of the variance comparison method found similar results for individuals with Down Syndrome in a finger force production task. In early testing, participants employed strategies that resulted in error amplification, indicating a level of discoordination. After training, the variance comparison suggested that synergy underlying finger force production was stabilizing the total force [Latash 2002] Both before and after training, the variance comparison showed improved coordination within repetitions. Similarly, impaired subjects herein exhibited improving coordination both within repetitions and across sets.

That the Curvature, but not the Minimum, is identifiable as a key feature of the dVI waveform during fine improvement is potentially suggestive of the nature of motor restoration that PAMI training yields. Subjects' brain injury type, stroke or TBI, was not well-correlated to the extent of Curvature. However, it may be that the location of the damage to the central nervous tissue affects the potential for improving coordination. Future work, involving more precise information about the location of brain tissue damage for more subjects, may be able to assess the relationship of dVI Curvature with specific areas of the brain.

While information pertaining to the location of damage for subjects in the present work was not available, it is possible to speculate what the source of dVI Curvature might be. It is unclear where primitives are organized (see Chapter 3). However, it can be conjectured that if the stabilization of function is affected by stroke or TBI, then the location of damage corresponds to the location of the organization of primitives. On the other hand, if the dVI Curvature is minimal, as was the case for a number of impaired subjects herein, then it could be that the location of damage is either “upstream” or "downstream" of synergy coordination. This would affect the spatial and temporal parameters of motor function, which would be reflected here in the Maximum and Slope features of the PAMI signal. Curvature of dVI, however, and likely the Jerk of the PAMI signal, would be less affected.

The waveform morphology of the dVI signal may also be useful in identifying the neurophysiology underlying the restoration of motor function with PAMI. In addition to the role of curvature, discussed above, its timing could be of importance. The curvature occurs early in the movement, generally during the first 400ms or less. As Zatsiorsky notes, this early feature occurs too quickly to be the result of peripheral feedback , which relates to the use of feed-forward generation of trajectory [Zatsiorsky 2004, Spoelstra 2000].

The role of decreasing early dVI could be related to the mechanism of changing motor function. This connection can be thought of as depending on the statistical significance of the difference in curvature between WF and NF training. If there is a significantly different trend of curvature between the two conditions, then it may be that motor planning is the impaired aspect of the motor control system in some individuals, and that the use of PAMI biofeedback facilitates the generation of a motor plan. Similar results have been found in preliminary testing of startle responses in the reaching behavior of stroke survivors [McCombe Waller, personal communication]. In this case, it would be possible to infer that the motor planning of thumb-index opposition is modified over training, which is correlated to the improvement of fine motor control.

While it is not certain how motor learning is accomplished at the neurological level, a number of possibilities in accordance with the present results have been suggested (see Chapter 3). It has been postulated that motor learning is the result of tuning motor primitives [Thoroughman 2005]. The modified combination of primitives would then result in changed motor function [Flash 2005]. The use of error signals to train a computer-based inverse kinetic model to approximate motor learning has given a more detailed possibility for that mechanism [Spoelstra 2000].

On the other hand, testing with more subjects may reveal that the difference between curvature during WF and NF training is minimal. In this case, the role of early muscle activation in restoring motor function would be insignificant. The greatest difference between the dVI records in the training conditions would therefore be in the steady state condition, reinforcing the idea that the use of task-relevant biofeedback motivates the repetitive performance of the task

The results of the present work appear to be concordant with possibilities introduced in the motor control literature. There is an apparent decrease in the discoordination of muscle activation, as measured by the dVI signal, during WF training, after which subjects show temporarily improved fine motor function. The feed-forward nature of control during early activation allows the inference from comparing dVI waveforms that previous feedback could be incorporated into the planning stage of each activation. The lower slope during training with the PAMI device than without supports the characterization of this modification. Thus, a mechanism by which PAMI biofeedback facilitates fine motor restoration could be the improvement of the motor plan prior to movement.

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