Chapter

Restoring Independent Living after Disability Using a Wearable Device: A Synergistic Physio-Neuro Approach to Leverage Neuroplasticity

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Abstract

The number of people living with various grades of disability is now in excess of 1 billion. A significant portion of this population is dependent on caregivers and unable to access or afford therapy. This emerging healthcare challenge coincides with new knowledge about the self-learning, self-organizing, neuroplastic nature of the brain, offering hope to those trying to regain independence after disability. As conditions such as stroke and dementia begin to affect more and more people in the younger age groups, there is an urgent, global need for a connected rehabilitation solution that leverages the advantages of neuroplasticity to restore cognitive and physical function. This chapter explains a novel approach using a Synergistic Physio-Neuro learning model (SynPhNe learning model), which mimics how babies learn. This learning model has been embedded into a wearable, biofeedback device that can be used to restore function after stroke, injury, the degenerative effects of aging or a childhood learning disability. This chapter enumerates the clinical studies conducted with adult stroke patients in two scenarios—with therapist supervision and with lay person supervision. The results indicate that such a learning model is effective and promises to be an accessible and affordable solution for patients striving for independence.

Keywords: SynPhNe, stroke, rehabilitation, wearables, biofeedback, neuroplasticity, EEG, EMG, sensors

1. Introduction

In a systematic review of 151 studies, there was insufficient evidence that traditional neurological treatment methods were effective in improving muscle strength, synergies, muscle tone, dexterity, or ADLs after stroke [1]. Kollen et al. reviewed 735 available published (clinical) stroke rehabilitation trials [2]. They concluded that conventional treatment approaches induce improvements that are confined to impairment level only and do not generalize at a functional improvement level. In contrast, they stated that the treatment strategies that incorporate a strong emphasis on functional training may hold the key to optimal stroke rehabilitation and that appropriate intensity and task-specific exercise therapy are important components of such an approach. This was later reconfirmed to various degrees by others [3, 4].

Several commercially available devices have been built to deliver repetitive movements to an impaired human hand for stroke survivors to regain the use of the hand. However, the dysfunction of the natural afferent feedback pathways and proprioception hampers the sensory learning process of the patient and its conversion to execution of movement. This contributes to an inadequate restoration of functionality despite reducing impairment at a gross motor level [4, 5]. External manifestations of movement such as trajectory, force, acceleration, range of motion and the like are ultimately dependent on adequate, appropriate, and timely self-regulation of brain and muscle activity specific to various tasks. After an event such as stroke, various compensatory strategies come into play to execute the same movements, which, left unaddressed, become learned behavior. Re-engaging the human being's innate sensory learning mechanisms to regain the appropriate muscle and neural strategies is, therefore, a challenge and an unmet need. If high repetition-based rehabilitation is embarked upon without such re-learning, one runs the risk of post-trauma compensatory strategies being unknowingly reinforced in the brain, thus restoring movement and function in only a limited manner [6, 7].

1.1 Learning in a rehabilitation context

The body learns coordination for task performance by using all the lessons learnt from neuro-muscular, inter-limb, intra-limb, and eye-hand co-ordination [8, 9]. The specific strategies used are not only different from task to task for a person, but also differ for any one task between persons [10]. Initially, it was thought that the muscle synergies eliminated the redundant degrees of freedom by constraining the movements of certain joints or muscle [10]. But this does not work very well with the initial pathological constraints of an impaired arm. It has also been shown that constraining the movement of certain joints and muscles requires more energy and neural commands, and hence increases the number of neural signals required to perform the task [11]. However, some strategies are fundamental to all movement, such as maintaining an agonist-antagonist balance in the appropriate muscle groups, a moderation of effort to make repetitions possible during rehabilitation without being confounded by fatigue, and an active brain state which allows one to bring attention to the task at hand in a consistent manner. Facilitating such general strategies with technology rather than directly and artificially controlling individual, task-specific strategies is less complex, requires lower computational power and could facilitate a generalization of such useful strategies to other activities. This could in turn result in higher degrees of independence.

As an illustration, let us consider how humans learn handwriting. This is usually done by tracing over an existing alphabet or joining dots in the shape of an alphabet. Here, constraints are mind imposed based on visual cues while no constraints are placed physically on the hand. These mind-imposed constraints involve seeing a pattern and responding with a pencil, like a sort of static imitation. Everyone may choose a different strategy to impose these constraints, based on the kinematics of the more proximal joints and natural synergies of muscles proximal to the point where control is desired. This is like the uncontrolled manifold hypothesis for motor learning and involves a mechanism by which brain and body complement each other in real-time in managing elemental and contextual variables [12]. Hence, there does seem to be some convergence between motor learning theory and how developmental biology describes babies and infants learning in an associative, Hebbian manner using their sensory and motor faculties. The next question is whether such learning can be used as a pathway to undo the maladaptive, compensatory brain-muscle strategies that are common among chronic stroke patients with upper arm disability and help re-educate the adoption of appropriate strategies.

1.2 Self-regulation and its impact on learning and neuroplasticity

Stroke is an injury that affects not only body but also cognition and cardiovascular health, among others. Hence, it resembles a systemic injury or trauma even in mild to moderate cases. Healing of such systemic injuries has the final pathway of self-management or self-regulation [13, 14]. Self-regulation is ingrained by a biological, natural model of learning driven by the feedback and feedforward of information [13]. Self-regulation essentially requires a measure (absolute or relative), some facility to monitor changes in real-time, and some training to help develop the skill to modify the measure and move it in a desired direction [14, 15]. In the area of motor recovery, similar benefits of "self-control" have been demonstrated [16] but it is not very clear whether it can result in improvement in functional tasks.

Exercise is one way of providing an enriched motor environment. It facilitates plasticity in the brain and protects against the erosive effects, and this is one of the fundamental principles of early mobilization and continuing long term therapy. However, not all exercise regimens are adaptive, and some may even be maladaptive. In animal studies, the location and type of injury appear to dictate to some extent whether the intensity of motor rehabilitation training results in pro-plasticity, neutral or adverse contralesional hemisphere effects [17]. Additionally, the contralesional hemisphere appears to benefit from early, intense, motor enrichment while the perilesional area may be most helped by a gradual, modest increase in therapy. On another note, if the motivation to use the impaired limb after stroke is reduced due to ineptitude, pain or fatigue in that limb and there is a corresponding increased reliance on the other extremity, "learned non-use" of the impaired limb is the result [18].

While remarkable improvements in function have been reported when the non-impaired arm is constrained, as in constraint-induced therapy [19], excessively intense therapy can also lead to increased chances of secondary tissue loss due to reduction of brain derived neurotrophic factor (BDNF) expression in the brain during recovery [20]. Thus, while early onset of therapy using repetitive practice is vital to recovery, too much of it can exaggerate the extent of injury. This becomes even more significant because commonly used clinical assessment tests are not sensitive to small changes and do not allow the experimenter to distinguish between actual neurological recovery and behavioral compensation [21]. Just as neuroplasticity is a mechanism which can be leveraged to regain function, training of inappropriate, compensatory muscle and neural strategies, adopted unknowingly, can just as easily get ingrained in the brain and may take a long time to undo. The chances of this happening are heightened after stroke, when touch function, proprioception and cognition are adversely affected, and self-regulation ability is reduced due to the disruption of the natural feedback loops. Hence, apart from re-learning brain and muscle strategies, self-regulation of intensity in order to consistently keep compensation at bay and maintain beneficial strategies during training is another important component in this learning-led recovery model.

Like in the handwriting example given earlier, any learning model must satisfy the requirements of an experience derived from a sensory-rich system, as well as a motor system free of artificial constraints, which can adequately choose the synergy and/or strategy necessary to respond to this sensory system [22]. This is very similar to infants who learn in a non-instructional manner rich in sensory experience, using a feedforward-feedback sampling process [23]. Like in infants, the presence of such plasticity may provide an opportunity for functional recovery after stroke, if the most appropriate strategies are learnt and the maladaptive ones unlearnt [24].

2. The synergistic physio-neuro (SynPhNe) learning model

2.1 Learning in babies

There is now a growing understanding about how the body affects learning. The embodiment hypothesis proposes that sensorimotor activity of the person as it interacts with the environment is central to the development of intelligence [23]. In this field of study, the six principles of learning that babies instinctively follow can be summarized as under [23]:

1. Being multi-modal.

2. Being incremental.

3. Being physical.

4. Exploring.

5. Being social.

6. Learning a language (symbolic representation).

2.1.1 Being multi-modal

A multi-modal experience of the world is achieved in humans through the sensory system which is made up of a vast array of sensors to provide vision, audition, touch, smell, balance, and proprioception. Any single function can be accomplished by more than one signal configuration from the neurons and different neuron clusters need not be limited to a single function. This type of redundancy ensures continuity in function where parts of the network can learn from each other without an external teacher.

The second characteristic is the time-locked correlations between several simultaneous inputs, which are a powerful tool for representation, both singly and in combination with various events and objects in the environment [25]. In real-time these activities are mapped to each other to discover "higher order regularities," for example, using a combination of touch and vision to understand texture or transparency.

2.1.2 Being incremental

In non-incremental learning, the entire training set is usually fixed and then presented in entirety or randomly sampled. However, it seems that systematic changes in the input patterns and their overlapping occurrence in time play a large part in determining the development process. As a child grows, the vision starts to couple with the hearing and helps organize attention. In hearing-impaired babies, we see disorganized attention and a consequent slower learning (this is common in stroke cases, where patients experience sensory overload and cognitive deficiencies). Co-ordination is a form of mapping of multi-modal learning and the way they map changes over the development time, using either changing patterns or additional sensory inputs which the infants are now able to voluntarily provide themselves through physical exploration. Shifts in inputs thus result from the infant's own behavior. Using the body and moving from one place to another presents new spatial-temporal patterns and alters the infant's perception of "objects, space and self." Experimental studies show that one of the factors that strongly influence biological intelligence is "ordering the training experiences in the right way" [26].

2.1.3 Being physical

Experiments by Ballard et al. [27] and Baldwin [28] show that children off-load short term memory to the world by linking objects and events to locations, using attention to selectively point to the world. It is an easy way to build coherence in the cognitive system and to keep contents of different information clusters separate from each other.

2.1.4 Exploring

Initially the baby does not know what there is to learn. Babies can discover both the tasks to be learned and the solution to those tasks through exploration or non-goal directed action. One of the ways of exploration is spontaneous movement. As they contact objects in the environment, they progress from non-reaching to reaching. Thus, they seem to move from arousal to exploration to a selection of solutions from whatever space they can explore, which initially is limited. This type of learning is possible because of the multi-modal sensory system that builds maps from time-locked correlations starting with smaller spatial maps and expanding to larger ones.

2.1.5 Being social

In early interaction with mothers, infants learn from a pattern of activity that tightly couples vision, audition, and touch to behavior. Mother and infant imitate each other to reinforce this coupling. A mature social partner can also build a cognitive framework by weaving their own behavior around the child's natural activity patterns. This is done by automatically selecting those patterns which they consider meaningful and helpful for the baby. They also serve to direct attention to an object or event to strengthen the coupling. This is done in the spatial as well as temporal aspects. The baby frequently looks for physical and directional support to manage the risks around exploration, to rest when tired and to crystallize goals through such imitation and coupling.

2.1.6 Learning a language

Language can be a regularity that is a "shared communicative system." It is also a symbol system where the relation between the symbol and events in the world are mainly arbitrary, e.g., there is no relation between the word "dog" and what it represents, by knowing the word we cannot know the animal. DeLoache [29] demonstrated the way children use scale models and pictures as symbols which are not too life-like. Children first learn subtle regularities from the words they absorb, and slowly it creates in them the ability to learn a word in one trial and do higher-order generalization. Efficient learning through a form of language thus itself becomes learned behavior.

While new born babies have non-goal directed exploratory behavior, they soon graduate into a more goal-directed behavior. These goals are a result of their decision-making process which takes inputs from their emotions, knowledge, intelligence, and social partners (in this case maybe parents or elder siblings). The mature partner moderates the child's emotions and value system and therefore, his or her early decisions during the learning process. This may be done through instruction, dialogue, feedback, and body language.

When this is considered in the context of a stroke patient, the goals he or she sets for recovery would be influenced by the same factors and more so with increasing disability and physical and emotional dependence. If we break down the learning process into its two broad components, exploratory and goal-directed, then one can line up the two components as an illustration shown in **Figure 1**. The patient formulates a goal (as in recovery of a specific function such as eating) and can begin exploratory learning in that specific context. However, there may exist cognitive as well as physical and social constraints due to post-stroke disability. If a technology could augment these aspects so that constraints are reduced through an appropriately designed user interface, it may facilitate such a patient re-booting how he learnt as a baby.

The goal dictates the quality, direction, and extent of the exploration. In stroke patients, the immediate and longer-term goals that the patient sets for himself/herself could significantly affect extent and speed of recovery [30]. Behavior generation is built around a distributed network of responses such as approach, play, avoidance of obstacles and attention requisition, all of which may be affected adversely after stroke. Behaviors may excite or inhibit each other, where non-conflicting behaviors fire motor commands with the brain and muscle complementing each other in real-time.

2.2 Integrating learning into functional recovery

In a learning environment which requires multiple repetitions, not all of which are identical, as in re-learning a skill, **Figure 1** forms the basic element of the learning iterations. Several iterations will be required as part of the exploratory strategy over time, which may be represented by a cyclic model as shown in **Figure 2**. In this figure, the feedback and feedforward loops drive subsequent iterations, which may be similar or dissimilar. Goals and decisions, as a feedforward, drive multi-modal exploration. Incremental changes or achievements seen at brain and body levels through measurable and quantifiable feedback drive modifications in belief systems, thus impacting goals and decisions for further learning.

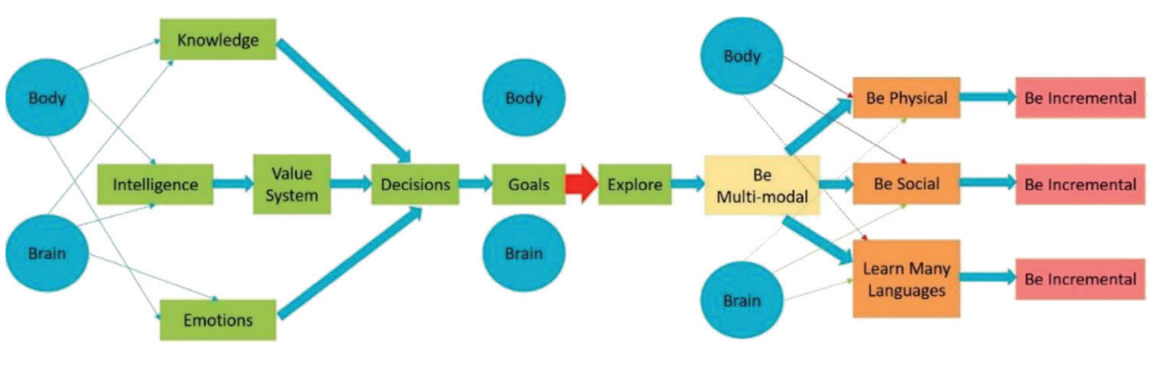


Figure 1.
A composite learning behavior using the mind and physical body in a multi-modal fashion for goal-oriented exploration.

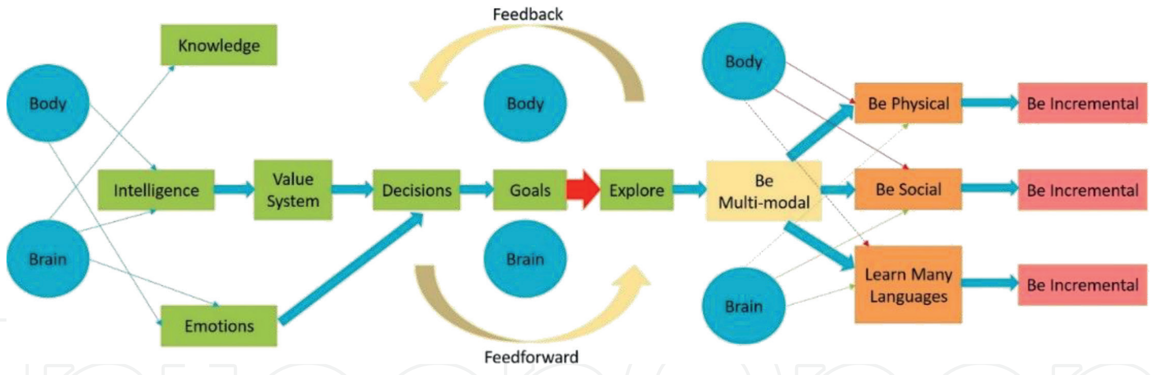


Figure 2.
The proposed natural learning model using iterative, incremental changes.

However, such faculties of learning available to a normal person may or may not be available to a stroke patient. A typical stroke model adapted from Ito et al. [31] of how stroke affects the human system resulting in motor function impairment is shown in **Figure 3** with an augmentation of such impaired feedforward and feedback superimposed. In this figure, the pathways for motor commands from motor cortex and proprioceptive feedback from the musculoskeletal system are disrupted and hence, some alternate pathway is recommended shown by the "motor intention" and "motor actuation" blocks. This is a popular model implemented by the rehabilitation robotics community and those adopting the stimulation approach. Motor intention is usually sensed by a brain-computer interface or artificially induced by stimulation methods such as transcranial magnetic stimulation. Motor actuation is achieved by either electrical stimulation or mechanically driven robotic movement. Intention and actuation are bridged typically by some adaptive algorithm which may be based on feature extraction, a control strategy, and a feedback

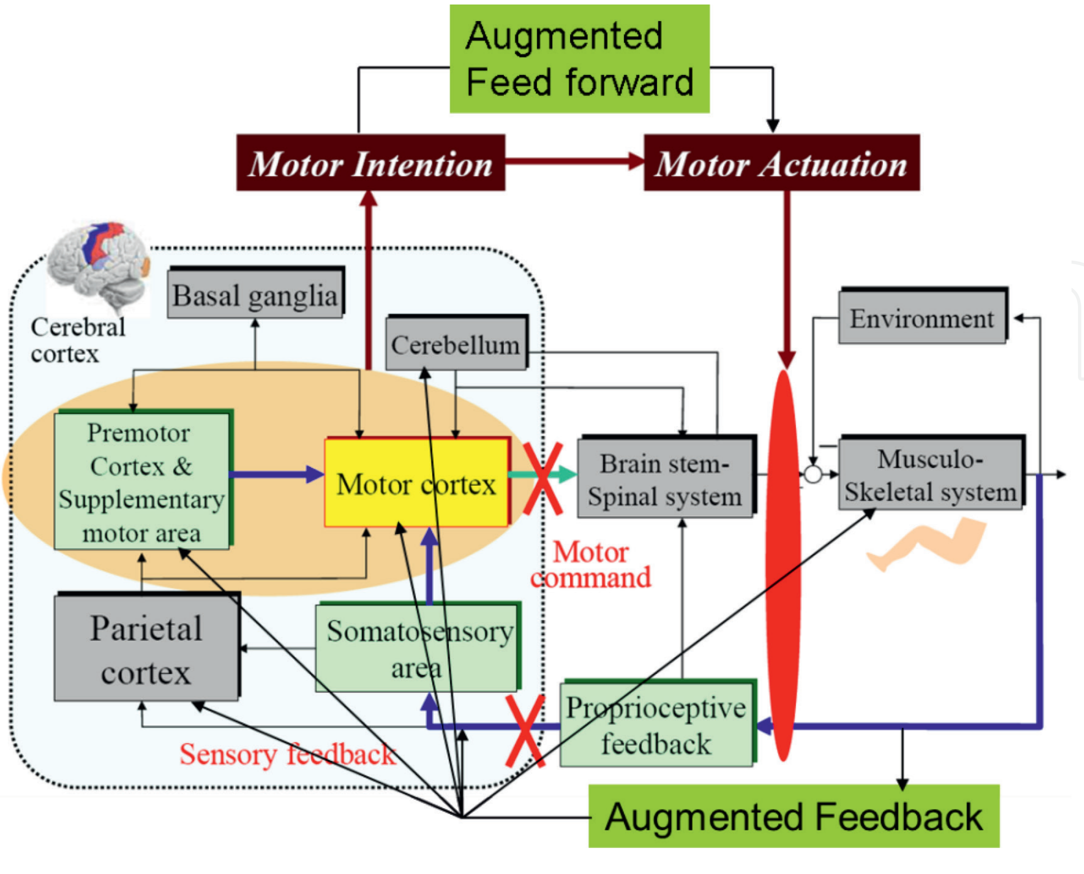


Figure 3.
The self-regulated model of recovery of motor impairment after stroke adapted from Ito et al. [31].

loop. Current technology, however, is not able to address the complex issue of hand function, which involves overlapping neuro-physio strategies and multiple degrees of freedom. At most, simple movements may be possible [32] which has been shown to not adequately impact function for the highly heterogeneous stroke affected population. Gross movements can be expected to improve with very high number of repetitions, thus enabling the brain to rewire itself in a limited way. However, there is poor evidence that such gross movement practice translates significantly into function. Therefore, the modification to the above model is proposed, incorporating the feedforward and feedback elements modeled in **Figure 2** as a form of augmentation to help overcome the deficits through the learning route.

The augmented feedback may be delivered visually via a muscle-brain-computer interface. The feedforward in the form of appropriate audio-visual inputs, which lead the human to attempt a series of desired actions through imitation, is known to facilitate recovery [33]. Moreover, there is evidence of perception transferring to action and more importantly, from action to perception [34]. The augmented feedback is expected to drive motor intention and exploration while the feedforward is expected to prime the brain for motor actuation and goal directed learning through imitation. From a functional improvement perspective, the augmented feedback may be customized for a person using time-locked parameters as follows:

1. EMG agonist-antagonist balance (muscle strategy).

2. EEG relaxation and attention states (brain strategy).

The brain and the body are inseparably linked, and both contribute significantly for neuroplasticity to occur and health parameters to improve [35]. Based on this understanding of how human learning may be applied practically in the context of post-stroke rehabilitation, this study was conceived with the following assumptions:

1. When EEG and EMG signals during activity are brought together in a time-synchronized manner for real-time feedback along with an audio-visual feedforward for imitation, it provides an opportunity for the patient to work with sensory, exploratory and goal-directed learning toward functional rehabilitation goals.

2. Displaying quantified, relative brain and muscle feedback in real-time while training activation and relaxation simultaneously during movement or while attempting to manipulate objects, will enhance the conditions for incremental associative learning of overlapping brain and muscle strategies to occur [36]. Under such conditions, subjects may potentially achieve systemic gains in functional performance, even though they may have tried existing rehabilitation methods and only partially succeeded.

This paper describes a bio-mechatronics approach to understanding where re-learning is misled or failing and uses a “feedforward-feedback” modality to help chronic stroke subjects train gross movements (as measured by Fugyl Meyer Upper Extremity Motor Assessment scale) and functional, timed-task capabilities (as measured by Action Research Arm Test). The SynPhNe system employs learning and training principles similar to that which babies seem to use in the design of its user interface, to leverage the mechanism of “self-regulation” or “self-correction.” The study explores to what extent such real-time “self-correction” alone, in the absence of any form of external stimulation or robotic assistance, impacts the recovery of functional ability in the stroke impaired, as a prelude to building a safe, effective, easy-to-use technology which would be useful for patients to augment therapy hours at home.

3. Methods

3.1 Technology description

3.1.1 Design principles for SynPhNe system

At the time of development, motor theory, learning principles and stroke rehabilitation challenges listed in Section 1 suggested that the SynPhNe rehabilitation platform should facilitate such learning keeping in mind the constraints faced by stroke patients.

- EEG and EMG biofeedback with video-based feed-forward provided the multi-modal environment.
- Incremental learning—use of biofeedback to highlight small changes in the muscle and the brain signals with their transitions and associating this with the gross movements and tasks performed with various degrees of success.
- Exploratory learning, using the hand for real world tasks perceived as important but difficult (for example, use of chopsticks), as well as understanding how to achieve various relaxation and attention states while in dynamic movement using the feedforward-feedback modality.
- Simulation of a "mature social partner" or instructor, perhaps in the form of an instructor led video which a patient could watch and follow and the smiley icon which indicates the successful management of the desired brain state while executing physical tasks.
- Teaching a new, universal language, i.e., making the subject aware of how to interpret and self-regulate muscle and brain activity at a signal level.
- Following the cyclic learning process shown in **Figure 2**, as a sensory-led, intuitive, self-sustaining, and reinforcing cycle.

3.1.2 System description

The wearable data capture unit (WDCU) acquires data from eight channels of EMG through an arm gear and eight channels of EEG data through a head gear and transmits the data simultaneously to the PC using a USB cable (**Figure 4**). The design of this arm gear has been previously reported in a separate paper by the authors along with design and testing of the amplification circuit [37]. The software running on the PC processes these signals from 16 channels and combines them in a time locked manner for presentation on the screen as real-time feedback showing muscle over-activation and under-activation as cartoon characters (EMG signal as agonist-antagonist koala bears climbing up or down a tree, EEG signal as a smiley face). While EMG signals are used as feedback by squaring and averaging the amplitude within a running window updated every 10 milliseconds, the EEG signals were converted to frequency band using a Fast Fourier Transform and the alpha

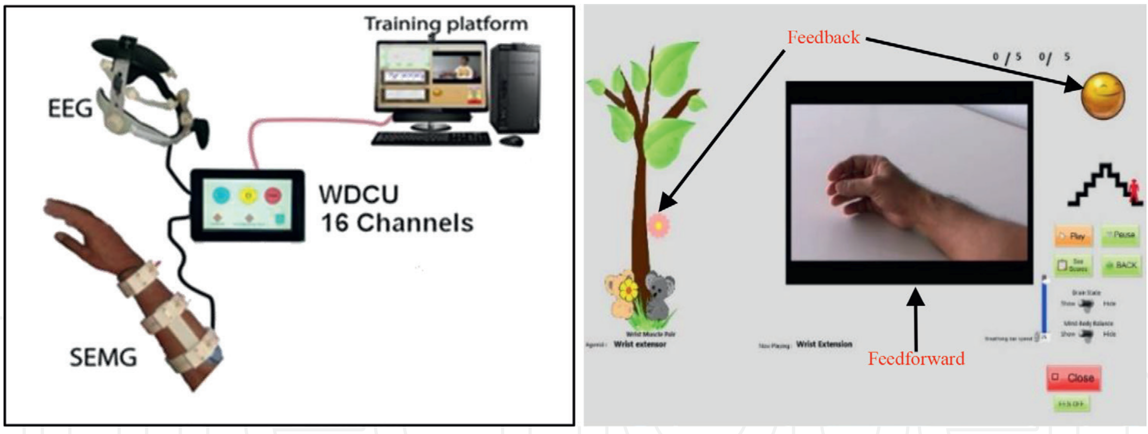


Figure 4.
SynPhNe learning model platform and user-interface.

band power (8–13 Hz) was used to represent a relaxed state, updated every 10 s as a proportion to total power in the 1–35 Hz frequency band. While EMG was sampled at 1000 samples/sec, EEG was sampled at 256 samples/s.

The goal of both the feedforward and feedback is to successfully attempt a movement or physical task while maintaining a relaxed brain-muscle state pre- and post-action comparable to resting state. If effort results in a deviation from resting state, return to resting state post-effort should be immediate. Brain and muscle influence each other too. Losing attention partially or fully may result in loss of ability to imitate the feedforward video and respond to feedback. Incremental changes in self-regulation are presented visually in the real-time user interface, which then provides an impetus for the patient to self-regulate further.

Figure 4 depicts the user interface on the computer screen. The subject observes the video as the feedforward in order to imitate it with the same speed. The koala bears, and tree serve as agonist and antagonist muscle EMG feedback during such imitation. The subject attempts to activate the appropriate muscle to raise the brown bear (agonist) to the top of the tree while keeping the gray bear (antagonist) as steady and close to the bottom of the tree as possible. The yellow smiley face represents EEG frequency band feedback as a measure of a relaxed brain state which needs to be maintained as best as possible while imitating the video-based physical movement or task.

In both the clinical studies, the subject tried to imitate an exercise and task practice video sequence running on the computer screen, while attempting to correct maladaptive over-activation and under-activation in opposing muscle pairs displayed on the same screen. Using a slower speed of execution than normal allowed proximal joints of the upper limb to stabilize and reduce temporal demands on the subject [38]. The slow-paced video sequences allowed time to train relaxation between repetitions. Also, the need to achieve a relaxation goal immediately after activation encouraged the subjects not to over-activate the muscles and to moderate their effort. This strategy was found to delay the onset of high dynamic muscle tone and allow for better repetition-based performance based on greater number of successful relaxations. When subjects experienced difficulties in being able to relax their muscles, they intuitively made postural corrections to let go and relax deeper before the next muscle activation. EMG thresholds displayed on the software gave them a clear indication on activation and relaxation targets appropriate for training, which were based on previously calibrated maximum voluntary contraction (targets were up to 40% of maximum) and resting state EMG respectively, for various muscle groups. In this paper, analysis of only the EMG peaks data as seen during activity and immediately post activity repetition is highlighted. The EEG and other metrics will be reported separately in subsequent papers since the primary objective of this paper is to highlight the thinking behind the user-interface design and the pre and post clinical outcomes.

3.2 Study methodology

In Trial 1, 15 adult chronic stroke subjects with a hemiplegic hand (31–69 years; 4 females, 11 males) were recruited for the study (**Table 1**). In Trial 2, 10 adult

Subject code	Age	Gender	Months poststroke	Nature of stroke
Demographics of subjects in Trial 1				
RH001	57	Female	22	Hemorrhage
RH002	44	Male	21	Infarct
RH003	54	Male	12	Infarct
RH004	61	Male	25	Infarct
RH005	69	Male	21	Infarct
RH006	38	Male	18	Hemorrhage
RH007	48	Male	18	Hemorrhage
LH001	31	Female	32	Infarct
LH002	53	Female	18	Hemorrhage
LH003	59	Female	37	Infarct
LH004	62	Male	8	Infarct
LH005	57	Male	10	Hemorrhage
LH007	65	Male	45	Hemorrhage
LH008	62	Male	15	Hemorrhage
Mean	54.3		21.6	
Std. dev.	10.3		10.0	
Demographic details of subjects in Trial 2				
NRH001	69	Male	21	Infarct
NRH002	60	Male	28	Infarct
NRH003	57	Female	23	Hemorrhage
NRH004	59	Male	7	Infarct
NRH005	65	Male	7	Infarct
NRH006	46	Male	60	Hemorrhage
NRH007	67	Male	49	Infarct
NLH001	61	Male	21	Infarct
NLH002	45	Male	49	Infarct
NLH003	62	Male	69	Infarct
Mean	60.0		32.3	
Std. dev	7.6		20.7	

Table 1.
Demographic of recruited subjects.

chronic stroke subjects with a hemiplegic hand (45–69 years; 1 female, 9 males) were recruited for the study (**Table 1**).

Both left and right limb impaired subjects were included for a better patient representation with at least 6 months post a first clinical stroke. Only paralysis with M.R.C. grade between 1 and 3 at elbow and digits was considered for inclusion. Passive, pain-free range of motion was at least 50% in all below elbow joints. No exclusion was made based on type of stroke and the group included those with ataxia and tactile sensory loss.

The experiments had only treatment group whose members had plateaued (those who had completed the rehabilitation program recommended by the hospital) in functional recovery and were ready to discontinue any other form of regular or alternative therapy during the study.

In Trial 1, the subjects were randomized between two clinical therapists, where either of them could conduct any session for any subject (as is common in a typical clinical setting). In Trial 2, to simulate a home-based, non-clinical environment, the therapy was not conducted in a standard hospital therapy/rehabilitation ward but rather in a normal spare room with a table and a chair. A research associate with a non-therapy background was trained to operate the SynPhNe system to deliver the sessions every day.

Each subject completed a 4-week, 3 sessions/week protocol using the automated SynPhNe device which delivers the learning modality. Each session lasted for 50–75 min including the setup time. In Trial 1, the EEG signals were captured during three sessions to track changes, i.e., in the beginning, midway and end of the study whereas in Trial 2, the EEG signals were captured in all 12 sessions, with the smiley face retained as a form of feedback on relaxed brain state represented by the relative alpha-band power as calibrated at rest. This brain-based feedback was introduced after it was observed that a significant component of therapist supervision in Trial 1 consisted of repeatedly nudging the subjects' attention back to task.

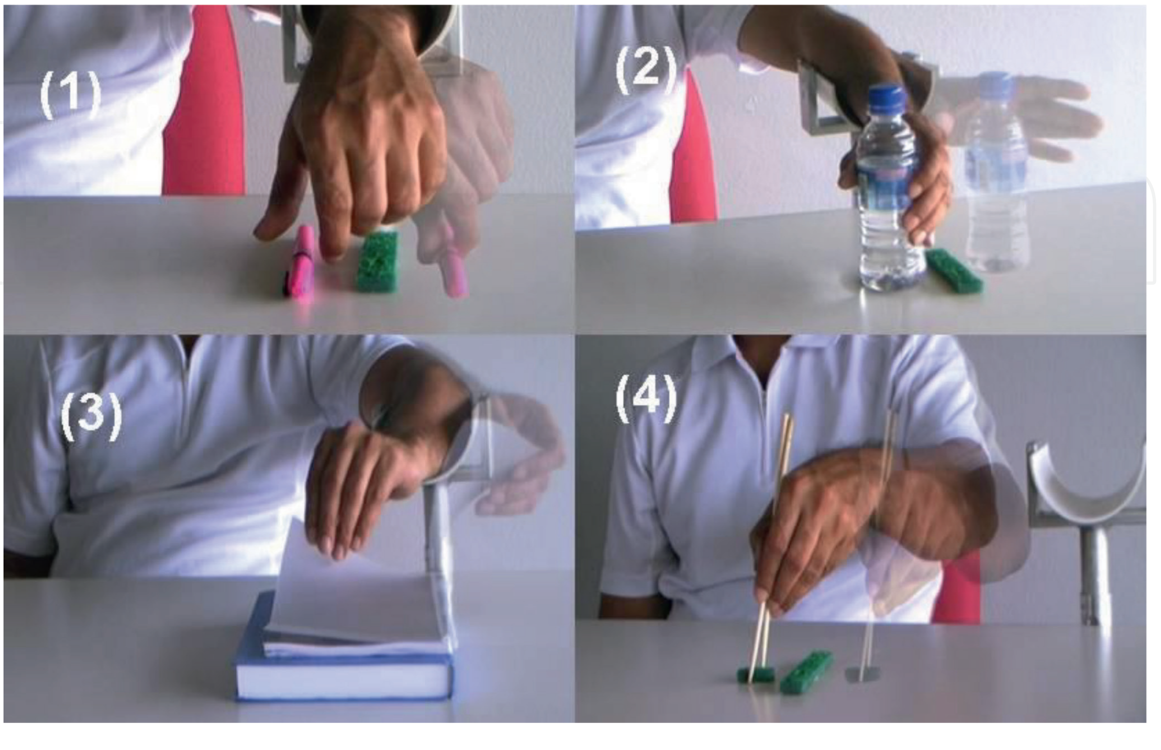
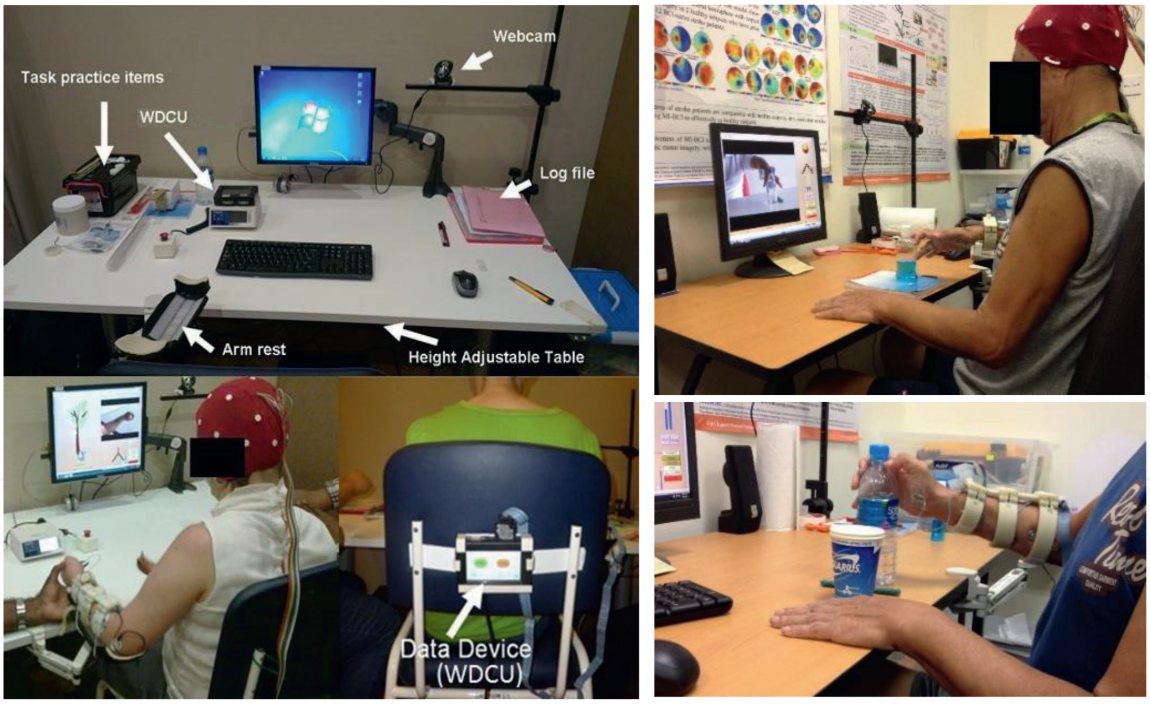


Figure 5.
Task practice (1) picking up a pen, (2) grasping a bottle, (3) flipping a page, (4) using a pair of chopsticks (pictures extracted from the instructional video created for the experiment).



(A) (B)

Figure 6.
Clinical trial setup in (A) Trial 1 (therapy ward) and (B) Trial 2 (outside therapy ward).

Imitating the video, subjects performed four basic hand movements—wrist extension and flexion, finger extension and flexion, pronation and supination, and open grasp. This was followed by four everyday tasks—picking up a pen, flipping a page, grasping a bottle and use of chopsticks (**Figure 5**).

These four tasks were chosen to represent a two-finger pinch with pronation, a cylindrical grasp, a key pinch with pronation and supination and a five-finger pinch which demands attention. Each exercise was repeated five times in the first three sessions and 10 times in the subsequent sessions while attempting to maintain a pre-calibrated agonist-antagonist balance using the biofeedback. In Trial 1, some of the more severely affected subjects (n = 7) were provided the facility for an automated triggering of electrical stimulation on extensor muscles for some or all sessions if the subject achieved an agonist EMG threshold while maintaining a relaxed antagonist [39]. In Trial 2, we did not use any FES as Trial 1 indicated that FES induced exaggerated, instantaneous antagonist-side reactions, which our protocol was, in fact, trying to minimize.

Pre-, mid-, and post-outcomes were measured using standard clinical scales [Fugl Meyer Upper Extremity Motor assessment (FMA) and Action Research Arm Test (ARAT)] to assess both gross and fine movements [40]. They were also randomized for assessment between two other therapists who were blinded to the study protocol. All subjects provided a signed written consent. Ethics approval was obtained from the Institutional Review Board of National Healthcare Group, Singapore. The set-up for the two experiments is shown in **Figure 6**.

4. Results and discussions

4.1 Association of muscle contraction to relaxation

On comparing the muscle activation and relaxation scores across all subjects in Trial 1 (168 sessions) and Trial 2 (total 120 sessions), it was seen that successful performance of higher repetitions of muscle contractions above an EMG threshold was associated with the ability to volitionally relax those muscles below an EMG threshold immediately after contraction (Trial 1: Pearson's coefficient = 0.78, CI = 99%; Trial 2: Pearson's coefficient = 0.74, CI = 99%).

Subjects who were unable to relax, volitionally, in a consistent manner had difficulties in performing simple actions such as extensions and flexions repeatedly as well as tasks. The antagonist was observed to be relatively stronger (the gray koala bear climbed higher up on the tree) in most subjects at week 0, whenever the subjects tried to activate the agonist and raise the golden koala bear up the tree. These subjects also demonstrated an inability to relax a muscle immediately on completion of a movement or task.

4.2 Clinical scale outcomes

The outcomes based on the FMA and ARAT clinical scales for both the trials are summarized in **Table 2**. Subjects have been categorized into mildly- (55–57), moderately- (32–54) and severely-impaired (≤31) based on their FMA scores at week 0. Subject LH006 encountered a personal accident at home resulting in a head injury during the study and was discontinued from the trial.

The scores for both the assessment scales were reduced to a common denominator by normalizing assessment scores against full scores of the respective scale. For FMA and ARAT, the full scores are 66 and 57 respectively.

Based on the nominalized scores, the percentage improvement in both the functional scales for the subjects in Trial 1 and Trial 2 can be summarized as shown in **Table 3**. Since these improvements are based on initial measurements of level of impairment (week 0), they capture both clinical and sub-clinical performance changes or incremental improvements or decline achieved by the subjects. The estimated minimum clinically important difference (MCID) of the upper limb FMA scores ranges from 4.25 to 7.25 points depending on the different facets of upper limb movement (overall upper limb function MCID is 5.25) while the MCID values for the ARAT were 5.7 points for chronic stroke patients [41, 42]. In Trial 1, there were two subjects who achieved MCIDs in FMA; RH003 (8 points) and RH007 (9 points) and four subjects who achieved MCIDs in ARAT; RH005 (7 points), LH005 (7 points), LH007 (12 points), LH003 (6 points). In Trial 2, subjects NRH006 (13 points), NLH003 (6 points), NRH001 (7 points) and NRH003 (6 points) achieved MCIDs in ARAT. These MCIDs were achieved with only 5–10 repetitions per exercise per session, which is about 10–30% of the number of exercise repetitions recommended per session in standard care.

Training in self-regulation of antagonist muscle relaxation during movement using the SynPhNe system contributed to positive pre-post changes in FMA (Trial 1: Mean = 6.855%, SD = 7.85; Trial 2: Mean = 5.05%, SD = 6.00) and ARAT (Trial 1: Mean = 25.84%, SD = 49.86; Trial 2: Mean = 30.17%, SD = 21.20).

4.3 Discussions

Results from the two separate trials are presented to illustrate the degree of consistency in two different patient samples. The inclusion and exclusion criteria in both studies were similar. However, in Trial 1 therapists fully supervised the therapy sessions while in Trial 2 non-therapists conducted the sessions. In both studies, a separate team of blinded therapists performed the pre- and post-assessments. Neither study reported any adverse events.

Impairment level	Subject code	Fugl Meyer (FMA)		Action research arm test (ARAT)	
		W0	W4	W0	W4
Clinical outcomes in Trial 1					
Mild	RH001	58	60	53	57
Moderate	RH003	36	44	9	11
	RH005	45	46	20	27
	RH007	50	59	45	49
	LH001	35	33	5	5
	LH002	44	45	25	28
	LH004	45	44	21	21
	LH005	52	56	32	39
	LH007	50	52	32	44
	LH008	43	47	32	32
Severe	RH002	16	19	6	7
	RH004	27	27	5	5
	RH006	29	31	17	17
	LH003	22	24	3	9
Mean		39.43	41.93	21.79	25.07
Std. dev		11.86	12.67	15.10	16.64
Clinical outcomes in Trial 2					
Moderate	NRH006	54	56	38	51
	NLH003	43	42	17	23
	NLH002	38	41	25	28
	NRH001	38	40	18	25
	NRH007	37	39	21	26
	NRH004	37	39	27	31
	NRH003	32	33	7	13
Severe	NRH005	31	30	9	10
	NRH002	20	24	8	9
	NLH001	19	20	3	4
Mean		34.90	36.40	17.30	22.00
Std. dev		9.78	9.69	10.31	13.05

Table 2.
FMA and ARAT clinical scores at week 0 (W0) and week 4 (W4).

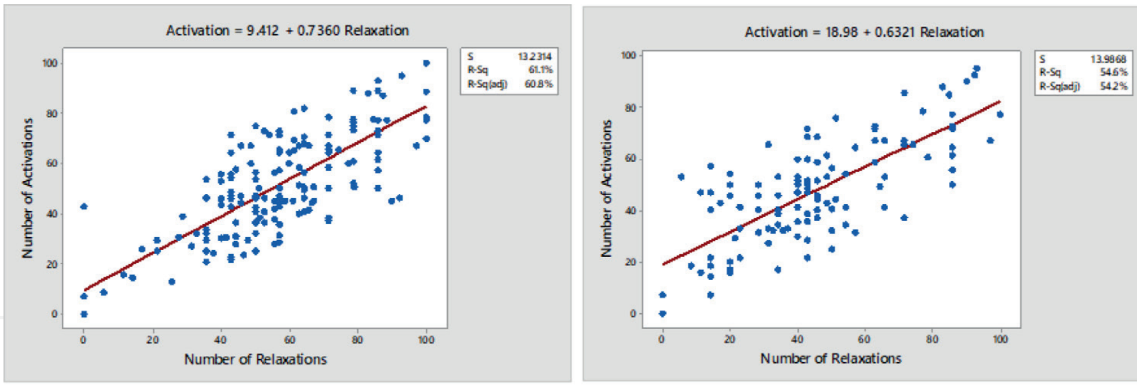
Figure 7 supported the research group's direction that both activation and relaxation must be trained specifically, as opposed to a pre-occupation with repeated muscle activation alone as is common in rehabilitation [43].

Both the studies reported a larger increase in ARAT scores as compared to FMA scores. This increase in ARAT was not necessarily linked to those who had high FMA scores at week 0. This suggests that functional task performance and object manipulation ability may improve even though reduction of impairment at a gross

Subject code	Fugl Meyer (FMA)	Action research arm test (ARAT)
Percentage improvement in Trial 1		
RH001	3.45	7.55
RH002	18.75	16.67
RH003	22.22	22.22
RH004	0.00	0.00
RH005	2.22	35.00
RH006	6.90	0.00
RH007	18.00	8.89
LH001	−5.71	0.00
LH002	2.27	12.00
LH003	9.09	200.00
LH004	−2.22	0.00
LH005	7.69	21.88
LH007	4.00	37.50
LH008	9.30	0.00
Mean	6.85	25.84
Std. dev	7.85	49.87
Percentage improvement in Trial 2		
NRH001	5.26	38.89
NRH002	20	12.5
NRH003	3.13	85.71
NRH004	5.41	14.81
NRH005	−3.23	11.11
NRH006	3.7	34.21
NRH007	5.41	23.81
NLH001	5.26	33.33
NLH002	7.89	12
NLH003	−2.33	35.29
Mean	5.05	30.17
Std. dev	5.72	20.22

Table 3.
Percentage improvement post-therapy (week 4) with respect to pre-therapy.

level is proportionately lower. Subjects who achieved MCIDs did so mostly in ARAT and not FMA, which is somewhat counter-intuitive. This may be because several functional tasks do not demand a full range of motion, e.g., Eating with chopsticks or Picking up a small object like a pen with a two-finger pinch. In the experience of the study team, it was noted that subjects were more motivated attempting to do actual functional tasks such as opening a book and manipulating chopsticks as compared to standard joint extension/flexion exercises that were repetitive and not directly linked to a perceived functional outcome. It may be noted that each exercise



(A) (B)

Figure 7.
Muscle activation is associated with relaxation during repetitive practice in (A) Trial 1 (B) Trial 2.

and activity was repeated only 5–10 times per session to produce the outcomes reported, which was about a fifth of the number usually recommended in rehabilitation settings, and about a tenth or less of that in high repetition therapy. This was done to ensure that compensatory strategies did not set in due to fatigue, boredom, or distraction. The results raise some questions about initial functional results being dependent on high repetitions and are, in fact, reminiscent about how babies learn with few, non-similar repetitions [29]. Since both studies exclusively recruited patients who were both chronic and plateaued, the chances of spontaneous recovery were minimized, although cannot be ruled out. The authors are of the opinion that restoration of function resembling spontaneous recovery may, in fact, be facilitated in the chronic phase of therapy by the re-learning of such brain and muscle strategies as described in these experiments, enhancement of relaxation and attention and the progressive reduction of compensation.

The gold standard for restoration of function and independence is still conventional, manual therapy. Kollen et al. reviewed more than 700 published studies and concluded that conventional robotic or stimulation treatment approaches induce improvements that are confined to impairment level only and do not generalize to functional improvement [2]. They stated that treatment strategies that incorporate a strong emphasis on functional training and task-specific therapy may hold the key to optimal stroke therapy. A search of systematic reviews in the Cochrane and other databases on well-known approaches such as electro-mechanical and robot-assisted arm training, electro-stimulation and EMG triggered neuromuscular stimulation of wrist and fingers showed that only electro-stimulation held certain advantages over conventional, manual therapy when comparing outcomes for motor ability [44–48]. However, conventional therapy continues to be superior in improving the complete spectrum ranging from gross motor, fine motor, strength, dexterity and ability to manipulate objects and perform timed tasks. Hence, the authors of this paper carried out a follow-up study with 30 subjects, comparing a group undergoing SynPhNe training to a group receiving standard care, which was a mix of conventional physiotherapy, physical therapy, occupational therapy and neuro therapy. Since the goal is to develop a system which can augment therapy effectively at home, the study was designed to prove that SynPhNe treatment was comparable to standard care. The results of this study have been published previously [49]. The conclusion was that SynPhNe training was comparable to standard care as seen in the FMA and ARAT scales.

The EMG data demonstrated that the stroke subjects had hitherto unknown antagonist over-activation in wrist and finger movements, which were moderated and subdued by starting the exercises with a reduced range of motion and reduced speed.

Once the antagonist activity was subdued and reinforced over 2–4 sessions, the range of motion and speed was progressively increased in subsequent sessions. This was effective particularly in wrist and finger extension, which is known to be a significant challenge for most stroke patients. Control deficiencies in approach, sequential steps and object release were similarly improved with slower execution speeds that were meant to effect better proximal stabilization and reduced compensation as often seen in shoulder elevation and abduction while reaching, pronating, and grasping with the affected arm. Since the most significant improvements in percentage terms were seen in the ARAT scale which evaluates functional and participation tasks, the authors propose that the SynPhNe system impacts independence positively, combined with enhanced self-regulation and the self-use of technology.

All subjects tolerated the multi-modal feedback well and did not report feeling overwhelmed by the user interface and demands of the feedforward-feedback loop. It was noticed that the distribution of the visual sampling of the feedforward and feedback during the sessions differed between subjects and within subjects as therapy sessions progressed. This could be an interesting area of investigation in future studies to better understand how adults learn in a non-instructional and sensory manner. This paradigm needs to be tested further with a larger study and a 30–60 day follow-up to evaluate retention of brain-muscle strategies learnt and further generalizations to other functional activities. Two larger, case-controlled studies are underway presently with sub-acute and chronic phase patients to understand how the transition from hospital to home-based therapy may be executed using the SynPhNe system, and the effect on outcomes and independence.

5. Conclusion

Training to relax specific muscles adequately and in a timely manner during therapy using a feedforward-feedback loop, instead of practicing repetitive muscle contraction alone, may help re-learn movement and daily functional activities in stroke subjects who have "plateaued" and not responding to further therapy.

Simultaneous activation-relaxation training of agonist-antagonist not only facilitated improvement of functional abilities but was also well tolerated by all subjects and did not cause them to get overwhelmed by the number of feedforward and feedback elements on the computer screen. This indicated that despite the challenges brought on by stroke, patients with impairments can still leverage their sensory learning abilities in an exploratory and then goal-directed manner while attempting to regain spatial and temporal aspects of movement and function of the upper limb. Thus, they appeared to be able to re-boot how they learnt in a sensory manner as babies using the feedforward-feedback modality. A wearable device such as the SynPhNe system may, therefore, help leverage neuroplasticity and act as a key complement to conventional therapy. Being patient-led and requiring reduced therapist supervision, it can effectively augment therapy hours at home or in the community, thus holding the promise of making daily therapy accessible and affordable to all.

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Conflict of interest

Subhasis Banerji and John Heng are founders and inventors of the SynPhNe system. While providing technical support and supervision to the studies, they were blinded to pre- and post-clinical assessment of subjects.

Daphne Menezes and Ponvignesh Ponnusamy are current employees of Synphne Pte. Ltd., Singapore. Daphne Menezes assisted the clinical study team as a trainer in the SynPhNe system and observer of therapy sessions. Ponvignesh Ponnusamy assisted with software programming and user interface development only. Both were blinded to pre- and post-clinical assessment of subjects.

The other authors have no conflict of interest.

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