

**PROTOCOL DEVELOPMENT AND FEASIBILITY STUDY OF
ENVIRONMENTAL ENRICHMENT IN ADULT ACQUIRED BRAIN
INJURY**

by

Devina S. Kumar

A dissertation submitted to the Faculty of the University of Delaware in partial
fulfillment of the requirements for the degree of Doctor of Philosophy in
Biomechanics and Movement Science

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I end with an inspirational quote from a poem my sister had on her pinboard growing up. Somewhere down the line, it became my source of inspiration too.

“Life’s battles don’t always go
To the stronger or faster man;
But sooner or later the man who wins
Is the man who thinks he can.”

~ by Walter D. Wintle

DEDICATION

To my parents,
Happy 35th Anniversary Ma and Papa!

To my sister,
the wind beneath my wings.

And to my husband,
the light of my life!

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ABSTRACT

Long-term physical, cognitive and psychosocial impairments are common after moderate to severe Acquired Brain Injury (ABI). Impairments associated with ABI decrease the well-being of the individual, their family, and the broader community. Also, challenges faced in the community drastically decrease the individual's ability to meaningful citizenship including work, socialization, participation in leisure activities, and activities related to daily independent living. Under most current models of care, individuals get discharged into the community well before their families, and healthcare professionals would recommend[1]. Community-based rehabilitation programs are essential to decrease long-term deficits of chronic individuals with ABI. ***Thus, this dissertation focuses on advancing community-based rehabilitation.***

Despite advancement in rehabilitation, research to support the effectiveness of different post-acute rehabilitation programs is still inadequate, raising several procedural concerns[2]–[4]. Information offered by ABI Model Systems provide different guidelines essentially developed by individual states based on state and federal budget, resources, and services available. Therefore, the treatment approach varies in different settings, therapies, and methodology[5]–[7]. Consequently, current evidence for traditional therapy and model systems lack provisions for determination of optimal dosage, timing, and intensity for each stage of recovery [8]–[10]. ***This dissertation takes the first step towards Protocol development and conducting a Feasibility study of a novel community-based intervention.***

As such, this dissertation addresses the national call for an integrated rehabilitation model to bridge the gap between discharge and meaningful community re-entry for individuals with moderate to severe ABI[11]. The primary objective is to develop a Protocol and test the Feasibility of the Go Baby Go Cafe, which combines a new body weight support technology with the enriched environment of a functioning business. *Chapter 1* provides background on the selected population and information on past and current rehabilitation techniques. Limitations of the literature guide the reader to the focus of the study. *Chapter 2* provides background and rationale for the major components of a formal clinical research protocol for a feasibility study of using a real-world environment equipped with a novel body weight support system. Components include study design, methodology, and intervention. The protocol will then set the guidelines for implementing the proposed feasibility study. *Chapter 3* provides information on the outcomes of the trial. Final results support moving forward with Phase 1 clinical trial with a few modifications to research design, recruitment, and outcome measures.

Conclusions from this dissertation will strengthen our understanding of developing, designing, and implementing a feasibility study located within a fully functional business. By developing the groundwork for the initial phase of a clinical study pipeline, the next step should focus on conducting a pilot study or Phase 1 clinical trial to establish the preliminary effectiveness of a real-world based community rehabilitation model

Chapter 1

IMPACT OF AND RECOVERY FROM ACQUIRED BRAIN INJURY

1.1 Introduction

1.1.1 Background and Significance of Acquired Brain Injury

This dissertation focuses on advancing community-based rehabilitation for adults with moderate to severe Acquired Brain Injury (ABI). ABI is an umbrella term to describe traumatic and non-traumatic injuries after birth (Figure 1) [3]. Traumatic injuries occur due to an external force to the head which disrupts brain function[12]. Common causes include penetration by a foreign body, striking or a blow to the head, rapid acceleration, and deceleration associated with coup contrecoup injuries, and blast-induced injuries[13], [14]. Examples of traumatic brain injury are falls, motor vehicle accidents, gunshot wounds, assault and concussion from a sports-related injury.

Non-traumatic injuries occur due to cardiovascular accidents, anoxic injuries, brain tumors, inflammation, and toxins. Examples of non-traumatic brain injuries are an ischemic/hemorrhagic stroke, encephalitis caused by a virus, anoxia caused due to drowning, choking, suffocation and benign/malignant brain tumors[15], [16].

Of all the types of ABI, Traumatic Brain Injury (TBI) and ischemic stroke are the leading causes of death and long-term disability[17]–[21]. TBI and stroke create substantial challenges for the individual, the family, and community. This

dissertation focuses on advancing interventions available to reduce these challenges.

Next, the primary impairments post-TBI and Stroke are reviewed.

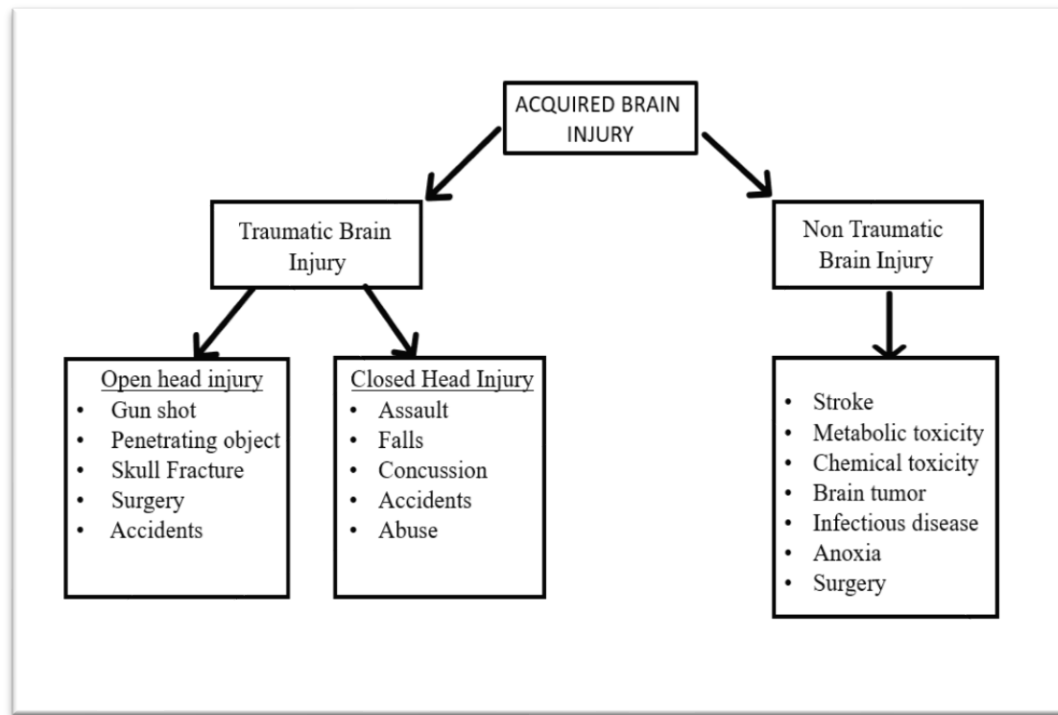


Figure 1 Types of ABI

Traumatic Brain Injury (TBI) is a major source of serious disability in the US and abroad. Thus, interventions that reduce an individual's disability post-TBI have the potential for significant impact on a large number of individuals and their caregivers as well as the society at large. TBI is the leading cause of *trauma*-related brain injuries resulting in the most severe disability[3], [19]. For example, in 2013, TBI accounted for 2.8 million visits to the emergency departments, 282,000 hospitalizations and 56,000 deaths[22]. TBI related medical visits are more common

in males (59%)[19], [23] compared to females[24]. The incidence of TBI related deaths for both genders is highest in minorities such as American Indian/Alaskan natives followed by African American men[23]. TBI related emergencies requiring hospitalizations are highest in adults > 75 years, children (0-4 years) and adolescents (15 – 19 years)[19], [22]. The three most common causes are falls (37%), motor vehicle accidents (17%), and blows to the head (17%)[19], [22].

TBI severity is classified based on the Glasgow Coma Scale (GCS) upon hospital admission [25], loss of consciousness, and post-traumatic amnesia (Figure 2). [26]– [28]. Often a TBI that requires admission to inpatient rehabilitation is associated with a higher risk of significant deficits and prolonged recovery[29], [30]. ***Long-term deficits for individuals with moderate to severe TBI include cognitive, physical, and behavioral impairments***[31].

Severity of Traumatic Brain Injury			
	GCS	PTA	LOC
Mild	13-15	<1 day	0-30 mins
Moderate	9-12	>1 to < 7 days	>30 mins to < 24 hrs
Severe	< 9	> 7 days	> 24 hrs

Figure 2: Diagnosis of TBI based on the severity

Cognitive function is essential for a person's life including critical components such as Activities of Daily Living (ADL)[32], [33], self-awareness[34], safety [35]and functional independence[36]. The frontal lobe is the most commonly bruised part of the brain. Thus, cognitive impairments are often considered a “hallmark” of TBI[37], [38]. Typical deficits caused by frontal lobe injury include impaired attention, a decrease in memory, processing speed, decision making, judgment, and reaction time[39]–[43].

Physical function is critical for most life activities including mobility, fine motor activities, ADLs, and independence in work or community-related tasks[44]. The distributed brain damage due to tearing/shearing of supraspinal structures in moderate to severe TBI often results in deficits with most physical functions. These include spasticity, ataxia, falls, gait deficits, loss of balance, and impaired coordination[45]–[47].

Behavioral function is how individuals maintain their personal, social, community, and work relationships[48]. Behavioral dysfunction results in deficits which affect the individual at the participation, work and social level[49], [50]. These deficits include mood disorders such as anxiety, depression, aggression, social inappropriateness, hallucinations, delusions, general confusion, and impulsiveness. Individual or a combination of behavioral impairments often prevent meaningful community re-entry [48], [51], [52].

Stroke, as with TBI, is a significant source of severe disability in the US and abroad. Thus, interventions that can reduce an individual's disability post Stroke have the potential for significant impact for a major portion of the neurological population as well as the community at large. Stroke is the leading cause of *non-trauma* related

brain injuries that result in severe disability (Figure 1). According to a 2017 report by the American Heart Association, 795,000 have a stroke annually in the US alone[53]. Currently, there are approximately 7 million people or 3% of the US population living with a stroke.

There are three types of Stroke: ischemic (87%), hemorrhagic (10%), and subarachnoid (3%)[54]. Typically, the incidence of stroke is higher in males than females. [55], and twice as high in African Americans compared to Caucasians [53]. While the incidence of stroke is known to increase with age, 34% of individuals diagnosed with a stroke are below 65 years of age[56].

Stroke severity classification was developed by the National Institutes of Health Stroke Scale (NIHSS) which diagnosis Stroke as minor, moderate, moderate to severe, and severe based on the total score(Figure 3). [57]. The scale consists of 11 items with a maximum score of 42. A higher score indicates greater severity, poorer outcomes, and associated long-term deficits. *Similar to TBI, stroke is associated with long-term cognitive, physical, and behavioral impairments.*

Severity of Stroke	
SEVERITY	NIHSS SCORE
No Stroke symptoms	0
Minor Stroke	1- 4
Moderate Stroke	5-15
Moderate to Severe Stroke	16 -20
Severe Stroke	21- 42

Figure 3: Diagnosis of stroke based on the severity

Cognitive impairments are associated in part with the site and size of the infarct[58]. As with TBI, cognitive impairments post-stroke can impair daily functioning, vocational ability, and socialization[59]. Common cognitive impairments include an increase in cognitive fatigue, attention deficit, a decrease in processing speed, concentration problems, spatial neglect, and impaired memory[60], [61].

Physical impairments are common post stroke[62] and disrupt routine functions such as walking, bathing, dressing, going to work and preparing meals [63], [64]. Common physical impairments include paralysis of the contralateral side, contractures, joint laxity, gait and balance disturbances, shoulder subluxation, chronic pain, and spasticity[65]–[69].

Behavioral impairments in Stroke are associated with long-term deficits [70]. Behavioral impairments can significantly affect a stroke individual's lifestyle, work setting, and personal relationships at the family and community level. Common behavioral impairments include anxiety, anger, depression, fear, social stigma and sense of loss[71], [72].

The personal and public health crisis created by TBI and Stroke [73] is compounded if the event occurs during young adulthood. These individuals will have permanent deficits resulting in challenges at school, home, work, and the community. For example, return to work is an important rehabilitation outcome for satisfaction with life, personal wellbeing, social engagement, and improving long-term outcomes[74]–[76]. However, even though an estimated 40% of individuals with severe ABI return to work initially, follow up studies report less than 20% of individuals can maintain their job 5-7 years post injury[77]–[79]. Another example is the disconnection from interpersonal roles and relationships common with moderate to

severe ABI. This disconnect, in turn, can lead to substantial social withdrawal and isolation[80].

In addition to the individual with an ABI, the family and primary caregivers are often deeply impacted by the injury and long-term consequences. Recently, caregivers are being recognized as an essential factor for rehabilitation and long-term well-being of the family member with an ABI [81]. Most caregivers report a high incidence of depression, stress, caregiver burden, poor work productivity, lack of sleep, social withdrawal and family distress[82]–[84]. *Therefore, novel approaches to prevent long-term social isolation, job instability, and family well-being are vital while developing rehabilitation goals.*

1.2 Current Stroke and Traumatic Brain Injury Rehabilitation

1.2.1 Factors influencing TBI/Stroke rehabilitation

ABI rehabilitation is influenced by various factors which can impact recovery and long-term outcomes. Below, are *three factors* that must be considered while deciding treatment goals to facilitate a smooth transition from hospital to home. [11]

- 1) *Individual* characteristics such as age at the time of injury play an essential role in functional outcomes. Older adults with ABI have a poorer prognosis compared to children and young adults[85], [86]. Additionally, those with higher preinjury cognitive functioning and education are directly correlated to having better clinical outcomes and recovery [87], [88].
- 2) *Social-environmental* factors post injury such as maintaining independence, job stability, marital status, personal relationships with friends and family is vital for

social integration[81]. Family well-being and caregiver support are important predictors of successful rehabilitation[83].

- 3) *Access to rehabilitation* can have a significant impact on recovery. Barriers such as limited technical and human resources can influence specialized care essential for severe ABI impairments[29], [89]. For example, according to the CDC Report to Congress, quality of care in a tertiary hospital of an urban area was more comprehensive compared to primary care in a rural area[11]. Additionally, limited insurance and lack of progress in recovery can lead to early discharge to a subacute rehabilitation setting [90].

1.2.2 TBI/Stroke Continuum of Care

“Recovery” from moderate to severe ABI is often discussed as lifelong and complex. Rehabilitation typically consists of a multidisciplinary team that includes physical, occupational, cognitive and speech therapist, and one or more physicians[91]. Physical Therapy (PT) and Occupational Therapy (OT) focus on improving gross and fine motor functions such as walking on a treadmill or performing table top activities. Speech Therapy (ST) focus on articulation and language intervention therapy. Cognitive Therapy (CT) focus on compensatory skill strategies and restorative intervention[92], [93] such as using an alarm as a reminder to take medicines or teaching individual steps for meal preparation.

Generally, the multidisciplinary team provides therapy separately within a clinic, hospital or rehabilitation setting. *Below are four major stages of the typical continuum of care for individuals diagnosed with ABI. (Figure 4).*

Acute care starts once the individual is medically stable. Typically provided within a trauma center or rehabilitation hospital, the primary goal of acute rehabilitation is to address basic body movements such as standing, reaching, and basic ADLs such as bathing, dressing, bed mobility, and eating[94]. Moderate to severe individuals with ABI may be discharged to subacute rehabilitation without achieving these goals.

Subacute rehabilitation is provided in various settings such as Skilled Nursing Facility (SNF) or specialty hospitals. The primary focus is to maintain medical stability while promoting recovery over a longer duration of time. The person's health condition and inability to tolerate the high intensity of treatment often results in less than three hours of combined therapy per day.

Post-acute programs occur as part of day treatment programs, residential rehabilitation, and behavioral programs. The primary goal is to increase the level of function towards some degree of community independence (aka community re-entry). Programs which typically provide high-intensity rehabilitation have been associated with better functional outcomes as compared to typical intensity programs[95].

Community programs focus on cognitive, motor, and social deficits that limit further community re-entry. Re-entry goals typically focus on employment, community safety, and independent living. Individuals typically live at home or under supervision.

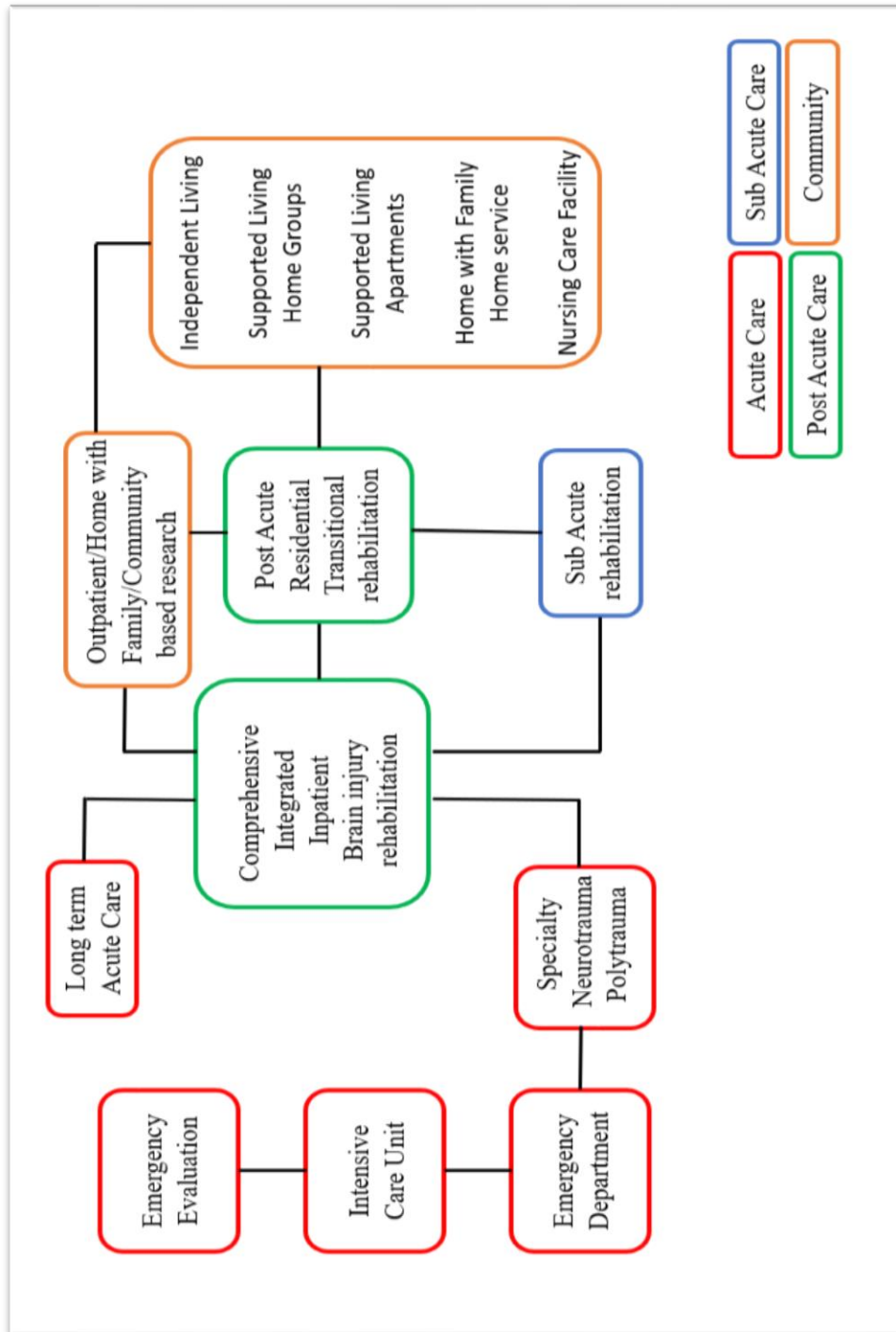


Figure 4 Moderate to severe brain injury continuum of care. Rehabilitation is typically comprehensive, long and consists of acute care (red) and post-acute care (green). Adapted from the Rocky Mountain Brain Injury Model System

Group-based, high-intensity programs are associated with better community integration as compared to the individual performance of low to moderate intensity programs[96], [97].

Based on the traditional continuum of care from acute rehabilitation to community-based programs mentioned above, it would seem that individuals with ABI have a smooth transition from hospital to home. Goals focused on family-centered outcomes, provision of community-based services like support groups and vocational rehabilitation activities would further promote a return to work and address long-term needs of the individuals and their family.

However, the literature on the prognosis of individuals with ABI often describes their recovery as non-linear and complex. For example, factors such as early discharge due to limited insurance, the inadequate regaining of skills, multiple re-hospitalizations, and secondary injuries due to falls significantly affect the long-term outcomes at home and in the society[11], [98], [99]. Alternative rehabilitation models have been recommended to address the above gaps and decrease deficits while improving functional skills.

Alternative rehabilitation models include a) *co-treating* where two or more therapeutic disciplines work together (PT +OT, PT + OT + CT) on similar goals for improving functional outcomes or b) *multiple tasks* performance simultaneously (cognitive + physical task). For example, *co-treating* could refer to a PT and an OT working different hours of the same day to improve an individual's goal of biking in the community. *Multi-tasks* [100], [101] could refer to a cognitive and motor task performed simultaneously (dual task) to improve an individual's goal of conversing while walking.

Focusing on task-specific skills is a conventional method for training of lost motor skills[102]–[104]. Based on the assumption that repetitive practice over time will eventually result in the acquisition of the practiced skill. Recent literature, however, provides little support for the transfer of task-specific skills to a more complicated and diverse activity[105]–[107], or greater participation in the community[108]. For example, a person may learn to lift a Styrofoam cup of water post-ABI. However, most individuals have difficulties with most basic ADL like dressing or preparing a meal.

There are a variety of community rehabilitation programs for individuals with ABI. Unfortunately, follow up studies have reported a cognitive decline, unresolved motor deficits, social isolation and even death [98], [99], [109]. Additionally, most community programs partner with local state-run agencies and support groups[11]. Therefore, available resources may well influence program outcomes. Subsequently, a general improvement in community services may be difficult as variability across programs regarding population served, dosage, timing, and duration prevent comparison of key characteristics[110].

1.2.3 Emerging Rehabilitation Techniques

Advancement in technology has given rise to emerging rehabilitation techniques as an adjunct to typical rehabilitation models. For example, Virtual Reality (VR) is one such approach where an “illusion of reality” is created using software and hardware for the users to interact and engage within the environment[111]. Feedback is given through a device mounted on the head or visually on the screen[112]. Studies on VR have assessed its effects on balance, fine motor function, arm posture

coordination, memory, attention, visuospatial navigation and emotions in individuals with ABI [112]–[115].

Another example is computer gaming options such as the Nintendo Wii TM. The Wii is a commercial game console with handheld controllers, equipped with inbuilt accelerometers and infrared technology to capture controller position. The user interfaces with games on the monitor through controller movement. Use of Wii games as an adjunct rehabilitation tool has been associated with an increase in balance and improve upper extremity function[116]–[118].

Another gaming option is the Microsoft Kinect TM. The Kinect is a low cost, off the shelf device which facilitates user interaction similar to the Wii. i.e., accelerometers and infrared technology to capture controller position. Use of Kinect games as an adjunct rehabilitation tool is associated with an increase in balance measures, hand function, decrease joint angle error, independence, and balance[119]–[121]. *Despite growing research on these interactive technologies, they are currently not considered as the standard of care in most acute, post-acute, and community rehabilitation programs. Below are potential reasons reported in the literature for this lack of implementation.*

Using the above technologies within the ABI continuum of care is likely limited by one or more of these factors: First, technology such as VR may not be possible for clinical utilization due to high costs associated with the setup and space constraints within a clinical setting[122]. Second, training clinical staff to set up, manage and collect data would also be too time-consuming given their caseload. Third, older adults demonstrate decreased adherence to digital technology. Currently, there is a lack of adjustable, user-friendly interfaces for aging populations[123], [124].

Fourth, off the shelf games have the added advantage of being low cost. However, they were not developed for rehabilitation[125]. For example, the Wii cannot be used by an aging stroke participant to work on balance alone at home due to safety concerns. **The above limitations highlight the urgency to design an intervention requiring less community space that is tailored to the individual's needs. At the same time, providing the engagement and motivation essential to increase satisfaction at a personal and community level.**

1.2.4 Advancing Current Rehabilitation

According to the 2015 CDC Report to Congress, “there is a need to establish integrated rehabilitation models that support ongoing treatment, community integration and cognitive behavioral support for people with TBI” [11]. Below, are three key factors this dissertation addresses in Chapter 2 (Protocol) and 3 (Feasibility).

- 1) *The first key factor is to pose a research question which answers how to improve an individual’s social interaction while motivating and challenging them in a work or leisure environment. Current ABI population comprises predominantly of individuals who lie within the working age group[59]. Often, moderate to severe individuals with ABI have long-term impairments which prevent successful community integration. Factors like returning to work, participation, and leisure activities are known to increase the quality of life, socialization and well-being[126], [127]. Therefore, by engaging in leisure activities to compensate for previously employed/social time, individuals with ABI may be able to achieve/maintain satisfaction with life [76].*

- 2) *The second key factor is to determine the method of application of an intervention that combines physical and cognitive tasks* (dual task activities) in combination with socialization (first key factor). Cognitive and physical decline are both common in ABI after discharge and directly related to a lack of meaningful community re-entry such as at home, and at work[42], [61]. The ability to dual task, i.e., divided attention is essential for real-world activities[128]. Additionally, benefits of physical activity on the brain and body has been widely acknowledged in animal and human literature[129], [130]. Therefore, engaging in the community while maintaining one's active physical profile may help prevent physical and cognitive decline.
- 3) *The third key factor is to provide adequate support structures in the environment* to facilitate an increase in independence, mobility, functional activities, and decrease fear of falls. The use of body weight support systems is widespread in hospitals, clinics, and rehabilitation settings. Unfortunately, early discharge or limited carryover of activities can leave the individuals feeling socially isolated and discriminated against due to difficulties with transportation, finances, and disability[80], [83]. Therefore, by providing a support structure in a work/leisure environment, individuals with ABI may improve physical, cognitive and social skills.

Combining the above three key factors help lay the foundation of the dissertation study. The first aim is to develop a Protocol for a clinical trial. The second aim is to conduct a Feasibility study based on the Protocol. Specifically, the

intervention is a functioning Café equipped with a novel Body Weight Support System for moderate to severe ABI. Development of a Protocol (Chapter 2) provides formal and specific guidelines for the proposed Café study. The Protocol study is tested for feasibility and safety (Chapter 3). Information gathered from the Protocol, and the Feasibility study would decide future action towards a clinical trial.

1.3 Specific Aims and Hypothesis

Our lab's research focus is to develop and test community-based technology and training programs for children and adults with severe mobility limitations. The focus of this proposed project is to develop a Protocol (Aim 1) and determine Feasibility (Aim 2) of a real-world Enriched Environment (EE) equipped with a fall arresting harness system (aka body weight support system, BWSS).

Typically, animals placed in EEs with dynamic, complex objects requiring active exploration and skill learning trigger greater neural plasticity and skill development compared to standard conditions[131]–[135]. EE has shown a positive impact on a range of brain and behavioral measures in a variety of animal models of disability across the lifespan [136]–[141].

Similarly, BWSS is well established for neurological rehabilitation for training for standing and walking across a range of adult disability populations.[142]–[147] However, despite robust literature on the application of EE in animals, there is limited research on the use of EE to promote recovery in brain-injured individuals[148]–[150].

With advancement in neurorehabilitation interventions, there is a growing need to develop novel, evidence-based rehabilitation environments that both a) advance

limitations, functional activities, and community participation and b) are feasible within the broader community outside of research lab.

The first aim is to provide the scientific rationale and methodology for study development and treatment for individuals with ABI (Protocol). The second aim is to determine the feasibility of different important parameters/objectives (see below) critical for proceeding to the next research study. These set objectives would be tested based on an “a priori” criteria to determine the feasibility and acceptance of the participants. Below, we highlight the specific aims and hypothesis:

Aim 1: To develop a Protocol for the Café as an intervention environment for individuals with ABI

A formal research Protocol based on Standard Protocol Items for Clinical Trials (SPIRIT) guidelines will be developed. Below, we call attention to critical factors addressed in the Protocol [151].

- *Scientific Background and Rationale* for conducting a feasibility study
- *Study Objectives* based on research questions and potential outcomes
- *Study Methodology* to include study design, population, inclusion and exclusion criteria, recruitment, and outcome measures
- *Study Intervention* with a description of the Café and tasks performed
- *Data Analysis* to determine the feasibility of outcome measures
- *Ethical Considerations* to ensure safety and confidentiality of vulnerable populations
- *Appendices* with all IRB documents used for conducting the study

Aim 2. To determine if the Protocol is feasible for future clinical trials

We hypothesize the Protocol will be feasible for the next Phase 1 clinical trial in the following areas:

Hypothesis 1.1: Recruitment of participants

Hypothesis 1.2: Attendance to the intervention

Hypothesis 1.4: Adherence to intervention

Hypothesis 1.5: Attrition to intervention

Hypothesis 1.6: Safety of the BWSS

Hypothesis 1.7: Acceptance of Intervention

Hypothesis 1.8: Selection of outcome measures

1.3.1 Significance

The protocol and feasibility study are significant in the following ways:

- The Protocol will provide future EE based clinical trials with concise guidelines to assist with data collections,
- The Protocol can be adapted to test feasibility in different neurorehabilitation populations,
- Results on safety, utilization, and feasibility of a commercially available, low-cost novel BWSS in a real-world business setting can be used to adapt to different work and hospital environments, and
- Knowledge gained on the selection and elimination of outcome measures would guide researchers with future population-specific EE trials.

1.3.2 Innovation

The protocol and feasibility study are the first to:

- Develop protocol guidelines for an actual business setting as the focus of rehabilitation,
- Determine the feasibility of conducting an EE based rehabilitation model in the community,
- Test the use a novel, commercially available FDA approved harness, and
- Use a multitask treatment approach to work on underlying impairments while performing typical job employee responsibilities.

Chapter 2

DEVELOPING A PROTOCOL FOR BWSS + EE: A COMPREHENSIVE INTERVENTION ENVIRONMENT FOR INDIVIDUALS WITH ABI

2.1 Abstract

The goal of chapter 2 is to develop a Protocol for a clinical intervention study. Protocols are an essential component of a typical clinical trial pipeline. They not only provide the guidelines to conduct the study, but also ensure transparency of data collection, management, and analysis. Thus, Protocols facilitate replication of studies, decreases bias and strengthens evidence-based practice.

Each stage of the developed Café Protocol is based on the selection of two established Protocol guidelines: Standard Protocol Items for Clinical Trials (SPIRIT) and World Health Organization (WHO). Background and Rationale for using two novel concepts (BWSS + EE) which form the foundation of the study are explained based on animal and human literature. The above section is followed by a description of the methodology which includes explanation and rationale for selection of participant population, study design, intervention, and outcome measures.

Finally, measures selected for the feasibility study are accompanied by an “a priori” cut off score to determine the minimal criteria for assessing the success of the Café trial. Additional information on ethical procedures, confidentiality, and potential risks and benefits are included. Thus, all items on the SPIRIT and WHO checklist applicable to the study are accounted for to ensure reporting of quality Protocol guidelines.

2.2 What is a Protocol?

Chapter 2 contains information on Aim 1 which was to develop a formal research Protocol for a clinical intervention by combining a Body Weight Support System (BWSS) with an Enriched Environment (EE) to form a fully functioning Café (aka Café Protocol). A protocol is an action plan used to provide guidelines for conducting a clinical research trial (Figure 5, Figure 6) [152]. The primary purpose of a protocol is to outline a scientific question, highlight its importance, adhere to international ethical rules while reporting data, ensure accountability, and provide a rationale for study design[152], [153].

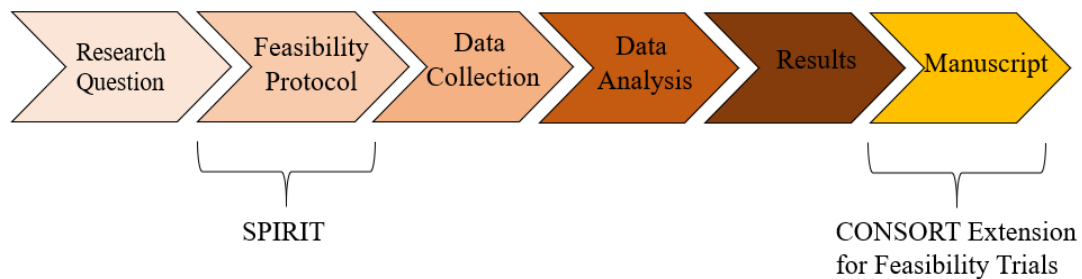


Figure 5 Procedure and Guidelines for Protocol Development (SPIRIT) Chapter 2 and Feasibility Study (CONSORT Extension) Chapter 3. Adapted from CONSORT and reporting trials in 2017: Who Should Do What by Larissa Shamsheer[154].

Providing a formal research protocol with precise details and guidelines enables other researchers to have access to study methodology and design for replication of the same study in a different population and evaluate potential study specifics. By providing clear guidelines on study methodology, a well-written Protocol controls for variability in data collection and management. This facilitates opportunities for multisite studies and international collaborations [153], [155].

Finally, the results obtained from a Protocol study can guide future clinical trials with valuable information on limitations, and recommended modifications[152], [153].

There are various common protocol templates available for descriptive (case report, case series), observational (case-control, cohort, and cross-sectional) studies, and Phase I – IV clinical trials. One initial step to the current Protocol was to critically review the guidelines provided by scientific research journals, funding agencies, and University of Delaware's Institutional Review Board (IRB). Though it is common to modify and change study aspects within suggested limitation, multiple studies have shown evidence of clinical trials providing incomplete information and missing outcome measures listed in the protocol[156]–[160].

In addition to incomplete information reported by researchers, current guidelines of protocols vary significantly in their content scope and recommendations[161]. This leads to a decrease in research transparency and validity with the increase in research bias. Consequently, the use and lack of reporting actual guidelines can lead to poor follow up studies, type 1 errors, prevention of setting a standardized trial design, and failure of replication studies by national and international researchers[156]. Thus, to prevent the above errors, Procedure and Guidelines for Protocol Development (SPIRIT) guidelines were used for Protocol development of the café study.

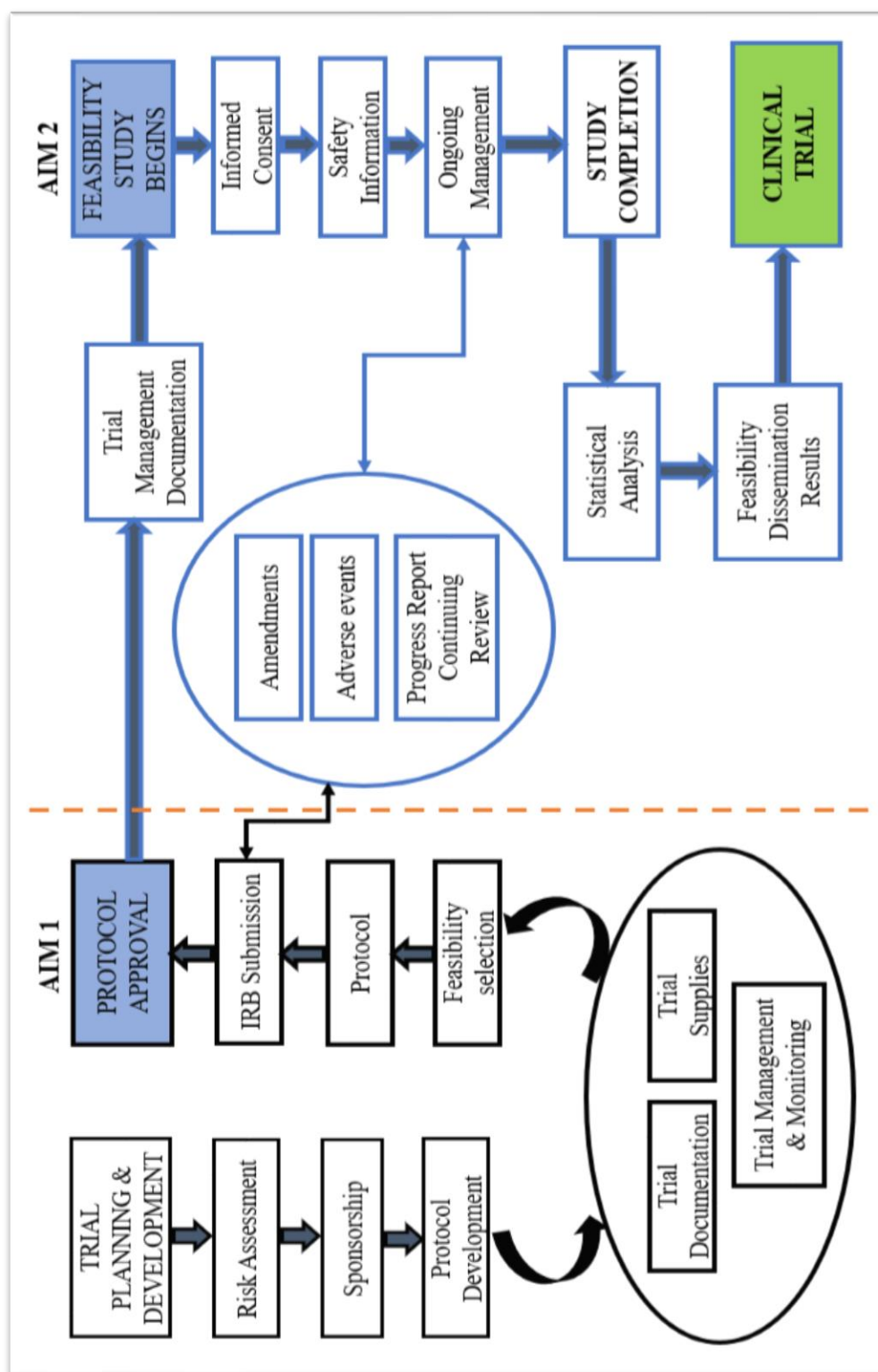


Figure 6 Pipeline for the development of a clinical trial. Aim 1 (Protocol) and Aim 2 (Feasibility) are essential components of the clinical trial pipeline. Adapted from Clinical Trials Toolkit Route-map by National Institute for Health Research.

2.2.1 Developing a Protocol for a Clinical Intervention

Conducting a small sample, relatively rapid feasibility study is often the first step in testing a research question and hypothesis (Figure 5). Results and experiences from a feasibility study would guide researchers on required modifications to the formal protocol. Depending on the results and level of modifications, researchers can accurately determine the cost/benefit ratio of perusing a large sample, more resource intensive pilot study, or phase 1 clinical trial. Thus, designing a feasibility protocol is essential to test essential objectives before conducting a large-scale intervention.

There are many guidelines for developing a protocol for a clinical trial. For example, the Standard Protocol Items for Clinical Trials (SPIRIT) 2013 Statement provides a 33-item checklist for recommended items included in a clinical trial protocol[151]. While the checklist ensures all essential factors are addressed in a Randomized Control Trial (RCT) Protocol, the scope of the checklist applies to most trials irrespective of study design[151].

Protocol templates are now being provided by other multiple sources including National Institute of Health[162], World Health Organization[163], Global Health Network[164], National Center for Complementary and Integrative Health (NCCIH)[165], Cancer Therapy Evaluation Program (CTEP)[166] and National Institute of Dental and Craniofacial Research (NIDCR). This is primarily to increase research transparency, prevent misconduct or omission of relevant information by authors in the clinical trial,

To our knowledge, there are no standard feasibility protocol templates. The current Café feasibility protocol was developed based on WHO and SPIRIT guidelines

to cover all relevant elements such as study design, methodology, deviations from protocol, quality assurance, data analysis, and interpretation of results (Figure 7).

The formal Protocol template used for this dissertation is outlined in detail in the upcoming sections. The first is Background and Rationale which focuses on two major scientific elements of designing the cafe: Body Weight Support System and Environmental Enrichment.

2.3 Introduction

2.3.1 Background and Rationale

2.3.1.1 Body Weight Support System (BWSS)

2.3.1.1.1 History of BWSS

This dissertation project uses a new FDA registered BWSS, which for the first time locates this technology within a community-based intervention program. The earliest use of BWSS in research was in laboratory animals. Sir Charles Sherrington first reported that despite surgical transection of the lower thoracic cord of dogs, they were still capable of “spinal stepping” [167]. This idea of holding the trunk and pelvis to facilitate stepping by the hind limbs was later tested over a treadmill. Forequarters of the cats were unloaded on a stationary platform and hindquarters were placed on the treadmill[168]. Results from this study provided evidence for patterned leg movements despite spinal transection. Additional studies on spinalized cats demonstrated the effects of changing treadmill speeds on locomotion with cats transitioning from walk to gallop to run[169], [170]. These studies are considered as landmark foundational work in systems neuroscience.

Section	Description
Title	
Funding	Funding source – Federal/Private/University
Introduction	
Background and Rationale	Introduction to research question, review of literature
Trial Objectives	Objective and research hypothesis
Trial Design	Type of study design – single, parallel, cross over
Methods	
Participants	Population, demographics, gender specific, acute/chronic
Study Setting	Location of study – single or multi-site
Inclusion/Exclusion	Eligibility criteria for participation in study
Intervention	
Outcomes	Description of Intervention, outcome measures used
Participant timeline	Total duration from screening to completion/follow up
Data collection	Procedure for data collection, tools required, resources
Data Management	Data entry, storage, safety of participant identification
Data Analysis	
Statistical method	Means of assessing measures collected for results
Data Monitoring	Fidelity of program, reason for interim analysis and stopping study
Adverse events	Procedure in case of adverse event, reporting policy
Ethical Considerations	All forms and testing measures require approval by IRB
Protocol Amendment	Procedure for application of protocol amendment to IRB
Confidentiality	Assigning number to participants, protecting personal
Appendices	
	Consent forms and outcome measures used for study

Figure 7 Key factors essential for the development of a Protocol. Adapted from WHO and SPIRIT Guidelines for human research trials[151], [163].

By the late 1980's, BWSS had expanded from being used to study animal locomotor patterns to study human gait and then used as a rehabilitation tool.[171], [172]. BWSS use in research and rehabilitation rapidly expanded as gait impairments are common in many neurological conditions such as stroke, TBI, cerebral palsy, spinal cord injury as well as orthopedic conditions such as osteoarthritis, sports-related fractures, and knee injuries.

There are two general types of BWSS's in rehabilitation – Body Weight Supported *Treadmill Training* (BWSTT) and Body Weight Supported *Overground Training* (BWSOG). The BWSS provides support, balance, and permits alteration in weight bearing as well as learning and relearning of a more functional gait pattern [173]. BWSSTT and BWSOG have been found to have positive effects on endurance, gait kinetics and kinematics, balance, and aerobic capacity in stroke and TBI populations[173]–[176].

In BWSTT, a mounting frame with an overhead apparatus connects to a harness garment worn around the chest of an individual. The frame is mounted over a standard motorized treadmill[177]. The BWSS itself allows for either fall arrest and reduced weight bearing. The amount of weight-bearing can be individualized for each. With repeated bouts of walking (mass motor practice) on the treadmill, underlying neuroplastic effects are known to enhance gait speed, symmetrical walking pattern and endurance[178], [179].

BWSTT have three primary advantages i) allows for early rehabilitation of patients who cannot wholly weight bear, ii) prevents falls during learning of gait patterns over the treadmill and, iii) symmetrical unloading of legs prevents compensatory strategies that typically cause asymmetrical walking patterns[173].

The use of BWSOG has significant importance for real-life ambulatory skills compared to the treadmill. Gain's noted with BWSTT have reported limited aftereffects to overground walking as compared to BWSOG. There are three reasons for this i) in BWSTT, the treadmill speed is predetermined whereas in BWSOG an individual adapts their own pace according to the factors such as surface conditions[180] ii) BWSTT may have different effects on joint angles and muscle activation compared BWSOG. This would then require some level of adaptation and potentially re-learning between the BWSS types [181], [182], and iii) similarly, propulsion and balance may differ between treadmill and overground training [180].

Attempts to develop modify and develop new types of BWSS's are emerging to address the limitations in older versions. For example, traditional BWSS's allow for walking in a) two directions along a single track, and b) non-community spaces such as clinical or laboratory settings. In contrast, for moderate to severe ABI populations, community ambulation is significantly impaired. Hence, attention to a regular walking pattern must be addressed by the new BWSS by facilitating i) the freedom to walk throughout a 2D if not 3D space, and ii) to do so outside of a clinical or laboratory setting.

In the above section available BWSS's that are widely used in clinical and laboratory settings were explored. This dissertation is the first project to place a new commercially available BWSS within a community setting.

2.3.1.1.2 New FDA registered community-based BWSS

The adult BWSS used in the current study originated from our lab's previous experiences with a portable pediatric BWSS. The Portable Mobility Aid for Children (PUMA, Enliten LLC, Newark, DE, USA, Figure 8) is relatively portable, easy to set

up, and lightweight. The PUMA can be equipped with a counterweight system to alter the amount of body weight support. This BWSS was designed to be relatively easy to place within play environments such as home and schools to encourage exploration by infants and children up to 50 lbs. In pilot studies using the PUMA, behavioral outcomes were positive. For example, infants with Down's syndrome demonstrated short-term changes in movement behaviors after a bout of exploration using the PUMA[183]. This initial success with infants led to our interest in studying the effects of a similarly designed adult BWSS with adult ABI populations.

The Open Area Support System (OASUS) is a BWSS for adults. It is composed of three components: frame, rolling car, and harness (Figure 9, Appendix Q). The frame forms the legs of the BWSS which is cut according to the height of the open area space. The four legs are connected at the top by interconnected beams to look like a four-legged square tent used for the PUMA. The rolling car is custom made to attach securely to the central frame while rolling with very little resistance. The support lines connect the harness garment to the rolling car. These support lines can either be regular straps or bungee cords to facilitate partial weight bearing if required.

The harness garment is worn by the individual and comprises of leg, shoulder, and chest straps that ensure fall prevention. In case of emergencies, red-colored quick release straps are installed at the junction of the harness garment and support lines. When pulled, it separates the harness from the support lines, thus freeing the individual from the BWSS. As outlined below, for this dissertation project, a 10 X 10' OASUS served as the infrastructure of a functioning Café as well as preventing falls and facilitating movement within a fully functional Café space, a.k.a. The Go Baby Go Cafe.



Figure 8 A PUMA shown with a constructed enriched environment and a doll within the harness garment near the weight stack that provides body weight support (right)

A collaboration between the UD Creamery and the Go Baby Go research program led to the development of The Go Baby Go Café. The GBG Café is a free-standing 10'x10' OASUS that provides both a fully-functioning small business through sales of ice cream, food, beverages and snacks (run by the UD Creamery), as well as a site for research participants to work on physical, mental and social activities under the direction of a research therapist (Go Baby Go Program).

For this dissertation, the OASUS was explicitly embedded within a functioning business to create an “Enriched Environment” where individuals with moderate to severe ABI might be able to address their functional goals.

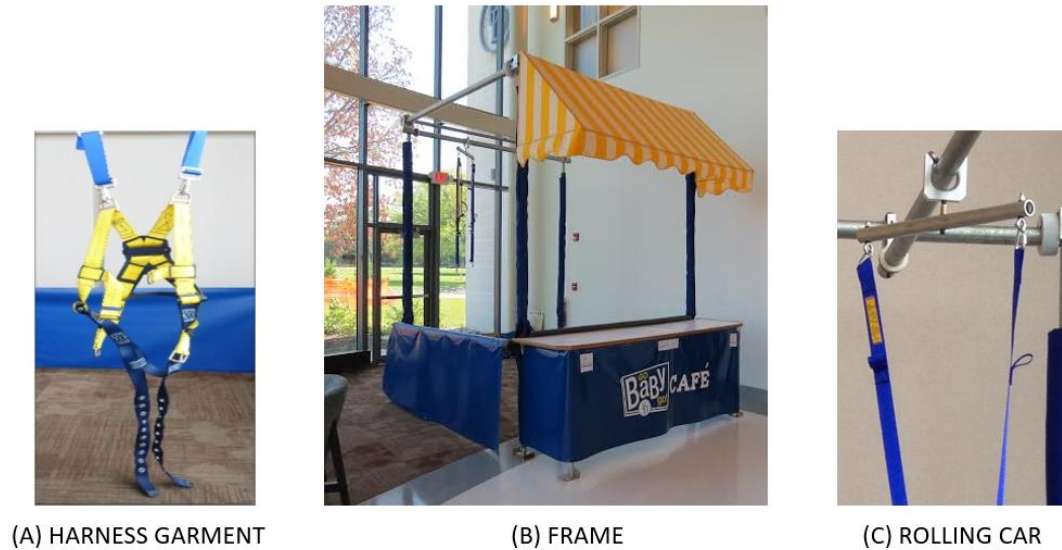


Figure 9 Open Area Support System (OASUS) unit with the (a) harness garment worn by the individual, (b) frame forming the kiosk, and (c) rolling car to allow smooth movement in space

2.4 Environmental Enrichment (EE) in animals

2.4.1 EE in healthy animals

The neurological impact of EEs in animals is one of the most robust and positive findings in all of the neuroscience research. Modern research on EE was first described by Donald Hebb in 1947[184]. He discovered that rats raised as pets performed better in problem-solving tasks as compared to rats raised in standard laboratory cages. Since then, countless studies have tested the effects of different EE

set up's on animal behavior, brain size, and molecular and cellular aspects of neuroplasticity in both, healthy and a wide range of adult and developmental neurological animal models [134], [135], [185], [186].

EE in animals typically refers to a relatively standardized laboratory experimental paradigm. In the *EE condition*, multiple rats are enclosed in a large cage with a variety of physical structures and novel toys which are replaced and reorganized every few days, with the provision of food and water (outlined in detail below). In the *standard housing condition*, a small number of rats are enclosed in a regular size cage with a few objects, and provision of food and water. In the *impoverished condition*, a single rat is enclosed in a regular size cage only with the provision of food and water [186] (Figure 10). **Below, description of building different types of EE's, influence of different EE's on brain structure and physiology in healthy animals[186] and neuroplastic effects in brain-injured animals are discussed[187].**

EE in animals is artificially created to answer specific research questions. For example, studies may focus on the effects of physical, cognitive, or social stimuli either in isolation or combination of multiple categories.

Physical Enrichment is provided by incorporating structures within the cage [188]. Cages may have one or more ramps, beams, ladders, tubes, running wheels, elevated platforms, and ropes. *Cognitive Enrichment* is provided by introducing unique toys and changing their position periodically[189]. For example, tunnels and balls may be incorporated in the cage to encourage navigation in and around objects. *Social Enrichment* is provided by including a pair or multiple rats together in one cage. Depending on the research focus, the rats may be genetically similar, may or

may not be related and could include young and old rats. *Sensory Enrichment* is provided by background noise (*auditory enrichment*) or special food (*tactile enrichment*). Auditory enrichment can consist of soft or loud sounds to increase or decrease the excitability of animals as an incentive for task performance[188]. Generic Enrichment refers to physical, cognitive and social stimuli provided simultaneously in a large cage containing physical structures, unique toys, and multiple rats. Thus, the entire environment is “non-selectively enriched” [189].

Physical Enrichment affects motor and cognitive domains of healthy, neurologically typical animals. The structures such as running wheels, ropes, and ramps are used to encourage general physical activity, exercise, running, and aerobic activities (Figure 11). The impact of the animal’s physical activity on their body and brain has been studied extensively in animal models. For example, exercise is known to strongly influence cognitive function such as spatial memory and learning[189], [191] . Exercise also affects age-related cognitive decline in older mice. High physical activity is associated with a decreased risk of cognitive decline and dementia[192].

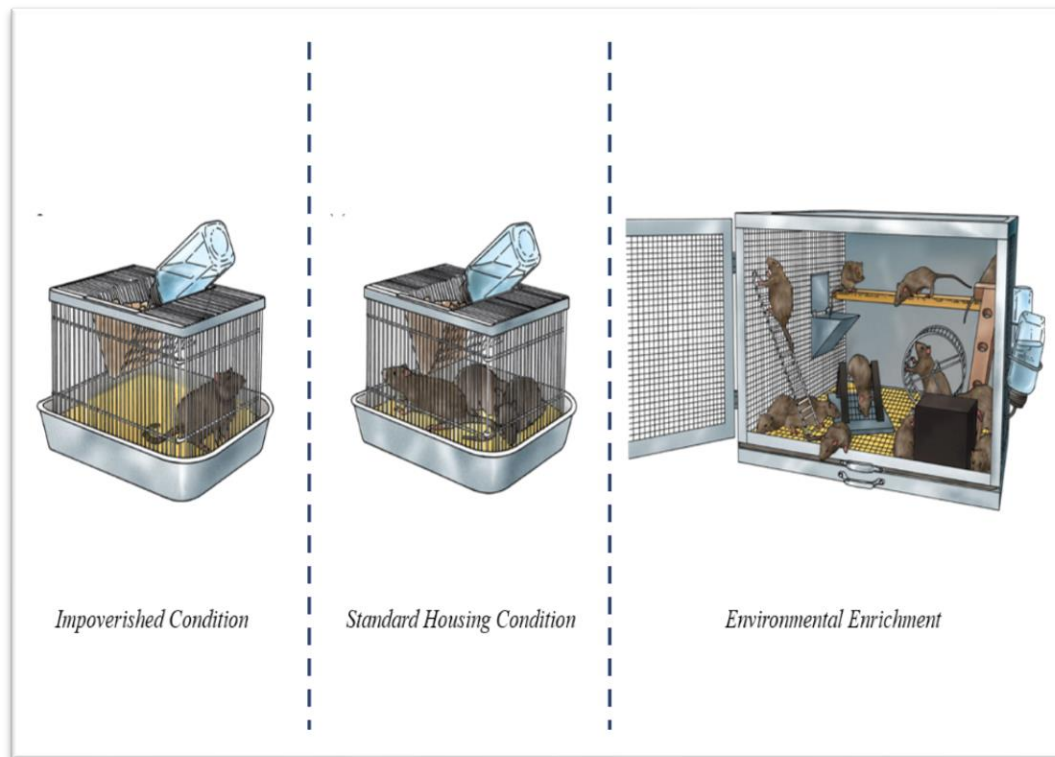


Figure 10 Types of housing conditions for testing the effects of the Environment on a rat's behavior, anatomy, motor skills, and cognition. Adapted from Biological Psychology, 6th Edition, 2010 [190].

Cognitive Enrichment also affects healthy, neurotypical animals. Introducing novel objects and rearranging them every few days leads to the formation of new spatial maps and increase in search behavior to detect new objects within the cage[193]. Thus, cognitive enrichment increases spatial learning, hippocampal long-term potentiation and memory, cognitive flexibility, visual and spatial recognition, and decreases anxiety. [194]– [198].

Social Enrichment also affects healthy animals. Having multiple rats living within the same cage decreases behavioral anxiety, stress, aggression and increases “harmonious living” and social learning [199]–[202]. Conversely, social isolation

results in neuropsychological abnormalities in animal model studies of depression, autism, attention deficit hyperactive disorder, and impaired social cognition [203]–[205]. *Molecular and Morphological changes* are consistently found in studies of EE in healthy animals. For example, morphological changes include an increase in brain weight, neuronal density, dendritic branching, increase in cortical and hippocampal weight, increase in synaptic connection, number of synapses, angiogenesis, neurogenesis, and better brain vascularization[196], [198], [207]–[209]. Molecular changes include an increase in the release of neurotrophic factors such as Brain-Derived Neurotrophic Factor (BDNF), Nerve Growth Factor (NGF), Neurotrophin – 3 (NT- 3) and Neurotrophin - 4 (NT-4) with exercise. Neurotransmitters such as acetylcholinesterase, serotonin, and norepinephrine also increase with social stimulation[210], [211]. Synaptic receptors such as AMPA and NMDA increase in size and are thought to relate to long-term potentiation with cognitive stimulation[187], [196].

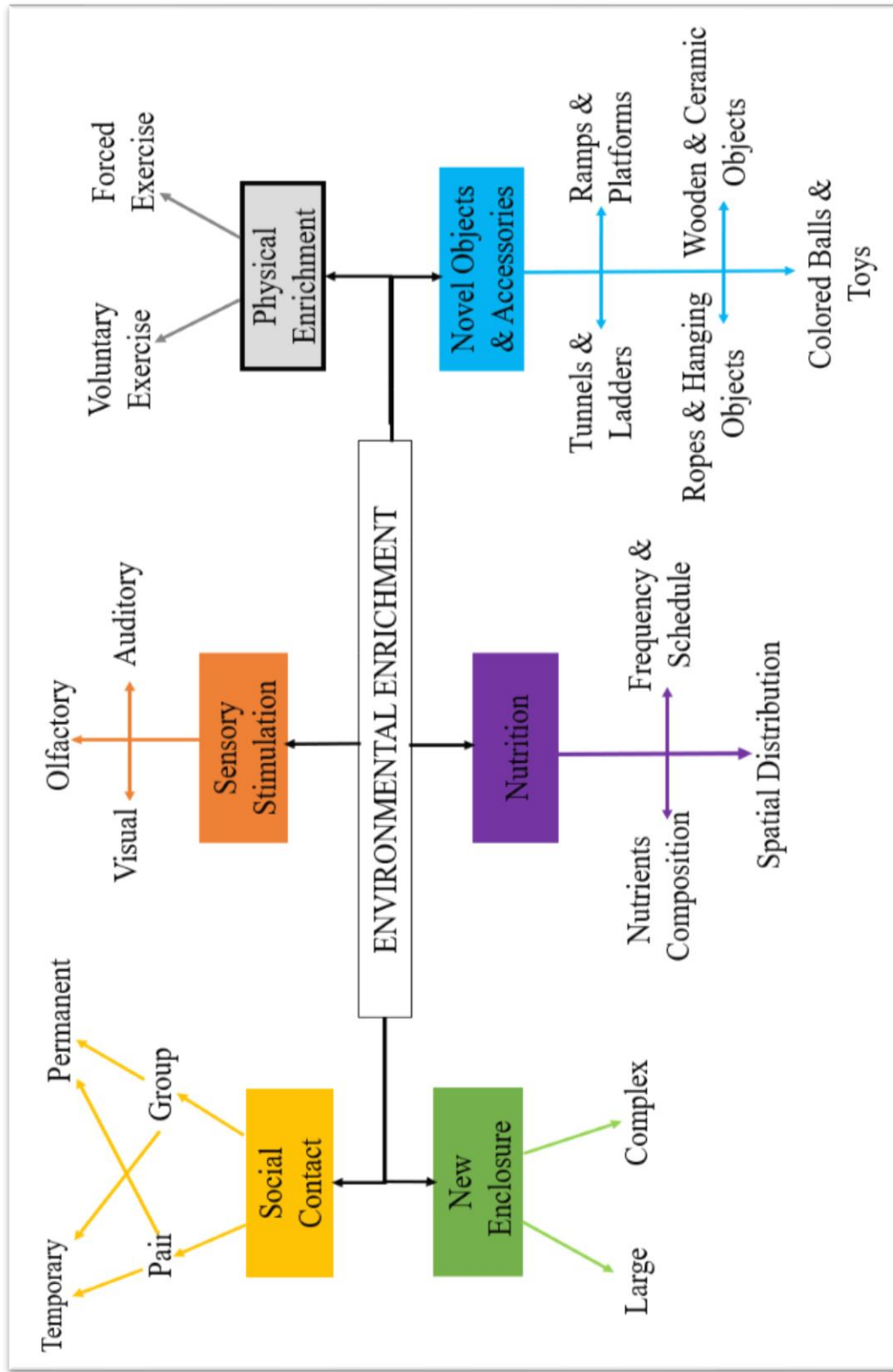


Figure 11 Different types of Enrichment can be provided depending on the research objective in healthy and brain injured animal models. Adapted from Gaurav Singhal et al., 2014[206]

2.4.2 EE in brain-injured animals

Physical Enrichment also affects motor and cognitive domains of ABI rat models (Figure 12). Exercise and running increase motor learning ability in ABI animals. Stroke-induced rats demonstrate better motor performance on the beam task, pole test, reaching, visuospatial navigation and memory tasks[212], [213]. Similarly, TBI induced animals demonstrate better performance on skilled paw reaching, ladder climbing, locomotor tasks, and rotarod motor performance test compared to control animals[214]–[216].



Figure 12 Different components of EE typically provided to study the effects of social, physical and cognitive changes. Adapted from Petrosini et al., 2009[217]

Cognitive Enrichment also advances cognitive domains of ABI rat model (Figure 12). The Morris water maze and radial arm maze are two standard measures of spatial memory abilities [191]. Therapeutic effects of EE on cognition in TBI rats include the superior acquisition of spatial learning compared to controls[218], [219]. Other effects of cognitive EE on neuroplasticity include enhanced learning, memory retention and a decrease in the size of cortical lesions in ABI rat population[219]–[222].

Social Enrichment has positive effects on ABI rat model (Figure 12). Most EE papers on neuroplasticity with social enrichment focus on motor and cognitive changes. Social enrichment post-stroke is associated with a decrease in infarct size and risk of cardiovascular diseases, increase in behavioral recovery, BDNF, and neurogenesis compared to socially isolated rats[223]–[225]. Conversely, social isolation increases neuroinflammatory responses associated with an increase in the incidence of multiple strokes and death[226].

Molecular and Morphological changes: Enrichment improves brain function at the morphological and molecular level in ABI rat model. ABI is associated with widespread morphological changes such as downregulation of neurotrophic factors, loss of cortical, thalamus, hypothalamus and hippocampal cells, the release of antioxidants, and an increase in inflammatory responses [227], [228]. Exposure to EE appears to be neuroprotective with decreases in apoptotic cell death, hippocampal volume loss, increase in synaptic density, spine density, dendritic branching, and changes in stem cell differentiation[196], [229]–[232]. Molecular changes associated with EE include upregulation of neurotrophic factors such as BDNF, VEGF, and NGF increasing survival and inducing plasticity through neurogenesis[233]–[235].

Thus, long-term EE has clear and consistent positive changes in neuroplasticity which are associated with therapeutic effects across motor, cognitive, social, and structural changes. Animal work provides several principles from which to build new rehabilitation interventions. First, generic EE has more significant effects as compared to a specific EE. For example, ABI rats receiving social EE in combination with physical EE performed better over time compared to rats solely assigned to social enrichment or solely to physical enrichment [236].

Second, the duration of EE impacts recovery. For example, a study randomly assigned TBI rats to one the six groups: TBI- no EE, TBI - early EE exposure, TBI - delayed EE exposure, TBI - continuous EE exposure, Sham - no EE, and Sham - continuous EE. TBI rats exposed to constant EE showed the maximum motor and cognitive improvement compared to early, delayed EE, and Sham conditions.

Thus, the therapeutic effects, underlying mechanisms, and neuroplastic principles of EE based animal models support a significant role of EE in human ABI rehabilitation[214].

2.5 Environmental Enrichment in adult humans

2.5.1 EE in healthy adult humans

Despite decades of consistently showing positive effects in animals, EE has not been as widely studied in adult humans [237]. The influence of environmental factors in healthy adults has primarily focused on studies looking at the impact of the environment on cognitive decline, being physically active, improve socialization within the community, and decrease incidence or onset of dementia. [238]– [240]. In the section below, the influence of various environmental factors on cognitive, motor

and social performance in healthy humans is discussed. This is followed by details on the neuroplastic and neuroprotective effects of EE in brain-injured humans.

Physical Enrichment affects motor and cognitive domains of healthy humans. In general, older individuals display a decrease in muscle strength, slow movements, difficulty with balance, slow processing speed, memory loss, and altered gait pattern compared to young adults. This decline is known to have a negative impact on their community life and increase the incidence of falls[241]. Physical exercise as enrichment positively impacts both brain and body in healthy and aging humans. For example, physical exercise and maintaining an ‘active lifestyle’ is associated with an increase in “cognitive reserve”, balance, coordination, longevity, flexibility, bone strength, density, better functional outcomes, and a decrease in risk of cardiovascular and metabolic conditions, incidence of falls and frailty (Figure 13) [242]–[246].

Cognitive Enrichment affects cognitive ability of healthy adult humans. Aging is associated with a decrease in attention, memory, learning, processing speed, language, visuospatial tasks, and problem-solving [239]. Cognitive reserve is related to a high level of cognitive functioning and performance of complex activities[187]. For example, the increased cognitive reserve is strongly associated with an ‘active lifestyle,’ cognitively challenging tasks like puzzles, community games like chess, participating in leisure activities, and socializing [247], [248].

Social Enrichment also impacts healthy adult humans. A metanalysis on the effects of social isolation on mortality indicates the importance of social relationships for survival[249]. Social engagement is known to decrease with aging typically. Social isolation leads to an increase in frailty, loneliness, cognitive decline and a decrease in functional activities[250]–[252]. Conversely, studies on social support have shown an

increase in cognitive functioning, satisfaction with life, daily functioning, and a decrease in dementia, stress and negative emotions[240], [253], [254].

Molecular and Morphological changes: EE improves brain function at the molecular and morphological level in healthy adult humans. Physical activity and exercise are associated with an increase in synaptic density, anterior hippocampal volume, BDNF, neurogenesis, grey and white matter volume, improved vascularization and blood flow to the brain, decreased atrophy, and increased functional connectivity[44], [241], [255], [256]. The specific mechanisms of participation and socialization are related to cognitive skills is still unclear[44]. Based on aging animals, complex activities such as multitasking, participating in challenging tasks are associated with increased brain volume, neural growth, and increase in dendrite formation[194], [196], [257]. ***Hence, maintaining an ‘active lifestyle,’ performing complex tasks, and socialization appears to be essential to decrease age-related structural and functional changes in healthy humans.***

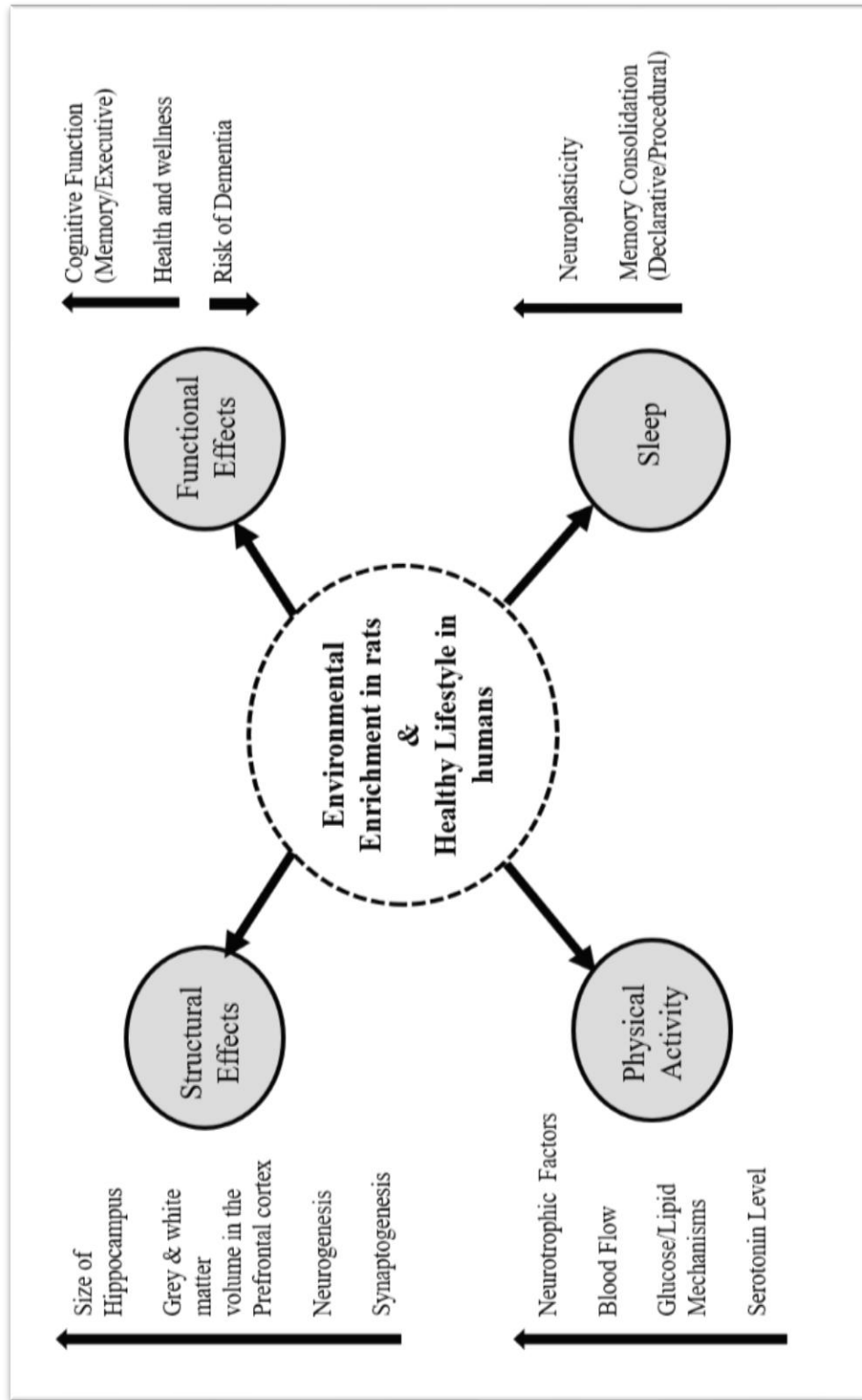


Figure 13 Common changes seen in healthy animals and humans with active lifestyles when exposed to Environmental Enrichment (EE). Adapted from Mandolesi et al., 2017[191]

2.5.2 EE in brain-injured adult humans

The primary objective of this dissertation is to advance the study of the relatively new field of EE in human rehabilitation. Adult neurorehabilitation studies in humans often consider “traditional rehabilitation” as EE through 1) increasing activity levels, intensity, and duration of therapy and 2) providing treatment to improve task-specific skills[237]. Although rehabilitation does not match the operational definitions of EE in animal work, it represents the basis for the current standards of clinical care from which to compare any new intervention. **Below, current literature on different types of EE for ABI adult humans is discussed.**

Physical EE improves motor learning in ABI humans. Some of the common physical impairments due to ABI are spasticity, ataxia, loss of balance, inability to walk, muscle weakness, impaired coordination and loss of fine motor function. Physical EE studies are almost exclusively conducted within a hospital or clinical setting. For example, a physical EE study on in-patient stroke participants has reported the ability to predict long-term function and walking ability based on functional status[106]. Another physical EE study reported that higher intensity of exercise dosage (increase in repetitions) in the first-week post-stroke was associated with faster walking speed and decreased dependence on assistive devices at discharge[258]. In a meta-analysis, effects of increasing exercise therapy time were measured stroke participants. Results indicated that a minimum of 16 hours of additional therapy within the first six months of stroke could increase walking speed as compared to standard treatment [259].

Cognitive EE improves specific executive abilities in ABI humans. Common cognitive impairments post-ABI include impaired attention, memory, processing speed, decision making, judgment, reaction time. Cognitive rehabilitation programs

are provided in a hospital, outpatient and also at home. For example, a cognitive EE study compared the effects of an Intensive Cognitive Rehabilitation Program (ICRP) with Standard Rehabilitation Program (SRP). Better outcomes were reported in the ICRP group who exhibited significant improvement in attention, processing speed, immediate recall, and better community integration[260]. Furthermore, home-based cognitive EE studies have demonstrated an increase in attention and memory through learning strategies[261].

Social EE improves community integration in ABI humans. Common social impairments after ABI are lack of awareness, decrease cognition, loss of emotional and behavioral control and language deficits[262]. Inappropriate behavior, lack of emotional control and self-awareness, language deficits and motor and cognitive deficits prevent return to work, increase social withdrawal, and social isolation[263]. Studies on the effectiveness of training social communication skills in ABI have demonstrated better community integration and satisfaction with life[264], [265].

Why is traditional therapy as EE a cause of concern in human ABI? Skills gained in an EE environment decrease when animals are transferred to an impoverished environment[266]. Insight from EE animal models has highlighted the dangerous reversal effects of EE on learning and memory[266]–[268]. Similarly, in ABI, a discharge or decrease from therapy (EE), has been associated with a reduction in cognitive and physical function[150], [269]. Therefore, applying the same EE principles to human ABI models raises concerns.

“Negative brain plasticity” refers to negative learning, decreased activity levels, and disuse of cognitive skills or motor function triggering a cascade of changes

causing a downward spiral of decline[237]. While therapy is considered a form of EE in humans, it is not “real world enriched,” i.e., it does not provide maximum global stimulation one would typically have in their real-life setting at home and the community. This is a significant cause of concern since most individuals with ABI have long-term deficits that prevent a return to work, social isolation, and interdependence on family and friends for ADL.

Therefore, in ABI adult humans, the application of continuous and long-term generic EE involving social, physical, and cognitive EE would be predicted to be essential to maintain and improve functional deficits. *Below, we discuss the use of EE for decreasing post-traumatic cognitive and physical decline in brain-injured adult humans.*

2.6 Protocol for the Go Baby Go Café (BWSS + EE) Study

The first objective is to provide detailed procedures for conducting a Go Baby Go Café Feasibility Study (Figure 14). We hypothesize that recruitment, attendance, adherence, attrition, participant satisfaction and ease of testing/using outcome measures will be feasible.

The second objective is to determine the safety of the novel BWSS and the ABI participants in the new EE. We hypothesize that the BWSS and the participants will be safe during the study. Specifically, we expect the BWSS to facilitate mobility and prevent falls without any adverse events. We also anticipate the BWSS itself and the Café environment, in general, will be safe for ABI participants.

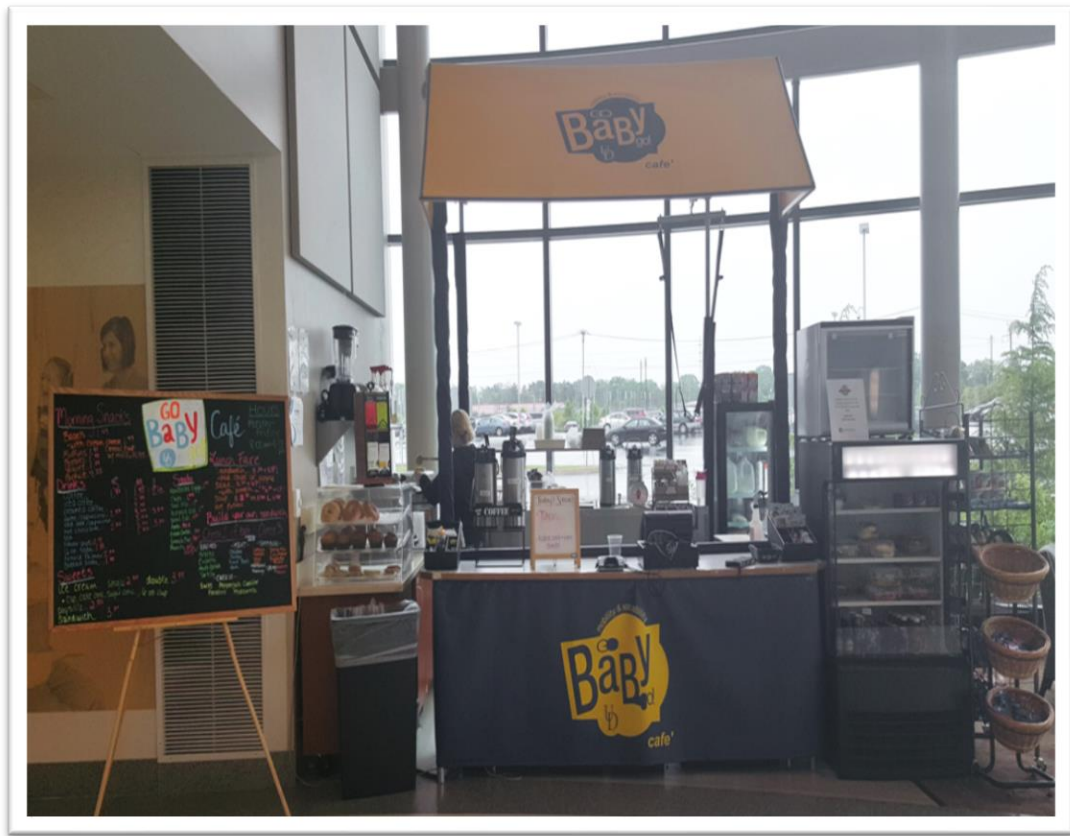


Figure 14 Go Baby Go Café (EE + novel BWSS) located in the atrium of STAR Health Science Complex.

2.7 Investigational Plan

2.7.1 Participants

Individuals with a diagnosis of moderate to severe ABI may be eligible to participate in the study. The rationale for selecting ABI in general and stroke and TBI is explicitly due to the a) long-term global deficits across cognitive, physical, and social domains, b) significant prevalence in the US and abroad and c) that both involve adults of working age such that deficits persist for decades post-event.

All participants will be screened for eligibility based on the Inclusion and Exclusion Criteria (Table 1). Feasibility and Pilot studies do not require a sample size calculation. Hence, different factors were considered before anticipating a recruitment size of 10 - 15 individuals with ABI (See section 2.8.3).

2.7.2 The inclusion of Women and Minorities

According to section 492B of the Public Health Service Act in conjunction with NIH guidelines, recruitment and inclusion of women and children, racial and ethnic minorities are highly recommended in clinical trials. This increases gender parity and diversity of individuals from different cultural and racial backgrounds. Recruitment targets are 55% females, 90% Caucasians with 8% African Americans and 2% from other races as per census data on Newark, Delaware [270].

Table 1 Inclusion and Exclusion Criteria for the Go Baby Go Café Trial

Inclusion Criteria	Exclusion Criteria
Age 21-85 years old	Unable to stand or walk
Diagnosed of a moderate to severe ABI by a physician based on hospital/clinical reports (GSC score <12, NIHSS >16)	Unable to communicate with others
Willing and able to attend all sessions and to provide informed consent	Cognitive impairment that limits the ability to provide informed consent (based on MOCA scores (>21/30))
Individuals requiring moderate to maximal assistance with most ADL	Active cancer or currently undergoing cancer treatment
	Cardiac event or cardiac surgery in the past three months
	Current participation in PT, OT or SLP

2.7.3 Recruitment

Participants will be recruited via local clinical facilities, media, physicians, support groups, fliers, and through generic advertisements for the Delaware Rehabilitation Institute. They will be contacted via phone to determine the type of ABI, time since injury, and if they reside within the tri-state area to commute for the feasibility trial.

2.7.4 Screening and Testing

An in-person interview will be conducted at the STAR Health Science Complex at the University of Delaware. Study objectives, procedures, and the intervention (dosage, EE setting, and assessments) will be explained in detail. If the participant is still willing to participate, a written consent approved by the Institutional Review Board (IRB) of the University of Delaware will be obtained. (Appendix L, Appendix M). Then, a final eligibility test using the Montreal Cognitive Assessment Scale (MOCA, see below for details on the MOCA) will be used to determine the level of cognitive impairment. Participants with a score below 21 out of 30 would not qualify for the study due to safety concerns (Table 1).

2.7.5 Duration of study participation

The total length for study participation from screening to completion of the 2-month study would be approximately two and a half to three months.

2.7.6 Choosing a research design

In many clinical fields, Randomized Controlled Trials (RCT) are often considered gold standard in clinical trials[271]. RCT's are typically costly, time-consuming, a high level of workload for the lead research team and require a high

number of participants[272], [273]. The café intervention has multiple novel elements and limited funding. Thus, an initial small sample study focused on feasibility and safety was needed to provide information to determine whether a formal pilot study was warranted.

Small sample designs have four advantages compared to RCT. First, small sample designs do not require a control group as compared to an RCT. Second, small sample designs allow for revisions of the intervention compared to RCT's, which have more protocol constraints. Third, small sample designs guide researchers on the interventions use since it is tailored to each participant. Fourth, they require fewer resources and shorter timeframe. These factors, together, help in establishing the foundation for evidence-based practice[271], [274].

Small sample research designs are also known by other names such as single case design, single subject research design, N of 1 trial and single systems design. In these designs, each subject serves as their control. However, researchers can control the influence of the treatment within the constraints of the design. *Below, different design types with a short description on their a) structure, b) purpose, c) advantages, d) disadvantages, e) reason for selection or not being selected for the feasibility study are given(Figure 15) [274].*

1) Withdrawal Designs (ABA or ABAB):

Consists of a Baseline Phase “A” followed by an Intervention Phase “B.” Removal of the intervention results in a second baseline period (ABA) which may be followed by reintroducing the intervention (ABAB) to illustrate experimental control.

This design methodology is primarily used to test the outcome of a study by adding and removing the influencing factor at certain intervals of the study.

Advantages: This study design demonstrates a high level of experimental control.

Disadvantages: Study design assumes that the intervention is reversible, i.e., on the removal of the intervention, the participant will go back to their baseline. Also, it often causes an ethical dilemma in case the intervention is effective.

The decision for the feasibility study: This study design was rejected since there is no previous literature in humans to test the effects of EE. Due to not knowing the reversible effects of the EE paradigm, this design was ruled out.

2) Multiple Baseline Design:

Comprise of many “AB designs stacked over each other.” They are used to determine the effects of a single intervention on three or more individuals, setting, and so forth. Experimental control can be obtained by introducing the intervention in a staggered fashion, i.e., the baseline period for all individuals begins at the same time. However, intervention is introduced at different points in time.

Advantages: Design does not require the withdrawal of the intervention and is suitable for interventions that are not reversible.

Disadvantage: Can be unethical if some individuals have a more extended baseline compared to others.

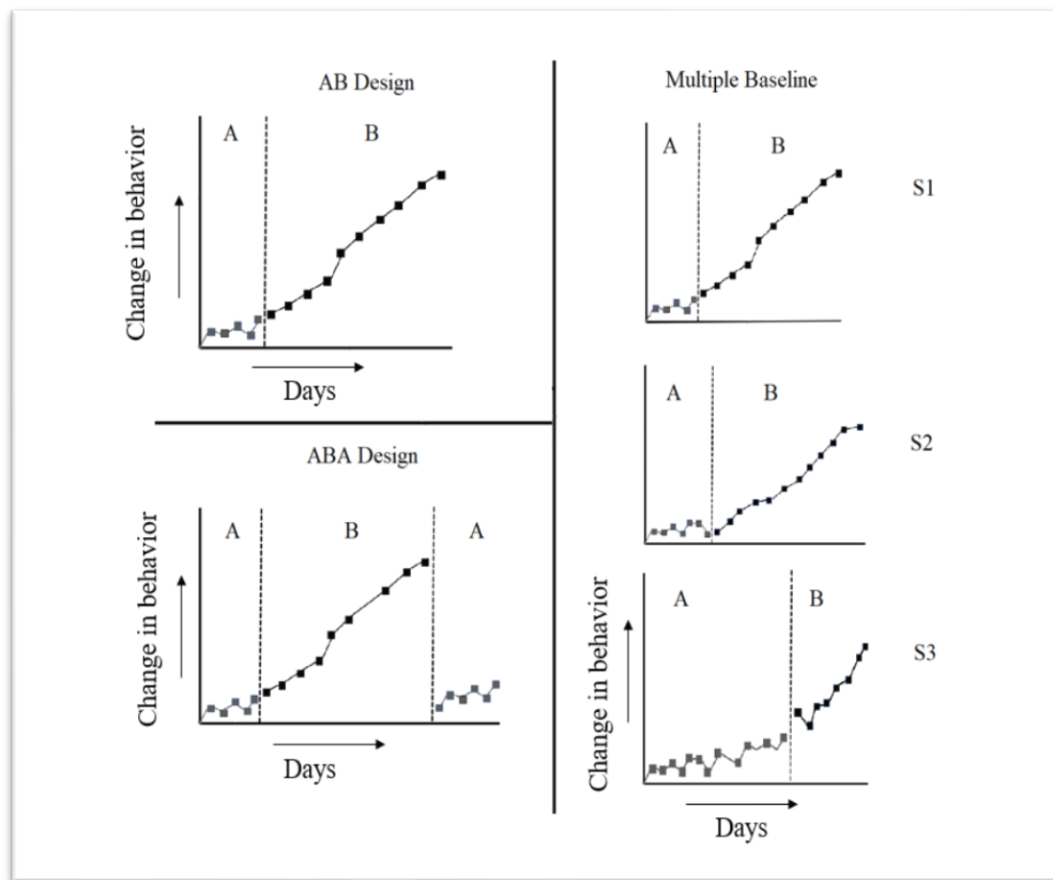


Figure 15 Different types of single-subject research design. Hypothetic data is used to show Baseline (A) and Intervention (B) for AB, ABA (withdrawal design), and Multiple baselines for different subjects starting at the same time but having different lengths of baseline

The decision for feasibility study: This study design was rejected since multiple participants were not anticipated to begin the study simultaneously.

3) Changing Criterion Design:

Considered as a variant of Multiple Baseline, each phase serves as a new baseline for the next phase. These designs are used to determine the effect of an intervention on the dependent variable. Unlike withdrawal where large immediate

changes are expected, this design is useful when the result is gradual. Thus, when the rate of behavior changes with each change in the criterion, experimental control can be obtained.

Advantages: Does not require the withdrawal of intervention and can be useful for interventions which show gradual change.

Disadvantages: Requires a consequence- based intervention, i.e., there is a reinforcement depending on the participant reaching a predefined criterion. Cannot expect substantial immediate changes in the dependent variable.

The decision for feasibility study: This study design was rejected since there is no literature yet on the gradual, substantial or immediate effects of EE in humans.

4) AB design/Preclinical

Consists of a Baseline Phase “A” followed by an Intervention Phase “B.” It is typically referred to as a pre-clinical design since it does not account for experimental control. Usually, multiple baseline measures help determine the current level of performance of individuals.

Advantages: Easy to use, especially when outcomes are unknown.

Disadvantages: It is not an exact experimental design since it does not account for internal validity. Hence, it cannot be used to determine a cause and effect relationship.

The AB design was selected as the feasibility study design since it was the most optimal option with the available funding, timeframe of the trial, and available resources for the initial feasibility study.

2.7.7 Dosage

Animal studies have suggested that the impact of the exposure to EE is not linearly dosed dependent. That is, the dose-effect relationship is complex and influenced by different factors including optimal dosage to expect recovery. Well et al. conducted a study to determine the effects of abbreviated and continuous EE in TBI induced rats. Rats were assigned to TBI + continuous EE, TBI + 2-hour EE, TBI + 4-hour EE, TBI + 6-hour EE, TBI + Standard Housing Condition (SHC) or sham group. Morris Water Maze Task was used to assess cognition, and the beam balance/beam walk test was used to determine changes in motor ability immediately post-surgery (day 1 – 5) and later in recovery (14 – 19 day).

TBI + 6-hour EE exposed rats not only performed significantly better than 2 and 4-hour EE groups but also, gave similar benefits as the TBI + continuous EE group. Interestingly, the 2 and 4-hour EE group did not demonstrate any significant difference from the SHC group[275]. These results suggest that bouts of at least several hours may be required to show meaningful changes in cognition and physical function post-ABI.

There is growing literature in humans to suggest a higher dosage leads to more significant improvement in functional outcomes of ABI population[276], [277]. Typically, the dosage in human rehabilitation is established by the frequency and duration of sessions for an intervention. Additionally, factors such as task specificity, variation in intensity tolerance, the actual time spent on therapy in clinical practice, and duration of treatment significantly affect rehabilitation outcomes in individuals with ABI [8]. *However, there is little data to support appropriate timing and optimal dosage during different stages of rehabilitation.*

The intensity of therapy at different stages of recovery may also be an essential factor in neurorehabilitation. High intensity during *early* rehabilitation in animal models has resulted in adverse outcomes compared to *delayed* therapy[278]. In the same way, studies such as the AVERT trial on human stroke participants suggests there may be a detrimental effect of higher dosage with *early* mobilization on functional recovery three months post injury[279]. *Therefore, there is no firm consensus on the time and dosage standardized for optimal recovery of individuals with ABI.*

Based on the effects of timing and intensity of dose on rehabilitation, it was decided to conduct the feasibility trial for three 2-hour sessions per week for a total duration of two months. While the primary objective is not to determine changes in clinical outcome measures over time, *an estimated dosage of 6 hours of Café exposure for two months was thought to be sufficient to assess feasibility and safety, as well as obtain to enough data for an effect size estimate.*

2.8 Study Assessments

2.8.1 Medical Records

Participants selected for the study based on the inclusion/exclusion criteria would be asked for their medical records for confirmation of a diagnosis of a moderate to severe ABI. This data would include their hospital admission sheet and discharge summary from their rehabilitation centers. Additionally, participants would also be asked to fill a Medical Health History form (Appendix A) and provide a list of current medications. This would ensure the investigator is updated on the participant's medical history and can take due action in case necessary.

2.8.2 Feasibility Outcome Measures

Outcome measures would be collected to determine the feasibility and potential risk factors which can compromise the safety of the participant, investigator and café employees for future trials (Table 2)

1) Recruitment and retention of participants are a vital aspect of any clinical study.

Current guidelines for minimal sample size in feasibility trials is unclear.

However, pilot studies which are conducted following a feasibility trial have reported findings with a range from 12 - 30 subjects in each arm. Since feasibility studies are performed before pilot studies, an estimated sample size of 10-15 participants was used to determine the feasibility of the Café study. Below, five factors are highlighted that influenced the small size for the feasibility study (Chapter 3)

i) Duration of project funding was for three years. An anticipated rate of five participants per year was thought to be feasible given that there were one PI and one research therapist working on the study.

ii) Total duration for each participant from screening to completion of the study was three months. As the Café was located in a University setting, allotted federal and winter holidays required the café to be closed.

Therefore, 5 participants per year with partial or complete overlap during a specific duration was anticipated to be sufficient within the time constraints.

iii) Published literature on feasibility studies with similar dosage and duration have typically recruited 10 – 15 participants.

iv) Given the limited funding, participant transportation and an honorarium were not included. These are common incentives which typically help

recruitment. This was taken into consideration while determining the sample size number.

- v) The idea of placing a new BWSS in a community-based EE is a novel concept based on animal literature. Previous EE studies in humans have typically looked at providing therapy in an enriched environment. Since the study measured feasibility, a sample size of 10-15 was thought to be sufficient to establish safety, attendance to the novel intervention, adherence, and acceptance by the participants.

Attendance: Each participant will be asked to attend training sessions in the Café three times a week for two months. The on-site researcher will note attendance and reasons for missing sessions for each of the participants. Participants rescheduling a session will not be considered absent. Participant canceling the second scheduled session will be considered absent. A cut off criteria of 80% for each participant would determine the feasibility of attending the intervention.

Adherence: Adherence is defined as the time spent working in the harness in the Café during each 2-hour session. Specifically, it is the total time spent working in the café minus the duration of rest breaks taken during each two-hour session. The research therapist would also enter additional notes on performance. A cut off criteria of 75% adherence for each participant would determine its feasibility.

Attrition: Attrition is the percentage of participants who did not complete the study. Attrition is typical in clinical trials due to a range of factors such as lack of

interest, transportation, and other health-related problems. For the feasibility study, attrition will be determined by the number of participants who dropped out at any point during the 2-month study and did not complete the evaluations every two weeks and could not be contacted after signing of the consent form. A drop-out rate of 20% and below will be considered feasible for the study based on a common drop-out rate used for feasibility and clinical trials.

Safety: There are two categories of safety that are important for this protocol. *The on-site research therapist will note the safety of the participant, coworkers, and public* during each training session in the Go Baby Go Café. Since each training session is 2 hours, participant safety will be determined by the following criteria 1) No dizziness or syncope 2) severe muscle soreness lasting more than 48 hours 3) fatigue causing early retirement from the training session and 4) serious adverse event or injury requiring immediate medical attention as reported by the participants. *BWSS safety* was determined by any adverse event caused by the equipment resulting in harm/injury to the participant, the researcher or the Café employees.

Acceptance: Acceptance of the novel intervention will be determined through participants' answers to a short self-constructed survey form upon completion of the 2-month intervention study (Appendix P). The questionnaire consists of a visual analog scale from 0 (very negative experience) to 10 (very positive experience).

Table 2 Feasibility measures with cut off criteria and rationale for selection

Feasibility Measure	Cut Off Criteria	Rationale
Recruitment	N = 10 - 15	Based on small-scale feasibility studies with comparable dosage [280]–[284], Internal and External Factors
Attendance	>80 (16/20 sessions)	Based on feasibility literature [285], [286]
Adherence	>75%	Based on feasibility protocols [285], [287]–[289]
Attrition	<20% drop out	Based on feasibility protocols and trials [285], [290], [291]
Safety		Reports on adverse events
Acceptance	>70%	Estimated criteria determined by investigators based on the study environment

Participants will be asked to rate their level of satisfaction, opinion on the novel approach, and if they would consider continuing to volunteer in the café. Since the café is the first of its kind, changes were not guaranteed. However, given the location of the café in a real-world community setting, it was anticipated that the participants would enjoy an increase in engagement with customers while performing goal-oriented tasks. Hence, a 70% cut off criteria was used.

2.8.3 Clinical Outcome Measures

Theoretical and empirical literature relevant to the use of EE in animals and humans suggested the Café has the potential to impact many physical and psychological aspects of ABI positively. The choice of which physical and psychological domains, as well as the specific measures within those domains, were based on three separate yet interconnecting factors:

- a) Comprehensiveness, such that a range of domains are included,
- b) Feasible, both regarding research resources (examples: study duration and funding) and participants resources (example: time, energy, attention/focus) and
- c) The necessity for a clinical trial based on the outcomes of the feasibility study

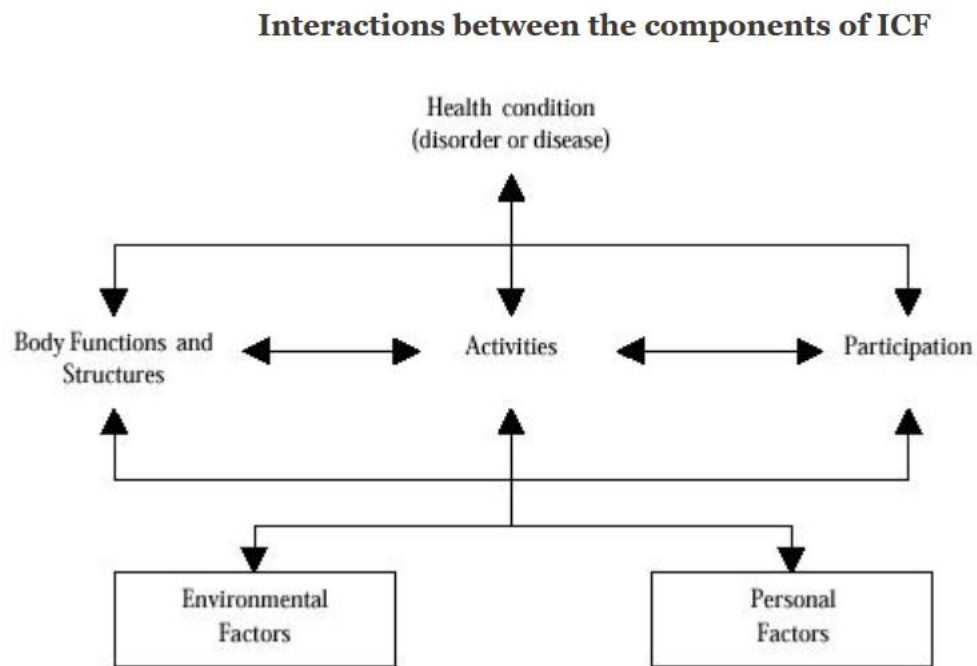


Figure 16 World Health Organization's International Classification of Functioning, Disability, and Health (2010)

The International Classification of Functioning, Disability, and Health (ICF) Model was used to determine the categories from which a comprehensive set of outcome measures were selected. The ICF framework developed by the World Health Organization is organized into two major components: Functioning and Disability and

Contextual Factors(Figure 16)[292]. Functioning and Disability includes Body structure and function, Activity, and Participation. Contextual Factors consist of Personal and Environmental factors. An individual's functioning is conceptualized as the interaction between the health condition and the contextual factors. Therefore, the ICF framework is commonly used to classify various assessment scales and assist with developing functional rehabilitation goals for different populations[293], [294].

Clinical outcome measures selected for the feasibility study are discussed below (Appendix B – K) with a summary on a) description of test b) what it measures c) how is it performed d) psychometric properties in ABI population e) limitations and f) rationale for selection or elimination from feasibility trial.

** Denotes selected for the Protocol

*** Denotes measures rejected for the Protocol

Body structure and function

The ICF defines body structure and function as anatomical parts of the body such as organs, limbs and their components, and body function as physiological functions of the body systems[295]. The literature on brain-injured animal models have demonstrated exposure to EE is associated with an increase in cognitive skills and ability. Based on animal models, the effects of complex cognitive environments have also been recommended for ABI rehabilitation[296]. *It was anticipated that working in the Café may result in cognitive changes over time due to the performance of various functional tasks in an enriched real-world environment. Hence, measures to detect changes in cognitive abilities were reviewed.*

Montreal Cognitive Assessment Scale (MOCA)**

Common, short screening scale used to detect cognitive impairment[297]. The assessment scale comprises of different cognitive domains such as visuospatial/executive, naming, language, memory, attention, concentration, delayed recall, and orientation. Individuals are scored based on the correct response with a total score of 30. Higher scores are associated with better cognitive ability. A score of 26 and above is considered normal. MOCA has strong reliability and validity in mild to moderate Stroke[298]. Higher scores have also been associated with better functional outcomes for subacute stroke patients[299]. In TBI, MOCA has good validity, high sensitivity, and can be used as a spot screening tool for determining global cognitive impairments [300], [301].

Trail Making Tests (TMT A and B) **

The common neuropsychological assessment used to assess cognitive functions such as attention, visual scanning, mental flexibility and set shifting. [297], [302]TMT tasks are to be completed as quickly and accurately as possible. TMT - A consists of 1-25 randomly scattered circled numbers, which should be connected through lines in ascending order. Primary cognitive measures tested by TMT A include motor speed, attention, and visual-perceptual tracking[303]. TMT – B comprises of 1-13 encircled numbers and letters A – L. The person connects these circles by alternating between the number and a letter. TMT B is more comprehensive and often considered a test to measure executive functions. In addition to all cognitive measures assessed by TMT A, the TMT B also measures task switching, divided attention, and reading skills[303], [304]. Performance for both TMT's is assessed by the time taken to complete each test. Higher scores are suggestive of more significant

cognitive deficits[305]. Normative data demographically adjusted for different age groups are available for both TMT A and B[306]. TMT A and B have low to moderate reliability in Stroke due to variability over time and across populations[307] [308]. However, TMT B has strong predictive validity in stroke and TBI[309]–[311]. TMT is known to report higher sensitivity in TBI with a strong dose-response relationship as compared to stroke[312], [313].

Limitations: Despite reports of high variability across age, IQ, demographics TMT A, and B were selected as it provides a quick screening of global cognitive impairments. [314], (Appendix C).

Activity Measures:

The ICF describes activity as the execution of a task or action by the individual and activity limitation as for the difficulties an individual might have while executing activities[292]. Physical activity such as ADL and exercise are known to improve motor and cognitive deficits in brain-injured and healthy animals. Similarly, the effects of an active lifestyle in healthy humans have been established[248]. Being physically active is known to have neuroplastic effects post-ABI [259]. The Café intervention would require the person to stand, balance and multitask while making salads, drinks, and sandwiches for a total of 40 hours over two months. Therefore, *it was anticipated that working in the Café may result in fine and gross motor function measures. Hence, measures to detect changes in gross and fine motor function were reviewed.*

6-minute walk test (6MWT) **

Common research and a clinical measure of submaximal assessment of aerobic capacity[315], [316]. The task is to cover as much distance as possible in 6 minutes. The total distance walked is measured using a stopwatch and GAITRite, using a measuring wheel or markings on the floor. This measure has good reliability in stroke [317] and excellent test-retest reliability in ABI[318]. Limitation: Is not tested on individuals who require physical assistance to walk. This is included in the final list of OM's due to strong psychometric properties in different neurological populations, and its clinical usefulness[174], [319]–[321](Appendix D).

10 Meter Walk Test (10 MWT) **

Common research and a clinical measure of gait speed[322]. The task is to walk for 10 meters with the middle 6 meters being timed. The remaining 2 meters on either side is to account for acceleration and deceleration of the person's walking speed. Two speeds are recorded– i) self-selected and ii) fast walking speed. Three trials are conducted at each speed. It has excellent test-retest intrarater (ICC =0.87) and interrater (ICC = 0.99) reliability in stroke population [323] and excellent test-retest inter-rater reliability in TBI (ICC=0.99)[318]. Limitation: Is not tested on individuals who require physical assistance to walk. This is included in the final OM list due to strong psychometric properties in different neurological populations[324]–[327](Appendix E).

Timed Up and Go (TUG), TUG Manual and TUG Cognitive**

Common research and a clinical measure of mobility, static and dynamic balance, and to differentiate fallers from non- fallers[328], [329]. The test measures the total time taken to get up from an armchair, walk 3 meters, turns around and sit down in the same chair. Two extensions of the TUG, the TUG Manual (Man) and TUG Cognitive (Cog) together these are called TUG – Dual Task (DT). These two tests consist of performing the original TUG task plus either carrying a glass full of water (Man) or counting backward in 3's from 100 (Cog)[330]. The purpose of this revised test is to assess the dual task ability of the individual. The TUG test has excellent test-retest reliability ($ICC=0.86$) in TBI children and adolescents[331]. It has excellent interrater ($ICC= 0.99$) and intra rater ($ICC = 0.99$) reliability [332] and validity [333], [334] in stroke population. Limitation: The TUG and TUG DT has not been validated in TBI population. These measures are included in the final list of OM's due to strong psychometric properties in the ABI population (Appendix F).

Jebsen Hand Function Test (JHFT)**

Common research and a clinical measure of hand function during activities of daily living [335], [336]. JHFT consists of 7 timed subtests performed first with the least or unaffected arm followed by the affected arm. The seven subtests include writing a 24-letter sentence, turning 3 X 5" cards, simulating feeding using five kidney beans and a teaspoon, picking small objects, stacking checkers, and lifting large, light and heavyweight objects. Total time for performance of tasks by each arm is recorded. It has moderate to excellent inter and intra rater reliability in stroke population for different subtasks[337]. Limitation: It has not been validated or has established

reliability in TBI population. This is included in the final OM's due to its high use in clinical and research practice [178], [338], [339] and since it is subtasks represent activities of daily living – ideal for the Café intervention(Appendix G).

Four Square Step Test (FSST) **

Common research and a clinical measure of dynamic balance and separate fallers from non-fallers[340]. The test consists of four single-point canes placed at 90 with their ends touching each other. The person starts from one square and moves forward and follows a clockwise pattern in the four squares followed by counterclockwise direction until they return to the original position. A variation of the FSST uses tape instead of canes. Three trials are taken with the best time taken for the final score. It has good intra-rater reliability (ICC = 0.82) and excellent inter-rater reliability (ICC = 0.99) in stroke population[341]. Limitation: It has not been validated or established reliability in the TBI population. This OM is selected for the trial since it requires movement in different directions (Appendix J).

Functional Gait Assessment (FGA)**

Common research and clinical measure, the FGA is a modification of the Dynamic Gait Index, this test measures the stability of posture during different walking tasks[342], [343]. The person is asked to perform each walking task and rated on a scale from 0 (severe impairment) to 3 (normal ambulation). There are ten tasks with a total score of 30. It has excellent test-retest intra-rater (ICC =0.97) and interrater (ICC = 0.94) reliability in stroke population with excellent convergent and construct validity in stroke population [344], [345]. Limitation: It has not been

validated or established reliability in the TBI population. This OM is selected for the trial since it looks at different aspects of walking (Appendix I).

Nine Hole Peg Test ***

Common clinical and research instrument used to measure manual dexterity of the hand being evaluated[346], [347]. Participant is asked to lift one peg at a time from a container and insert them into the holes on the board as fast as possible; once all are inserted, they remove each peg and put it back into the container. Total time taken is recorded as the final score. It has adequate to excellent intra rater ($r = 0.68 - 0.99$) and interrater ($r = 0.75 - 0.99$) reliability, excellent validity, and moderate responsiveness in stroke population[348]–[350]. Limitation: It has not been validated or established reliability in the TBI population. This was not selected for the final list of OM's since it was not a functional test and doesn't mimic tasks specific to activities of daily living.

Box and Block Test ***

Commonly used measure to assess gross unilateral manual dexterity [351]. Tests consist of a rectangular board divided into two with a partition. 150 cubes (2.5 centimeters each side) is placed into one compartment. Participant is asked to transfer as many cubes in 1 minute over the partition into the adjacent compartment. Scoring is based on a total number of blocks transferred with higher scores indicating better gross manual dexterity. It has excellent test-retest reliability for the more affected arm ($r = 0.98$) and concurrent validity in stroke population[348], [350]. Limitation: It has not been validated or established reliability in the TBI population. This was not selected

for the final list of OM's since it was not a functional test and doesn't mimic tasks specific to activities of daily living.

Action Research Arm Test (ARAT)**

An assessment of arm function, dexterity, and coordination, the ARAT measures four subscales of grasp, grip, pinch and gross movement [352]. 19 different observer-rated tasks are performed with various sized objects with a total score of 57. Performance is rated on a 4-point scale ranging from performing the task normally to unable to perform or complete the entire task. Total time required to complete the test is 10 minutes. It has excellent test-retest intra rater (ICC =0.98) and interrater (ICC = 0.99) reliability and validity in stroke population [353], [354]. Limitation: It has not been validated or established reliability in the TBI population. This OM is selected for the study to determine changes in hand function (Appendix H).

Participation Measures

The ICF defines participation as involvement in a life situation and participation restriction as the problems one might experience during community engagement [292]. Based on ICF recommendations, participation measures most commonly used in physical therapy neurorehabilitation are described below.

Functional Independence Measure (FIM) ***

A measure used to determine patient disability and amount of assistance required to carry out activities of daily living[355], [356]. It consists of 18 tasks (13 motor and five cognitive) of different activities. Participant is scored on a 7-point

ordinal scale from complete dependence to complete independence. It has excellent internal consistency and validity in stroke patients [357]. It also has excellent inter-rater reliability (ICC = 0.85) but limited content validity in TBI[358], [359].

Limitation: It has high ceiling effects, and hence this OM was not taken[360].

Functional Assessment Measure (FAM)***

Developed as an adjunct to the FIM to address areas not previously covered in communication, cognition, behavioral and community-based questions. It consists of 12 questions that are added to the FIM. Together is commonly done as FIM + FAM. Participant is scored on a 7-point ordinal scale from complete dependence to complete independence. It has excellent reliability, validity and internal consistency in the TBI population[358], [361]. Limitation: It has high ceiling effects, and hence this OM was not taken[360].

Community Integration Questionnaire ***

The assessment used to determine limitations in social roles and community integration in the ABI population[362]. It consists of 15 questions covering three major domains – home integration, social integration, and productive activity. The participants rate their community integration on a score from 0 to 2 with higher scores indicating greater integration and independence. Total score possible is 29. It has excellent test-retest reliability (ICC= 0.93) and internal consistency and validity in TBI [363], [364]. Limitation: It has high ceiling effects, and hence this OM was not taken[360].

A significant drawback of the above measures was the absence of reporting the level of satisfaction and engagement fundamental to the posed research question. The above measures defined participation based on performance alone[365]. This raised several concerns since participation varies across individuals and different age groups. Therefore, a participation measure must not only reflect performance but also, the satisfaction and sense of accomplishment an individual gets from social activities and maintaining relationships in the community[366].

Everything considered, the Café intervention was based on the concept of i) encouraging social participation with café employees and customers, ii) increasing engagement with work-related activities such as preparing meals and trying new recipes, and iii) providing some level of satisfaction through customer tips or preparing a meal without assistance. Hence, a broader review of the literature on participation measures was conducted. Ultimately, Health-Related Quality of Life (HR- QOL) measures were considered as they capture multidimensional aspects of a person's QOL.

For example, Trudy et al., have described participation as the intersection of what the person wants to do, can do, and has the chance to do without any limitation in the community[367]. Therefore, participation not only takes different forms of social activities and social relationships in society but also portrays means through which the individual can engage in the community regardless of their disability [367]. With advancement in conceptualization and implementation of new measures, psychometric models are becoming very common to grade a person's HR-QOL[366]. **Given the potential effects (physical, mental and social) that were anticipated from the Café's EE, the Neuro - QOL measure was selected. The Neuro-QOL not only**

comprises of health-related physical and mental domains but also measures their influence on the individual's ability to participate and amount of satisfaction with personal and social relationships within the community.

Neuro QOL **

Is a set of self-report questionnaires used to assess HR-QOL in pediatric and adult neurological populations (Appendix K). Sponsored by the NINDS, it has strong psychometric properties in adults with Stroke, Multiple Sclerosis, Parkinson's disease, Epilepsy, and Muscular Dystrophy.[368] The Neuro- QOL comprises of three primary health measures: physical, mental and social with 17 HR QOL domains. Test administration can be done by computerized adapted tests or short forms selected from the available item banks. Short forms typically have 5 - 9 questions per item bank[368]–[370].

Most item bank questions begin by asking the individual to recall their experience in the “last seven days.” Answers are based on a scale with five possible options ranging from “not at all” to “very much” or “never” to “always.” Scoring of Neuro-QOL test can be done through the assessment center (computerized adaptive test) or summing the numbers below each response for all questions of a specific short form.

Scores are converted into an IRT based T scores readily available in the manual. The T score represents standardized scores with a mean of 50 and a standard deviation of 10. Therefore, a score of 60 or 40 (10) deviations from mean indicative of the individual being one standard deviation above or below the mean of the US general or clinical population for the specific item bank[368].

Below, item banks (dependent variables) suitable to the objective of the study are provided with the accompanying rationale for inclusion.

Physical Health: Short Forms of Upper Extremity (UE) and Lower Extremity (LE) function, Fatigue, and Sleep disturbance were selected for the feasibility trial. It was anticipated that working in the Café would require preparation of different meals (Upper Extremity function), continuous standing and maintaining balance (lower extremity function). Subsequently, the intense physical activity for otherwise sedentary individuals may increase fatigue leading to longer and better sleep durations. As a result, changes observed by the individual may result in a positive response by them over time.

Mental Health: Short forms of Anxiety, Depression, Stigma, Emotional and Behavioral Control, Positive Affect, and Well-Being were selected for the feasibility trial. It was anticipated that working in the Café may increase socializing, interaction, participation, and making new friends. A combination of the above could increase positive affect and well-being. As a result, behavioral changes associated with ABI such as anxiety, depression, stigma, emotional and behavioral control may be perceived to decrease over time.

Social Health: Short forms of Satisfaction with Social Roles and Activities, Participation in Social Roles and Activities were selected for the feasibility trial. It was anticipated that working in the Café with other employees, could increase participation and satisfaction with time spent in the community, increase in socialization, and performing meaningful tasks. Consequently, an increase in performance and functional skills may provide the satisfaction with their community

based social roles and relationships at home and in the community. As a result, changes observed by the individual may result in a positive response by them over time.

2.9 Intervention

2.9.1 Session Setup and Safety

Before each Café session, the BWSS and the harness garment will be inspected for wear and tear, loose parts and missing equipment. The research therapist working in the Café is responsible for ensuring the safety of the equipment and participant during the training. Once the participant enters the Café, the research therapist will help him/her don the harness garment. The research therapist will also ensure that the straps on the garment are not twisted and that the participant feels comfortable, relaxed and safe. As a safety precaution, a semi-squat test will be done to ensure that the participant is secured and safe in the harness.

2.9.2 Café

The Café serves as a fully functional business. The participants will be volunteers who function as Café employees, assisting paid staff with serving food and drinks and managing the register. Depending on participant goals/abilities, activities may include: standing at the counter, greeting customers, taking and filling orders. The overall goal for participants is to practice job activities that simultaneously involve motor, social and cognitive skills embedded within an ecologically valid and enriched environment. During the intervention, the research therapist will assist the participant

in performing various goal-directed actions while guiding movements as necessary during each session.

Goals set by the on-site research therapist and participant will be aimed at upper and lower extremity functions, executive functioning and communication for a 2-week period. Once goals are achieved, the tasks will either be changed or modified to make it more complicated. For example, if the goal is to improve cognitive ability, participants would be asked to work at the register and make meals requiring multiple steps. Working at the register will need attention, short-term memory, and ability to recall the order. Making sandwiches would also need cognitive ability as the participant would have to remember specific requests of the customers.

During this process, the researcher will guide the participant and provide cues to enable successful accomplishment of tasks. If the goal is to improve fine motor functions, the researcher will work with the participants to use their more affected arm to perform different tasks such as serving ice cream, making sandwiches, salads, and drinks. This may improve grip, pinch and grasp components as well as improve eye-hand coordination and attention.

2.9.3 Intervention Fidelity

Intervention fidelity refers to the researcher's and participant's compliance with the designed study intervention. Fidelity of the feasibility trial will be determined by the total time spent in the harness, the frequency, and duration of rest breaks and attendance by the participants.

2.10 Safety and Adverse events

The on-site research therapist will note the safety of the participant, coworkers, and public during each training session in the Go Baby Go Café and assessments. Since each training session is 2 hours, participant safety will be determined by the following criteria 1) No dizziness or syncope 2) severe muscle soreness lasting more than 48 hours 3) fatigue causing early retirement from the training session and 4) serious adverse event or injury requiring immediate medical attention as reported by the participants.

In case of an adverse event, information regarding the time, place, and type of adverse event will be submitted to the IRB. Compliance with IRB policies on the investigation will follow. Following a response from IRB's inquiry, the feasibility trial will be temporarily stopped, or data collection will be resumed.

2.11 Withdrawal or Elimination

Taking part in any study is entirely voluntary. Participants do not have to participate in the feasibility trial and have the right to stop at any time without any negative consequences. That is, if, they decide not to participate there will be no penalty or loss of benefits to which they are otherwise entitled.

The investigators could terminate participation in the study if they deem it inappropriate for the participant to continue if participant status changes and they fail to meet all inclusion/exclusion criteria. Additionally, if being a part of the study puts participants at risk medically or psychologically, they may be eliminated from the study.

2.12 Data Management and Quality Control

Participant identities will be kept confidential to the extent possible. Participants will be assigned a code that will replace a name or other identifying information on all data forms or electronic records, excluding video recordings. All paper records will be stored in a locked file cabinet in a locked office or lab. All electronic records will be encrypted and saved on password-protected desktop computers and backed-up and stored on University-managed servers to maintain data security. However, because the intervention will be performed in a fully public environment, the research team cannot prevent participants from being identified by Creamery staff, Café customers, or any other passers-by during Café sessions. Quality control would be conducted by the principal investigator or the co-principal investigator to ensure the accuracy of data entry in electronic data storage

2.13 Potential Risks

There are primarily three types of risks

- 1) *Psychological risks* include possible discomfort, frustration, anxiety, and embarrassment during testing or training sessions because some activities may be difficult to perform. Although it is not anticipated, there may be unexpected, or potentially adverse interactions with members of the public. In order to address the above concerns, different café scenarios will be described to the participant and their family. This would help decrease their frustration, anxiety, and fears.
- 2) *Fall and loss of balance risks* can occur during assessments. To minimize risks of loss of balance, fall or fatigue, a physical therapist will present to complete all testing. In order to address the above concerns, the participant will be

appropriately guarded by a CITI trained volunteer. The participant will wear standard clinical safety measures such as a gait belt or over-ground harness system during all walking tests.

- 3) Work-based risks in the Café include minor cuts, burns, and bruises associated with handling hot drinks or the coffee machine. In order to address the above concerns, the onsite researcher would be present at all times to prevent the likelihood of an injury. For example, participants will be allowed to take rest breaks when fatigued. In addition to rest, first aid will also be available for minor injuries.

2.14 Ethical Consideration

This feasibility study will be conducted by the University of Delaware's Institutional Review Board (IRB) research policies and procedures. Purpose of the study, assessment procedure, potential risks, voluntary withdrawal, and IRB office contact information, will be explained to all participants by the on-site researcher. Once the participant signs the stamped consent form approved by the IRB, all participants will be assigned a subject number, to be used for research communications except when identifying information is necessary.

All data sheets, participant information, and signed consent forms will be stored in the participant's folder in a locked file cabinet. Participants may also be videotaped or photographed during the study. An optional photo release form will be signed by participants who agree to this before initiation of the study.

Chapter 3

TO DETERMINE FEASIBILITY OF THE GO BABY GO CAFÉ TRIAL

3.1 Abstract

Background. The use of Environmental Enrichment has been widely studied in animal models. The application of the same in humans is limited to inpatient rehabilitation settings. The objective of this study (Chapter 3) is to determine the feasibility and safety of a formal clinical research protocol (Chapter 2). The Protocol focused on the use of a real-world Café setting equipped with a novel Body Weight Support System (BWSS) as an alternative rehabilitation intervention for individuals with moderate to severe Acquired Brain Injury. **Method.** Individuals with a diagnosis of moderate to severe Acquired Brain Injury (ABI) were recruited during the study. Of the total individuals screened, six individuals with TBI were eligible to participate in the study. The Go Baby Go Café intervention (Café) was conducted for two-hour sessions, three times a week, for two months. In neuroscience terminology, the Café served as a sophisticated “enriched environment” where participants gained social, cognitive and physical abilities by volunteering as a Café employee. Feasibility measures and safety of the participants and BWSS were assessed. **Results.** Despite recruitment for individuals with ABI, only six chronic severe TBI participants enrolled and completed the study. Overall, the study demonstrated safety and feasibility of most measures in the TBI specific population. Most notably, all participants reported high levels of acceptability to the novel intervention. **Discussion.** Even though the protocol suggested the inclusion of individuals with ABI, only individuals with a

history of moderate to severe TBI participated in the study. Nevertheless, the current protocol is appropriate for a phase 1 clinical trial with modifications for the specific population. In preparation for the clinical trial, the Protocol needs revision in the areas of recruitment strategy, outcome measures, study design, and resources. **Conclusion.** A commercially available, low cost, high impact BWSS in a real-world business setting is feasible and safe. Additionally, it also provides community engagement, social interaction, and the opportunity to work on functional goals. Future studies must consider conducting a pre-study survey to determine the enriched environment most suitable for the population and age group of interest. Consequently, specific protocol revisions will then increase the potential success of formal clinical trials to determine efficacy and effectiveness in target populations.

PREFACE

The focus of Chapter 2 was on Protocol development using established Standard Protocol Items for Clinical Trials (SPIRIT) and World Health Organization (WHO) guidelines for a feasibility study. In Chapter 3 feasibility study is described by taking the CONSORT 2010 Statement guidelines into consideration for implementing feasibility trials. The use of established guidelines for the Protocol and Feasibility study helped ensure compliance in reporting quality clinical research. Concerning the chapters mentioned above, partial overlap of some aspects of the Methodology (study design, outcome measures, and mode of recruitment) from Chapter 2 will be noted in Chapter 3. Before initiating the study, the Protocol (Chapter 2) and Feasibility trial (Chapter 3) was approved by the Institutional Review Board (IRB) of the University of Delaware. Outcomes from Chapter 3 will decide the potential for future phase I and II clinical trials.

3.2 Introduction

Despite a decrease in mortality of Acquired Brain Injury (ABI) individuals, long-term disability is still a major cause of public health concern[18], [19], [21]. Often, individuals with moderate to severe ABI re-enter their communities with a range of challenges such as decreased cognitive ability, gait disturbances, paralysis, communication, and sensory-perceptual impairments[45], [65], [66], [77]. Consequently, quality of life and independence become impacted by decades of decreased participation in daily and leisure activities, social withdrawal, and even employment[45], [46]. *Therefore, ABI rehabilitation must be comprehensive, high impact, adaptive, and across the lifespan.*

Current adult neurorehabilitation typically includes multidisciplinary teams comprised of physical, occupational, speech, and cognitive therapists who provide therapy independently within the same clinical or rehabilitation setting[11]. Despite a multidisciplinary approach to achieve common functional goals, many individuals are discharged into the community well before they can reach the level of skills required for ADL's[371]–[374]. *This is a significant cause of concern as most rehabilitation programs consider successful community integration as an essential discharge goal*[89].

There is growing evidence to highlight the limitations of current rehabilitation programs regarding carryover for real-world skills needed for meaningful community re-entry[92], [260], [261]. First, task-specific skills within a single clinical environment may have a limited transfer to community/work-based settings[92], [261]. For example, repetition of tabletop activities such as peg boards and manipulating putty may not carry over to lifting objects of different weights, shapes, and sizes at home. Second, early discharge due to limited insurance and progress in

recovery can decrease the ability for obtaining the skill sets required for community integration. For example, insufficient locomotor training before discharge can result in increased dependence on the use of a wheelchair for mobility at home and the community. Third, unsatisfactory programs with inadequate funding can hamper rehabilitation of an individual with ABI. For example, limited resources due to insufficient funding and lack of program guidelines can cause generalization of therapy. This, in turn, prevents customization of treatment approaches tailored to an individual's needs.

Consequently, follow up studies on community-dwelling individuals with ABI have reported decreased involvement with ADL and diminished skills acquired from previous rehabilitation[269], [373]. At the individual level, this “negative plasticity” can be attributed to a decrease in ADL's, decrease in cognitively demanding tasks, social isolation, and learned nonuse of the impaired side/limb. At the community level, this could be due to lack of resources, necessary adaptations, and long-term community-based services which typically encourage physical, cognitive and social activities. Therefore, emphasis on long-term community rehabilitation is vital to decrease and prevent long-term cognitive, social, and physical deterioration.

Environmental Enrichment (EE) is an emerging rehabilitation concept in humans. The influence of EE on social, physical, and cognitive domains has been widely studied in animal models including those of brain injury [1]-[11]. However, the use of EE in clinical neurorehabilitation is less common [375]. What is an EE? In traditional animal model neuroscience, EE refers to an experimental paradigm *artificially created* by building large cages equipped with multiple rats, different toys and natural bedding [189], [376].

Conversely, impoverished cages typically contain bedding and one or two objects or a small group of rats. For example, cognitive enrichment is generally provided by introducing novel objects and rearranging them frequently to increase the formation of spatial maps and the detection of new objects within the cage[193]. A change in cognitive ability is then tested in rats using the Morris Water Maze Task. Rats enclosed in cognitively enriched versus impoverished cages demonstrate an increase in spatial learning, cognitive flexibility, visual and spatial recognition[194]–[196].

However, in human neurological rehabilitation, there are none to a few studies on constructed physical and cognitive and social EEs[237]. Instead, human rehabilitation work has used a much broader definition of EE that merely includes *greater intensity, dosage, frequency, and duration of physical, occupational and speech therapy compared with standard rehabilitation conditions* [377]. For example, occupational EE is provided through an increase in frequency/duration of tabletop activities and functional activities in a simulated kitchen, cognitive EE is delivered through comprehensive compensatory or restorative strategies, and physical EE is provided through high-intensity treadmill training for a longer duration.

Consequently, if one applies the traditional EE definitions, clinical environments are relatively non-enriched compared to the real world for adult humans (Figure 17). This study sought to determine the feasibility and safety of a real-world environment using a new BWSS (see below) for humans that meet the accurate EE definitions.

Furthermore, the lack of necessary adaptations and environmental supports in the community may be an essential factor in the relatively unsuccessful transition to

the community in moderate to severe ABI[237]. The effectiveness of traditional BWSS has been extensively covered in literature from BWSS over a treadmill to BWSS over ground in neurological and healthy populations [12]-[17]. However, most BWSS's permit two directional movements in space and are restricted to hospitals, clinics, and research settings. Consequently, once discharged from the hospital/rehabilitation setting individuals with ABI have residual motor deficits with no access to community-based BWSS's to maintain learned motor skills. This results in a downward spiral of previously gained skills which affects not only the individual but also their family members and caregivers.

In animals, EE's are created by constructing structures and supports to facilitate mobility in a large cage set up for physical enrichment. *Consequently, if one applies the traditional EE definition to BWSS in humans, BWSS's which promote "natural" walking could provide the support and structure currently lacking in the community.* Therefore, by providing necessary adaptations, individuals with ABI can continue to achieve physical, cognitive, and social gains in society. For example, after discharge, a chronic individual with ABI will significant residual mobility could use a community-based BWSS to practice walking, balance, and stepping for a certain number of hours per week.

When designing EE based studies for adult neurological populations, a central concept to think of is that humans, like rats, are highly social animals. Therefore, exploration, navigation, socialization, and mobility are critical for a meaningful life. Consequently, it can be hypothesized that the combination of real-life enriched environment combined with a new BWSS that permits "natural" walking pattern, individuals with ABI could achieve and maintain physical,

cognitive, and social gains. Thus, this study sought to determine the feasibility and safety of a constructed environment for humans that met the traditional EE definitions.

This study aimed to fill the above gaps in literature:

- 1) Investigate the feasibility of the Café intervention by using measures such as recruitment, attendance, adherence, attrition of the participants,
- 2) Determine the safety of the participants and the new BWSS,
- 3) Determine the acceptance of the program by the participants, and
- 4) Determine the use of selected outcome measures.

We hypothesize that the Café intervention and the new BWSS would be feasible and safe. Results from this study will provide information on safety, modifications in the protocol if necessary, the feasibility of using multiple measures, and reports on any adverse events in and outside the cafe.

Current Environmental Enrichment for ABI humans

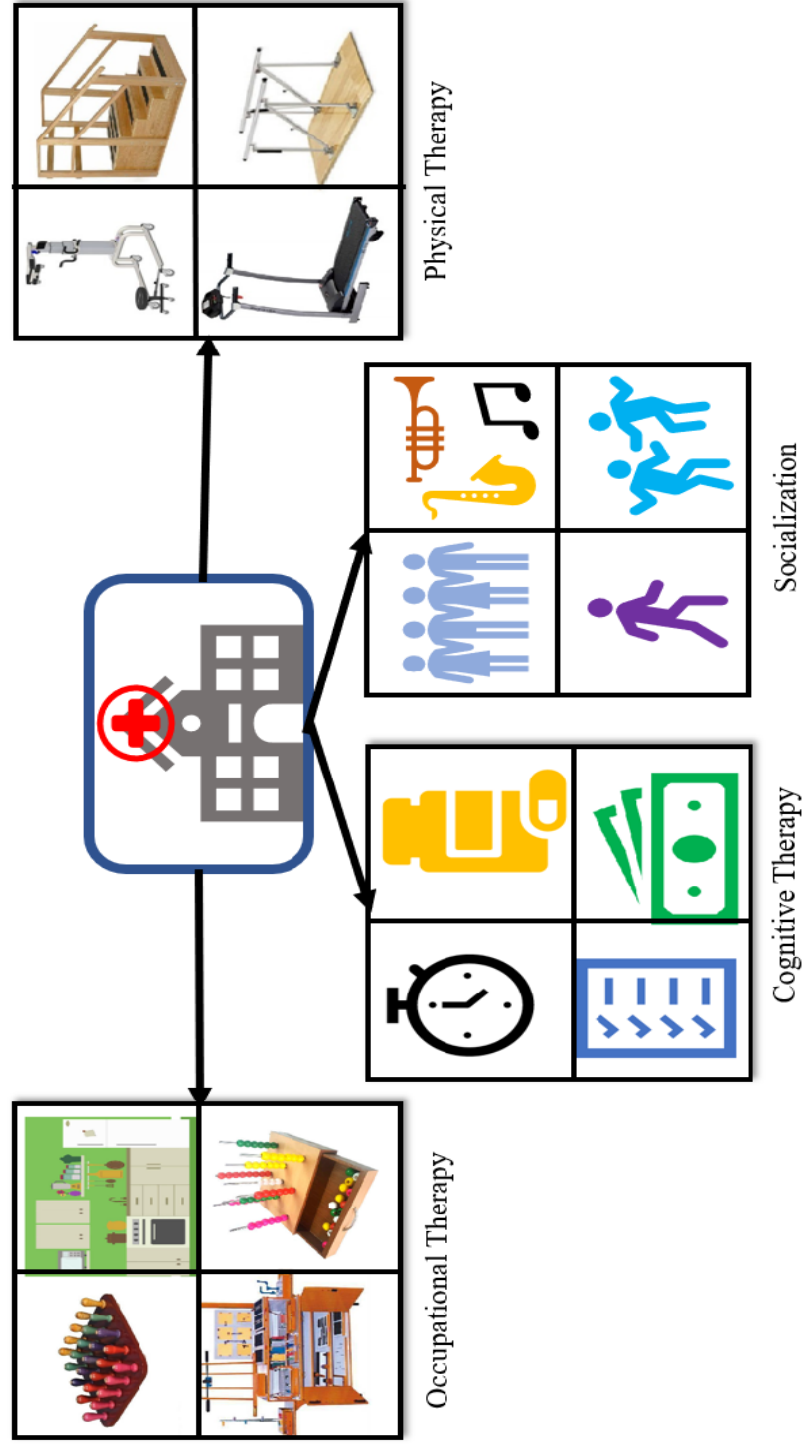


Figure 17 EE for human adults with ABI is typically provided in a hospital or rehabilitation center. Occupational EE is provided through tabletop activities such as peg boards, performing functional activities in a simulated kitchen, and improving skills by using a complex work desk space. Cognitive EE is provided through compensatory strategies such as setting the alarm to take medicines or restorative strategies such as making a complex task simple by breaking it into multiple components such as counting money. Physical EE is provided through physical therapy such as postural training, staircase climbing, balance training, and BWSS for over-ground and treadmill training

3.3 Methodology

3.3.1 Study Design

A single subject experimental trial using the AB design was selected for the feasibility study. All participants signed an informed consent approved by the Institutional Review Board (IRB) of the University of Delaware. The study included two initial baseline sessions (A) spread two weeks apart (Figure 18 first two arrows). This was followed by 2-months of intervention (B) in the Go Baby Go Café (Figure 18 Go Baby Go Intervention block in grey). Baseline measurement sessions were repeated every two weeks until completion of the study. (Figure 18 arrows after 2, 4, 6, and eight weeks of intervention). The total duration of the study from the first baseline session was ten weeks. The entire period of the study from in-person screening to completion of intervention was 2.5 - 3 months.



Figure 18 Study design of the Café intervention. AB design with Baseline (A) for two weeks, and Intervention (B) for eight weeks

3.3.2 Study Population and Recruitment

Individuals with moderate to severe ABI have cognitive and physical deficits that persist after discharge. This typically results in decreased socialization and the risk for various degrees of withdrawal from society[254], [263], [265]. Knowledge on the influence of a novel EE based intervention on community-dwelling individuals with ABI was selected as the study population. It was based on the belief that the global deficits associated with the population would provide new insights into the effects of global stimulation in the brain.

Participant recruitment and data collection were conducted between 5/30/2014 to 12/31/2017. After families of potential participants contacted the research therapist, two screening procedures were initiated: 1) phone call with family members and/or the individual with ABI to determine diagnosis, time since injury, severity of injury, and 2) an in-person interview at the STAR Health Science Complex for eligibility based on the inclusion/exclusion criteria. Individuals with ABI were eligible to participate irrespective of gender, race, and ethnicity. There was no reason to expect differences in feasibility and outcome measures in minorities compared to other participants.

After the initiation of the study, three changes were made in the Protocol and Consent form with the approval of the IRB. First, the Montreal Cognitive Assessment Scale (MOCA, see details below) scores for exclusion was modified to allow more severely affected participants to become eligible (Table 3). Specifically, at the beginning of the study, a few participants with severe cognitive deficits were unable to pass the MOCA test due to strict grading criteria set by the MOCA scoring manual. Second, by decreasing the cutoff score of MOCA, the IRB recommended the addition of a Parental Guardian Approval Form (Appendix N) and Assent Form (Appendix O) to ensure the safety of the vulnerable population.

Table 3: Inclusion/Exclusion Criteria with modifications after study commencement

Inclusion Criteria	Exclusion Criteria	Modified Exclusion Criteria
Age 21-85 years old	Unable to stand or walk	
Diagnosed of a moderate to severe ABI by a physician based on hospital/clinical reports (GSC score <12, NIHSS >16)	Unable to communicate with others	<i>Diagnosis of moderate to severe TBI by a physician, based on a severity scale (GSC score <12)</i>
Willing and able to attend all sessions and provide informed consent	Cognitive impairment that limits the ability to provide informed consent* (based on MOCA scores – cut off 21/30)	<i>Cognitive impairment that limits the ability to provide informed consent (based on MOCA scores - (>10/30)</i>
Individuals requiring moderate to maximal assistance with most ADL	Active cancer or currently undergoing cancer treatment	
	Cardiac event or cardiac surgery in the past three months	
	Current participation in PT, OT or SLP	

Therefore, if a participant scored above 21/30, they would sign the consent form. However, if they scored between 10 and 21, their guardian would sign the parental guardian permission form first. Only then, the participant would sign the Assent Form. Third, at the initiation of the study, recruitment of individuals with ABI was emphasized as per protocol guidelines. However, midway through the study timeline, the most common type of ABI being recruited were individuals with severe

TBI. The primary mode of recruitment was through word of mouth of previous participants of the study. Hence, given the limited duration of the study, a decision to allow the sample population to deviate from the initially expected population of ABI was proposed. Modifications made in the Inclusion/Exclusion criteria were then implemented to aid with the recruitment and *enrollment of individuals with only moderate to severe TBI*.

Table 4 Feasibility Measures with the rationale for cut off criteria

Feasibility Measure	Cut Off Criteria	Rationale
Recruitment	N = 10 - 15	Based on small-scale feasibility studies with comparable dosage [280]–[284], internal and external factors discussed in Protocol
Attendance	>80 (16/20 training sessions)	Common cut off in feasibility literature [285], [286]
Adherence	>75%	Common cut off in feasibility literature [285], [287]–[289]
Attrition	20% drop out	Common cut off in most clinical trials [285], [290], [291]
Safety		Reports on adverse events
Acceptance	>70%	Anticipated participants would enjoy the study environment

3.3.3 Testing Measures

Testing measures comprised of two groups: Feasibility and Clinical

3.3.3.1 Feasibility Measures

Feasibility outcome measures were collected by the research therapist who worked with the participants in the Café. The Café is open to the public. The majority

of the customers are the several hundred individuals that come through the building each day for classes, laboratory research, clinical and academic work or as clinic patients. The Café is located in the atrium of the STAR health Science Complex of the University of Delaware. The potential factors to establish the feasibility of the Café Protocol (detailed explanation in Chapter 2) are discussed below (Table 4):

Recruitment:

A single research therapist coordinated recruitment. Primary recruitment outlets were nearby area clinical facilities, physicians, support groups, use of fliers and generic advertisements through the University of Delaware's Delaware Rehabilitation Institute (DRI) and Department of Physical Therapy Clinic. As established by the Protocol in Chapter 2, 10 – 15 TBI participants were estimated to enroll for the study.

Attendance:

Attendance was defined as the total number of sessions attended by each participant. According to the Protocol (Chapter 2), attendance for each participant was expected to be at least 80% (16 of 20 training sessions) in the Café for the Café study to be considered feasible.

Adherence:

Adherence was determined by the total time spent working in the Café during each session minus the total duration of rest break(s) taken by the participant in that session. According to the Protocol (Chapter 2), adherence to intervention was set at 75% for the study to be feasible.

Attrition:

Attrition or the dropout rate was determined by the percentage of participants who did not complete the study. This included participants who dropped out at any point during the entire duration of the study. A cut off criteria of 20%, and below of total screened participants were considered to determine feasibility.

Safety:

According to the Protocol (Chapter 2), *Participant safety* was determined by the following criteria 1) no dizziness or syncope 2) severe muscle soreness lasting more than 48 hours 3) fatigue causing early retirement from the training session and 4) serious adverse event or injury requiring immediate medical attention as reported by the participants (Table 4). *BWSS safety* was determined by any adverse event caused by the equipment resulting in harm/injury to the participant, researcher or Café employees.

Acceptance:

A self-constructed survey (Appendix P) was used to establish acceptance with a combined cut off of 70% (Table 4). Participants were asked to answer the survey questions only if they completed the 2-month intervention study. Answers to the questions were scored by the participants using a visual analog scale from 0 (very negative experience) to 10 (very positive experience). Acceptance was determined by the extent to which participants were i) satisfied with the intervention, ii) showing

willingness to continue volunteering, and iii) provide feedback on the concept of using a BWSS within a real-world setting to address impairments.

3.3.3.2 Clinical Outcome Measures

The on-site researcher collected clinical Outcome Measures during the two baseline evaluations and repeated every two weeks until completion of the study. All testing was done in a quiet research laboratory with minimal distractions on the ground floor of the STAR Health Science Complex.

To determine the feasibility of using a comprehensive set of outcome measures, the ICF framework by WHO was used to ensure coverage of all ICF domains while evaluating the TBI participants[292]. This provides two significant benefits as it assisted with selection of measures specific to anticipated study outcomes and it helped establish functional goals tailored to each participant.

Few clinical outcome measures were included in the Protocol but were later eliminated after initiation of the feasibility trial. Table 5 provides the outcome measures excluded from the study with the rationale for the decision. Specific to the feasibility study, ease of conducting a comprehensive set of outcome measures were assessed.

Body Structure and Function

Montreal Cognitive Assessment Scale (MOCA)**

Common, short screening scale used to detect cognitive impairment[297]. The assessment comprises of different cognitive domains such as visuospatial/executive, naming, language, memory, attention, concentration, delayed recall, and orientation. Individuals are scored based on the correct response with a total score of 30. Higher

scores are associated with better cognitive ability. A score of 26 and above is considered normal. In TBI, MOCA has good validity, high sensitivity, and can be used as a spot screening tool for determining global cognitive impairments [300], [301].

Trail Making Tests (TMT A and B)

Common neuropsychological assessment thought to reflect cognitive functions such as attention, visual scanning, mental flexibility and set shifting. [297], [302]TMT tasks are to be completed as quickly and accurately as possible. TMT - A consists of 1-25 randomly scattered circled numbers, which should be connected through lines in ascending order. Primary cognitive measures tested in TMT A include motor speed, attention, and visual-perceptual tracking[303]. TMT – B comprises of 1-13 encircled numbers and letters A – L. The person connects these circles by alternating between the number and a letter. TMT B is more comprehensive and often considered as a test for measuring executive functions. In addition to all cognitive measures tested in TMT A, TMT B also measures processes involved with task switching, divided attention, and reading skill[303], [304]. Performance for both TMT's is assessed by the time taken to complete each test. Higher scores are suggestive of greater cognitive deficits[305]. Normative data demographically adjusted for different age groups are available for both TMT A and B[306]. TMT B has strong predictive validity and sensitivity with a strong dose-response relationship in TBI[309]–[311].

Activity Limitations

6-minute walk test (6MWT)

Common research and a clinical measure of submaximal assessment of aerobic capacity[315], [316]. The objective is to cover as much distance as possible in 6 minutes. The total distance walked is measured using a stopwatch and GAITRite, using a measuring wheel or markings on the floor. It has excellent test-retest reliability in TBI [318].

10 Meter Walk Test (10 MWT)

Common research and a clinical measure of gait speed[322]. The objective is to take three trials of i) self-selected walking and ii) fast walking for 10 meters each. The middle 6 meters are timed, and average speed is determined for self-selected and slow walking. Two meters on either side of the 10-meter track is to account for acceleration and deceleration of the participant's speed. It has excellent test-retest inter-rater reliability in TBI (ICC=0.99)[318].

Table 5 List of Measures eliminated after Feasibility study initiation

Domain of ICF	Outcome Measures Eliminated	Rationale for elimination
Activity Measure	Action Research Arm Test (ARAT)[354]	Severe deficits/functional impairments increased the time-dependent test duration resulting in fatigue and frustration
Activity Measure	Functional Gait Assessment (FGA)[343]	Major gait deviations led to variability in the scoring of the gait assessment. Flooring effects on certain items prevented accurate assessment
Activity Measure	Four Square Step Test (FSST)[341]	Severe gait deficits significantly increased flooring effects due to inability to maintain balance and achieve required knee flexion.

Timed Up and Go (TUG) and TUG Cognitive

Common research and a clinical measure of mobility, static and dynamic balance, and to differentiate fallers from non- fallers[328], [329]. The objective is to time the participant from getting up from an armchair, walking 3 meters, turning around and walking back to sit down in the same chair. The TUG Cognitive consists of performing the TUG test while counting backward in 3's from 100[330]. The purpose of this revised test is to assess the dual task ability of the individual. The TUG test has excellent test-retest reliability (ICC=0.86) in TBI children and adolescents[331].

Jebsen Hand Function Test (JHFT)

Conventional research and a clinical measure of hand function for activities of daily living [335], [336]. JHFT consists of seven timed subtests performed first with the least or unaffected arm followed by the affected arm. The seven subtests include of writing a 24-letter sentence, turning 3 X 5" cards, simulating feeding using five kidney beans and a teaspoon, picking small objects, stacking checkers, and lifting large, light and heavyweight objects. Total time for performance of tasks by each arm is recorded.

Participation Measures

NeuroQOL

The Neuro-QOL is a self-report questionnaire to assess the health-related quality of life in various neurological populations, including those with stroke, multiple sclerosis, and [368]. The item banks consist of questions related to physical, cognitive, social, and emotional health domains relevant across disorders. It has 17 health-related quality of life domains and subdomains. Each subdomain can be administered through computer-adapted tests (CAT) or short forms comprising of 5-9 questions. Questions are answered based on a 5- point scale based on intensity (not at all to very much) or frequency (never to always). It has good reliability and concurrent validity in stroke. [368].

3.3.4 Environmental Enrichment (EE)

For this study, the EE is a functioning business - Go Baby Go Café located within the atrium of the Health Science Complex building, University of Delaware (UD). The Café lies within is a 10'x 10' metal 'kiosk' equipped with an overhead harness system used for fall prevention. The kiosk is the central physical structure making up the Café, a commercial business (Figure 17). The Café is a collaboration between the UD creamery and the Go Baby Go research program. The Café serves beverages, ice cream, hot and cold snacks, and soups, etc. The structure and body weight support system (BWSS) is a commercially available, FDA registered device (Enliten, LLC, Newark, DE). The BWSS was reviewed in detail in Chapter 2.

Participants underwent training in the Café for three two-hour sessions per week for a total duration of two months. The participants were volunteers but functioned as Café employees, who assisted paid staff in serving food and drinks. Depending on participant goals/abilities, activities included standing at the counter,

greeting customers, taking orders and preparing food and drinks (Figure 19). The overall goals set up for the participants were tailored to the needs of the individual and his or her family.

Goals were typically built around actual Café job activities. Each activity simultaneously involved motor, social and cognitive skills. During the intervention, the on-site researcher assisted the participant in performing various goal-directed actions while guiding movements as necessary during each session. For example, S1 was keen to improve her balance, socialization, and cognitive abilities. Therefore, a functional goal for S1 was to walk from the back to the front counter while conversing with a customer without losing balance within 50 seconds.

Goals were also modified on a biweekly basis by the on-site researcher based on participants performance and inability to complete the goal. Conversations with the respective participant and their family about general progress outside the Café were also discussed on a biweekly basis. If the participant was unable to complete the goal, it was modified and made easier to achieve. For example, once S1 was able to accomplish the task within 50 seconds, the time was changed to 40 seconds. Conversely, if the goal was easy and attained sooner, the speed of task performance and the addition of multiple steps were added to increase task complexity. For example, to improve socialization, S1 worked at the register. However, task complexity was increased by encouraging her to concentrate on taking orders and returning exact change while conversing with the customers.



Figure 19 Activities done by a participant in the Go Baby Go Café. The participant performed various tasks using upper and lower extremity, executive functions and/or communication as a Café volunteer employee (A) Serving a packet of carrots (B) Carrying an ice cream bar while interacting with a customer (C) and (D) making hot and cold beverages[378](Participant provided photo consent).

3.3.5 Data analysis

As the sample size is small, descriptive statistics such as percentage, mean, and lower and upper-level range of scores are used to indicate the feasibility of collecting a quality data set in timely fashion.

3.3.6 Results

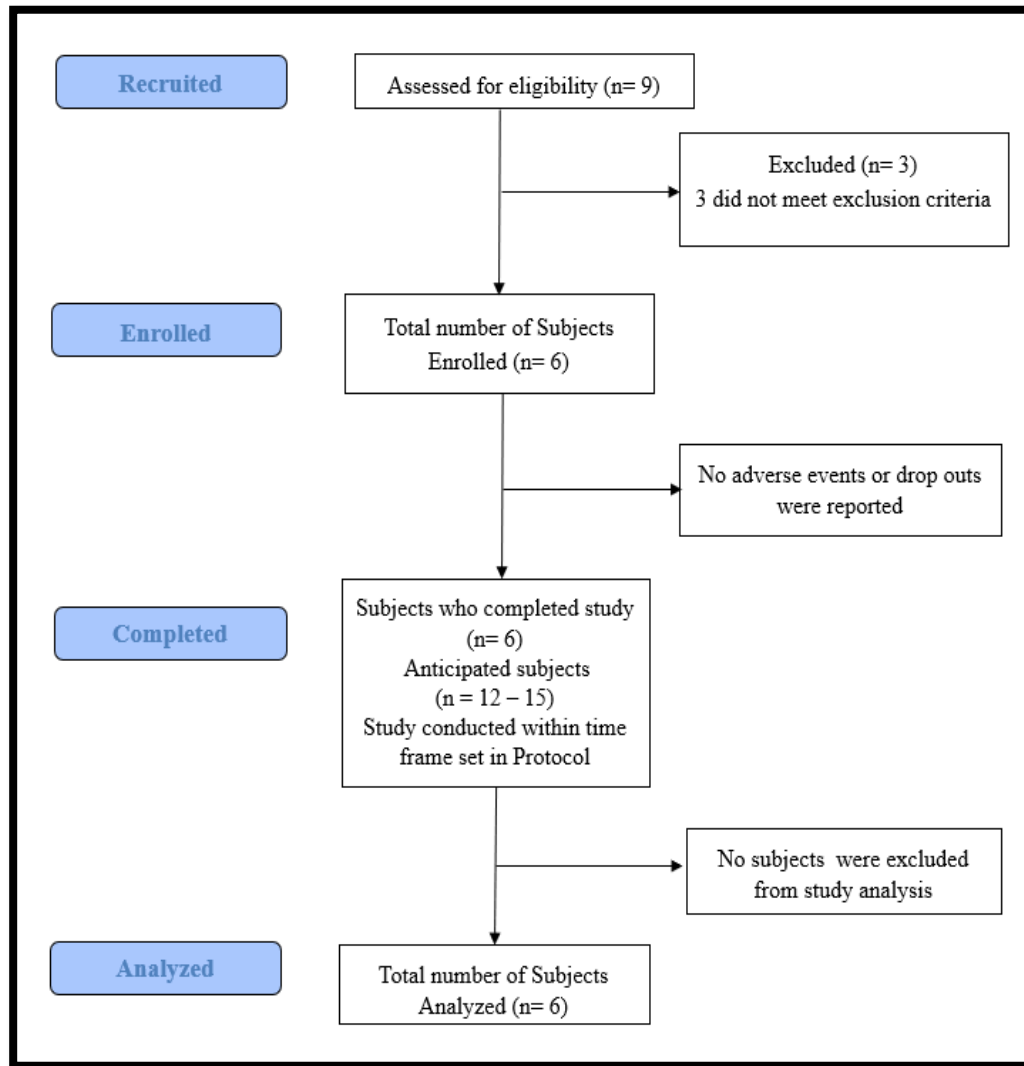


Figure 20 Flowchart of participants from recruitment to data analysis for feasibility trial

Recruitment: Of the nine individuals with chronic TBI, three individuals did not meet the eligibility criteria mentioned in Table 3. Of these, one individual had minimal motor impairments, which made the use of the BWSS unnecessary (See

Exclusion Criteria). The second individual did not meet the modified minimum criteria for a score of 10 and above on the MOCA scale. The third individual was eliminated due to a history of uncontrolled seizures. Therefore, a total of six individuals with TBI were enrolled in the study (Figure 20). All six participants had a severe TBI (as per the medical records made available by the participants family). All except S5 could provide medical records due to the longevity of time (>25 years) since the injury. The family was unable to obtain the records from the hospital due to disposal after 10 years post-injury.

However, a verbal report from the family confirmed a diagnosis of severe TBI Diffuse Axonal Injury (DAI) causing global brain damage was a commonality for all participants. Five of six participants had a TBI from a Motor Vehicle Accident (MVA). Only S6 had a TBI resulting from a fall from a significant height. Table 6 provides information on the cause of injury, GCS and MOCA score, type of injury and assistive device used by the participants at the time of enrollment (Table 6). Demographic information revealed all participants were Caucasians with a gender ratio of two women for each man with a mean age of 30 years (Table 7).

Attendance: For the total number of sessions that were possible, no absentees were noted. If a participant was unable to come due to illness or bad weather, the session was rescheduled. None of the participants canceled the rescheduled appointments. Since the Café is located in a University setting, academic breaks were taken into consideration for a total number of sessions. Therefore, one participant (S2) could only attend 15 sessions due to winter break at the University. The remaining participants attended 20 of 20 sessions (Table 8).

Adherence: All six participants demonstrated high adherence to the intervention (Table 8). Despite requiring rest breaks, participants were able to stand for most of the two-hour sessions and practiced several different functional tasks.

Attrition: All participants enrolled in the study completed the Café intervention without any dropouts (Table 8).

Table 6 Diagnosis of enrolled individuals with TBI

	Cause	GCS Score	MOCA Score	TBI Severity	Type of TBI	Assistive Device used for community ambulation
S1	MVA	6	20	Severe	DAI	Motorized Scooter
S2	MVA	2	13	Severe	DAI	Manual wheelchair (propelled by a caregiver)
S3	MVA	3	19	Severe	DAI	Manual wheelchair (propelled by a caregiver)
S4	MVA	4	21	Severe	DAI	Rolling Walker
S5	MVA	N/A	18	Severe	DAI	Manual wheelchair (propelled by a caregiver)
S6	Fall	3	21	Severe	DAI	Manual wheelchair (self-propelled)

Table 7 Participants demographics

Participant demographics	Mean (SD)
Age (years)	30.6 (10.74)
Time since injury (years)	9.3 (1– 25)
Gender	2 males, 4 females
Race	Caucasians

Safety:

Participant safety: All participants found the Café intervention to be safe.

None of the participants reported no incidents of dizziness/syncope, muscle soreness lasting more than 48 hours that required medical intervention. Only in two different participants, one session was stopped early due to fatigue (S2) and fever (S6).

BWSS safety: No injury or adverse events due to the assistive technology were reported during the 2-month study. The BWSS did not require replacement of parts or any repairs. No wear and tear to harness garment were reported (Table 8).

Table 8 Feasibility Measures: Attendance, Adherence, Attrition and Safety Measures

Feasibility Outcome Measures	Mean as a % (Range)
Attendance	100 (0)
Adherence	87.31 (78 – 94)
Attrition	0 (0)
Safety	
Participant	No adverse events reported
BWSS	No adverse events reported
Acceptance	
Satisfaction with intervention	85 (70 – 100)
Desire to continue volunteering	100 (0)
Novelty of BWSS+EE with focus on multi-task performance	95 (90-100)

Acceptance: All participants enjoyed the study. A self-constructed survey was filled by the participants upon completion of the study (Appendix P). Participants were asked if a) if they were satisfied with the intervention, b) they would like to continue volunteering in the Café, and c) their input on the concept of combining novel BWSS with a real-world EE for rehabilitation. An average rating of i) 85% participant satisfaction with the Café intervention, ii) 100% willingness to continue volunteering in the Café, and iii) the participants reported 95% approval for the novel concept of Café.

Outcome measures: The outcome measures selected at the beginning of the study were too exhaustive for participants. The average time was 2 – 2.5 hours. After consultation with the participants, their families and senior research therapists, several measures were removed for reasons outlined in Table 4. After modifications, no complaints were reported during the evaluation. After that, the average time reported was 1.5 – 2 hours. Two of six participants with severe memory impairments required assistance from their caregivers or personal assistants to fill the NeuroQOL questionnaire at home. In such cases, family members and personal assistants were asked to recap the Café activities with the participant before selecting their verbal response.

Though the primary purpose of the study was to determine feasibility and safety, Table 9 and 10 provide data on clinical outcome measures at baseline and eight weeks. To demonstrate the feasibility of obtaining quality data from participants by following a formal protocol. No conclusions about the effectiveness can be drawn from the study.

Table 9 Data on body function and activity outcome measures for enrolled participants at baseline and two months. Measures in shaded cells must decrease with time and measures in white cells must increase with time to indicate improvement.

OUTCOME MEASURE (unit)	S1		S2		S3		S4		S5		S6	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
TMT A (seconds)	55	53	204	139	83	57	59	42	62	45	44	34
TMTB (seconds)	131	61	552	268	187	168	95	84	111	77	126	87
10 MWT Self-Selected (m/s)	0.09	0.14	0.23	0.28	0.35	0.46	0.42	0.75	0.3	0.33	0.57	0.72
10 M Walk Fast Speed (m/s)	0.16	0.19	0.32	0.39	0.42	0.41	0.61	0.86	0.33	0.42	0.7	0.9
TUG (seconds)	59	40	62	38	34	18	28	20	46	28	23	15
TUG COG (seconds)	53	47	67	51	43	24	31	18	40	28	28	25
6 Minute Walk Test (feet)	305	302	325	389	393	596	559	851	187	300	695	770
JHFT Dominant (Seconds)	250	190	114	93	130	179	187	138	103	76	105	77
JHFT Non-Dominant (Seconds)	327	214	658	442	495	349	330	261	489	398	199	120

Table 10 Neuro – QOL outcome measures at baseline and two months. Item banks with an asterisk indicate high scores signifying better outcomes. Conversely, item banks without an asterisk indicate high scores signifying poor outcomes.

Neuro-QOL Domain	S1		S2		S3		S4		S5		S6	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Physical Health												
Upper Extremity*	35.6	51.7	28.7	30.2	53.8	41.2	30.9	28.7	39.3	30.9	28.7	30.9
Lower Extremity*	38.3	54	16.5	27.2	43.9	43.6	39.1	33	39.1	38.3	40.8	38.3
Fatigue	44.7	40.8	43.8	43.8	29.5	29.5	41.8	41.8	51.3	51.3	41.8	51.3
Sleep Disturbance	58	32.6	56.8	59.2	32	32	48.9	47.3	43.8	58	56.8	58
Mental Health												
Depression	60.6	46.7	54.3	54.3	46.8	36.9	47.9	43.1	51.3	47.9	45.3	47.9
Anxiety	44.3	50.6	59.3	60.1	36.4	36.4	52.3	50.5	44.3	49.5	44.3	49.5
Stigma	51.7	60.5	59.3	56.2	55.4	51.7	51.7	52.8	54.6	52.8	53.7	52.8
Positive affect and well-being*	52.3	54.4	48.1	47.2	54	63.3	49	55.8	39.4	56.8	57.8	56.8
Social Health												
Satisfaction with social roles and activities*	52	50.9	36.7	34	48.9	46.9	39.1	44.7	43.7	46.9	46.3	46.9
Ability to participate in social roles and activities*	46.1	49.5	59.3	35.7	42	60.2	39.9	43.4	43.4	46.1	44.7	46.1

3.3.7 Discussion

The objective of this study was to determine the feasibility and safety of an EE based intervention using a new commercially available BWSS in a business environment. Findings indicate that the EE (Go Baby Go Café) is safe and potentially feasible for a pilot project involving two-month intervention with TBI participants (Figure 17). There were four indications of feasibility and safety as reflected by attrition, adherence, attendance, and acceptance. *Below, recruitment and clinical outcome measures are discussed first as they likely require protocol modifications for future clinical trials. This is followed by addressing the four feasibility measures.*

Recruitment

Anticipated recruitment was 10 – 15 individuals with ABI between 5/30/2014 to 12/31/2017. Of the 9 participants screened only 50% were eligible and agreed to participate in the study. Also, despite significant steps to increase recruitment for individuals with ABI, only those with chronic TBI ultimately participated in the study.

Another concern was the lack of participation of any minority group and more participation of females than males. As per NIH, females, and minorities are often underrepresented in clinical trials leading to gender bias and racial disparity in the research literature. Efficient recruitment is an essential component of any clinical trial. Almost 30% of clinical trials are discarded due to recruitment and retention issues [379]. Therefore, even though the intervention may be useful, a small sample size can reduce its validity leading to inconclusive results and abandonment [291]. Some common causes for slow recruitment that are relevant for the current feasibility study were **1) unforeseen obstacles at the initiation of the study, 2) complex protocols,**

and 3) barriers to study site[379]–[381]. Below some strategies are highlighted with recommended modifications in recruitment for the Phase 1 clinical trial.

Unforeseen obstacles at the initiation of study: Inadequate connections or networking with local rehabilitation hospitals, adult day care, and outpatient programs can affect recruitment of participants[380]. A lack of established relationships before initiation of the Café study may have led to slow recruitment. Networking with local support groups, clinics, and rehabilitation centers after the launch of the study were unsuccessful to increase participant enrollment to achieve the anticipated sample size. Upon completion of the study, the most common enrollment method was determined to be through word of mouth of previously enrolled participants and a rehabilitation center in the neighboring state.

Therefore, recommendations for future clinical trials on small funds and/or time limit are: i) establish network with local hospitals, clinics, and rehabilitation centers “prior” to initiation of the study, ii) prescreen the vicinity to determine demographics of required population, iii) set up a multi-site study to ensure better recruitment, and iv) identify specific resources within the available funds such as number of on-site researchers, therapists, and evaluators.

Complex Protocols: Complex protocols and/or going over the consent form over the telephone can slow recruitment[291], [380], [381]. For the feasibility study, one mode of recruitment was calling potential participants and family members. Though the protocol was not complex, it may be possible that the family found the study intervention too complex, i.e., PT, OT, CT provided simultaneously in a real-life environment. Inconvenience and issues with participating during business hours of the weekday can further decrease interest of ABI families [380], [382]. Therefore,

recommendations for future clinical trials are: i) Simplify the explanation over the phone, ii) Provide images or videos to explain the study via email, or in person, and iii) use feasibility data to explain the outcomes of participation.

Barriers to study site: The inability of participants to physically get to the assessment and/intervention location is a common factor for decreased participation. [380].

Specific to the Café study, transportation may have been a big factor for the slow recruitment of participants. A common question during a screening of individuals with ABI was whether there is provision for transport to the research site. Therefore, recommendations for future clinical trials are i) Funding for adequate transportation is often much more expensive than initially thought. Thus, transportation budget must be well accounted for when writing a small pilot grant proposal such as an NIH R03 or R21, ii) Using budgeted funds for transportation, validate parking and provide an honorarium to increase the incentive for participation.

Use of selected outcome measures:

Clinical outcome measures were feasible with the removal of specific outcome measures (Table 4). However, four modifications must be considered for future trials.

Population Specific Outcome Measures: This study was initially designed to measure the change in individuals from any ABI population including stroke, TBI and brain injury due to other etiologies from substance abuse to brain tumors. Hence, measures considered and ultimately selected were from commonly used assessments in clinical practice and research across ABI.

Since ABI is an umbrella term encompassing many neurological conditions, some measures that were not explicitly validated in a target neurological population but were widely used in other neurological populations clinically and in research were still incorporated in the study. For example, the Timed Up and Go Test is a commonly used measure in neurological clinical practice across ABI population and, has excellent reliability and validity in stroke but not in TBI.

Future clinical trials should consider taking outcome measures with strong psychometric properties specific to the population being tested. This would ensure the quality of data collected and provide an accurate representation of results for evidence-based practice. Recommended measures for HR-QOL and cognitive tests for TBI specific population includes TBI – QOL, NIH toolbox cognitive battery, Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), WAIS-IV-digit span subtest. Given the real-world environment of the study, another approach for comprehensive data collection could include the use of naturalistic assessments such as Multiple Errands Test (MET), Multi-level Action Test (MLAT), Naturalistic Action Test (NAT), Cooking Task, and Executive Function Performance Test (EFPT).

Practice effects: There is abundant evidence on the learning or practice effect where participants remember the test and perform better due to memory than actual skills [383], [384]. This results in better performance with each evaluation. All participants in the study performed the assessments every two weeks. Even though, most of our measures focused on mobility (fine and gross motor function), participants may become skilled at memory tests such as TMT A and B, and the MOCA. Future clinical

trials should consider using control groups for testing practice effects and use new cognitive tests such as the Executive Function Performance Test. This test provides a naturalistic setting and helps assess executive function based on functional task performance.

Short Comprehensive Clinical Measures: Specific to the study, all participants had severe cognitive and mobility impairments. Time constraint tests such as the ARAT required the individual to perform the subtask within a given duration of time. Severe functional limitations prevented the initial participants to accomplish the subtask. Consequently, as per rules, the participant had to perform all the remaining tasks within that section. Furthermore, participants complained of fatigue, frustration due to the inability to complete the subtask on time which prolonged the total test time to 45 minutes. Future clinical trials must consider two important aspects of preventing participant fatigue and frustration: i) assessment time for each measure should be short to prevent early onset of cognitive overload. and ii) consider two-day evaluations to prevent fatigue.

Attendance:

Participant attendance is a vital feasibility measure for many reasons: 1) it reflects, in part, participant motivation, 2) provides additional data on adherence and attrition to be collected, and 3) is essential for determining treatment effects of an intervention. The current study showed excellent attendance (100%) by all participants. This may be attributed to the rescheduling of the session to make up for illness or family vacation. However, participants were aware that they could choose to not attend up to four sessions as the minimum criteria were 16/20 sessions. The willingness and

motivation of the participants and their families suggest they enjoyed the community intervention and experiences. *No modifications are recommended regarding attendance for future clinical trials.*

Adherence:

According to the Protocol (Chapter 2), participants were required to adhere to the intervention for at least 75% of the total duration. This required all participants to stand for at least one and a half hours in the Café during the two-hour session. Results demonstrated that the average adherence of participants over two months was 87% (range 78 - 94%). Thus, all participants met the adherence threshold. The lowest adherence value (78%) was for the oldest and longest post TBI participant who had the most mobility impairments. Specifically, she was 28 years post-TBI and primarily used a wheelchair for mobility. She often needed multiple rest breaks due to leg fatigue from standing. Future clinical trials that retain rest breaks within the protocol should have no problem with adherence even with participants who are several decades post-injury.

Attrition:

Participant attrition (aka dropouts) are typical and thus are typically accounted for while recruiting participants for a study. Usually, attrition rates above 30-40% indicate severe errors with study design and methodology[385]. Our study reported no dropouts after formal entry into the study via completing the consent form. This excellent attrition rate in combination with high attendance and adherence indicate strong study vigor and motivation of participants [385]–[387].

Safety: As technology is increasingly being used in neurorehabilitation, safety continues to be a significant factor in feasibility studies[388]. This is especially true for this study, as it uses a newly FDA registered device for the first time. Therefore, information on safety was necessary as the six individuals had a history of chronic severe TBI with significant mobility and cognitive impairments. Additionally, the new three-dimensional BWSS was incorporated in a real-world environment for the first time as compared to the typical laboratory or clinical settings equipped with traditional two-dimensional BWSS's for the last few decades.

No adverse events occurred during the study. That is, there were no adverse events reported for the participants and no breaks/repairs/malfunctions of the BWSS itself. Additionally, for families that continued to volunteer, donning and doffing the harness garment was reportedly found to be easy. *Therefore, no modifications are recommended for improving the safety of participants and the BWSS in future clinical trials.*

Recommended Enriched Environment for ABI humans

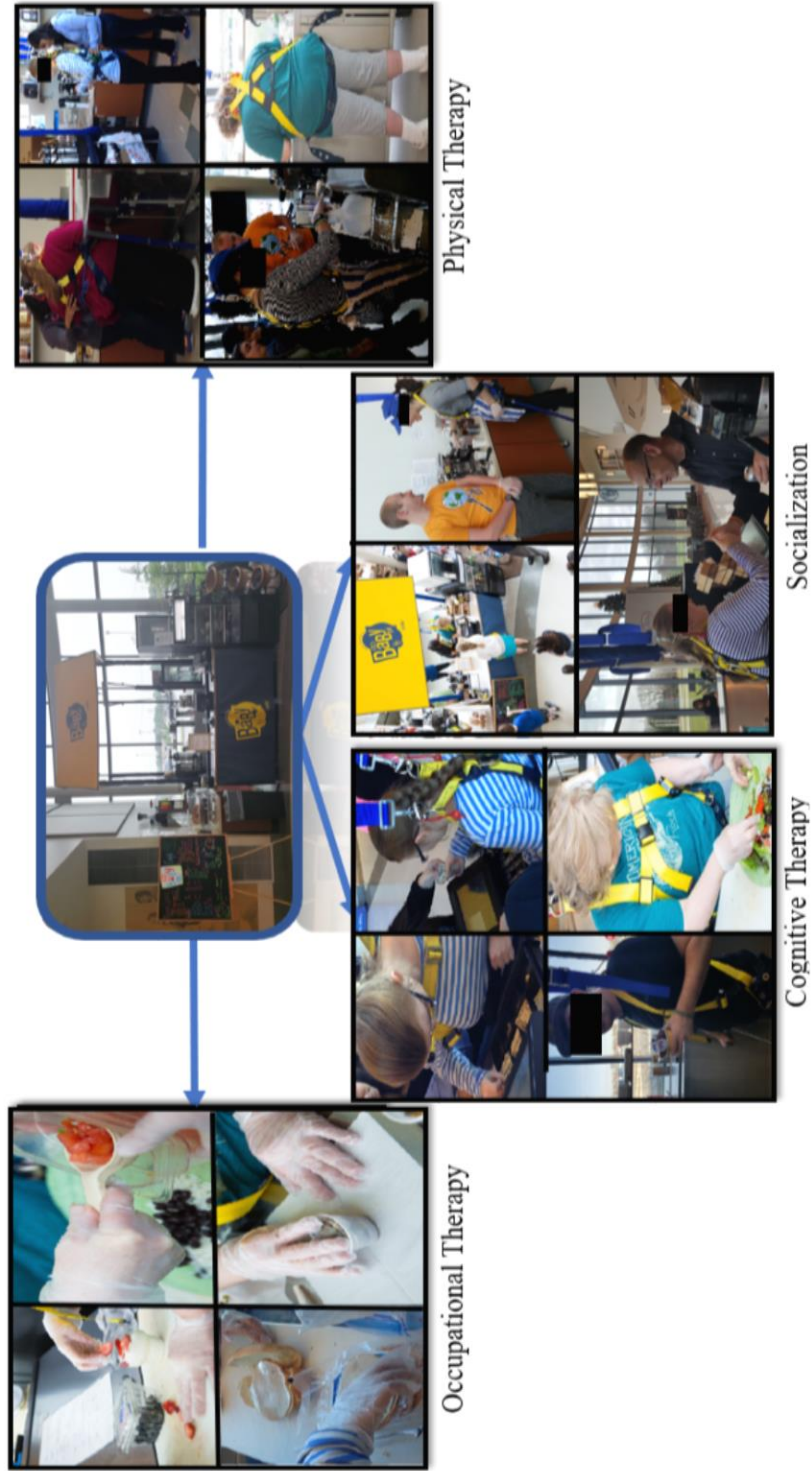


Figure 21 Recommended EE for adult ABI humans. Occupational EE is provided through preparing different foods. Cognitive EE is provided by working at the register. Physical EE is provided by dual tasking. Social EE is provided through interaction with Café and customers in a real-world business setting

Acceptance:

The use of EE in Individuals with ABI has primarily been tested in acute and rehabilitation settings[148], [149], [389]. Additionally, satisfaction with daily activities is an essential measure for long-term rehabilitation goals[264], [265]. The objective of the survey questionnaire (Appendix P) provided at the end of the study was to get participant feedback on the novelty of using a community-based business setting for rehabilitation. The outcomes from the survey reported that all participants were not only satisfied and wished to continue volunteering, but also liked the novel approach to rehabilitation.

Three of the six participants continued to volunteer for several months. Three participants were unable to volunteer for the following reasons: i) caregivers were not able to commit due to work schedules, and ii) the participant did not want to be with the parent in the Café. Overall, the outcomes of the survey were positive and indicative that *no modifications are required regarding the satisfaction and EE based intervention for future clinical trials.*

3.4 Limitations

This study has several limitations given that it is the first to assess the feasibility of a novel community-based intervention using a commercial, low-cost BWSS. First, despite additional recruitment efforts such as distributing fliers to support groups, local outpatient clinics, and a nearby TBI Model System (Moss rehabilitation center) database, the study failed to recruit enough participants.

Second, the selection of outcome measures was generalized to the ABI population. Consequently, enrollment of only TBI participants affected the psychometric properties of the test. For example, Neuro-QOL has robust psychometric

properties in Stroke. However, an optimized version of several item banks of Neuro – QOL has been explicitly published to TBI populations (TBI – QOL).

Third, screening information was not documented while recruiting participants. This was an immense drawback as several people were interviewed, but information on the total number of people screened is unavailable. Instead, the only documentation available was of individuals who signed the consent form and tested for eligibility using the MOCA. Thus, the results only highlight the number of people who signed the consent form and not the actual number of people approached to participate in the study. Future studies must include a screening test to have an estimate of the actual number of individuals screened for the study.

Fourth, two of the six participants required the assistance of their respective caregiver to complete the Neuro – QOL questionnaire due to severe cognitive deficits. While proxy-reported outcome measures are commonly used for HR-QOL measures, proxy response bias has also been reported[390], [391]. Proxies (typically provided by the caregiver or family member who works closely with the individual) report a higher level of impairment in HR QOL measures as compared to self-reported outcome measures. Hence, the occurrence of proxy bias must be accounted for in studies. A recent study by Kisala et al. (in press) reported equivalence between conducting interviewer-administered measures and self-reported measures[392]. This is an important find as people with significant cognitive and physical impairments may not always be able to complete computerized tests. Hence, recommendations for future studies on individuals with moderate to severe TBI can consider the application of i) proxy-reported outcome measures for all participants to reduce bias or ii) conduct both

interviewer-administered and self-reported measures to ensure the reliability of participant's responses.

Fifth, while the BWSS allowed for movements in all directions, the participants were unable to perform any bent over activities due to the fixed lengths of the harness straps. The next generation of BWSS's must consider modifying the straps to adjust according to standing, sitting and bending over postures, while preventing falls. Additionally, expansion of the BWSS to different real-world settings would provide valuable information on its feasibility and importance of the selected work/leisure environment in the community.

3.5 Conclusion

This study lays the foundation for feasibility and safety of a community-based EE equipped with a BWSS for individuals with severe TBI. Young adults often get injured due to road traffic accidents[11]. Therefore, most individuals will spend decades of their life with long-term deficits. Despite successful community integration being a vital rehabilitation goal, most individuals with TBI get discharged, unprepared, and unaware of the challenges they would face in the community[11], [264], [393]. This not only affects the recovering individual but also becomes a significant burden to family and friends[82], [83].

Providing community-based opportunities may provide the functional environment, socialization, and leisure activities that, in part, can dramatically reduce physical and cognitive decline. This study advances our understanding of the advantages and feasibility of using real-world environments. It also provides insight into the use of low- cost, commercially available technology for rehabilitation. Finally,

knowledge gained from this study would provide the necessary information and critical modifications to increase the probability of a meaningful Phase 1 clinical trial.

Chapter 4

DISSERTATION SUMMARY

The overall objectives of this dissertation were to provide a survey of comprehensive nature of the deficits and rehabilitation associated with ABI recovery (Chapter 1), establish a formal research Protocol for a novel community-based intervention based on EE principles (Chapter 2), and conduct a small sample Feasibility study (Chapter 3). Below, four key findings of the study are summarized.

Theoretical concepts in favor of EE in human rehabilitation - The last few decades have highlighted the significance and impact of EE in human neurorehabilitation. Some emerging concepts for providing EE include:

i) *Environmental Complexity* governed by stimulus and demands. i.e., greater the challenges in a complex environment, greater the following actions and decision-making process by the individual[394]. A Café example of a complex task is working at the register. It requires the participant to interact with the customer while entering the order into the register. Thus, this requires a high level of cognitive functioning including attention, concentration, working memory and the ability to the dual task.

ii) *Multi-Context Treatment Approach* comprising of five essential components: use of different environments, metacognitive training, performing meaningful tasks, processing strategy, and learner's characteristics such as motivation and inspiration to maximize treatment benefits, improve generalization, and transfer of skills in individuals with brain injury. [395], [396]. A Café example of a multi-context

treatment approach is making sandwiches in the Café and returning home to a Harnessed kitchen to prepare dinner. This not only allows for the transfer of skill from work to the home environment but also facilitates in learning new strategies for increasing speed of preparing meals and motivation to test new recipes.

iii) *Cognitive Reinforcement* directed toward motivation and engagement in complex, stimulating environments which is associated with improvement in cognitive ability[296]. A Café example is doing an activity that requires fine motor function. Participants were asked to use their affected arm to scoop out ice cream and serve it to the customer. This involved not only fine motor function but also cognitive functions like attention, memory, and visuospatial navigation to bring it to the front counter.

Participation in a real-world community-based setting: The Cafe feasibility study is the first to test the concept of EE in a real-world community setting. Previous studies in ABI have stereotypically examined principles of EE with focus on the dosage of therapy or more recently, the provision of puzzles, entertainment and dining options with other stroke inpatients[148], [258], [260]. However, one important caveat to these approaches is the lack of transition to real life experiences and events. For example, an occupational therapist may assist an individual to make food in a simulated kitchen within a clinical setting. While this methodology ensures safety, it may not provide the motivation nor mental energy essential for best effort [296].

The Café provided an opportunity for the participants to not only be present in the community but also work on their multiple deficits through functional goals while engaging with other community dwellers. For example, preparing sandwiches for different customers involved various steps and different types of sandwiches. More

importantly, the lunches made went to real customers who gave actual tips. Therefore, provision of incentives can be encouraging to boost morale and functionality of individuals with TBI.

The gap in community-based supports for individuals with TBI: The Café study is the first to incorporate a commercially available, low cost, FDA registered BWSS allowing for three directional movements within a fully functional business setting. Common grievances of the individuals include being unprepared to re-enter the community, unproductiveness, social isolation, transportation barriers, and struggling to adapt to their new life[30], [43], [51], [397].

A recent review paper argued against the use of conventional methods for post-discharge environments[237]. They highlight and recommend the use of cognitive, community resources, socialization, and physical activity to prevent overall decline (Figure 21). The Café (EE + BWSS) serves the purpose of addressing all the above concerns for young and middle age individuals with TBI who become withdrawn from friends and family members over time.

Provisions to support long-term volunteering in the Café: All participants were provided with the option to continue volunteering post completion of the study. One participant continued to volunteer for 2.5 years before getting a part-time job for the first time in 17 years. Another participant found a part-time job a few months after the Café. Two other participants proceeded to have the harness installed in their house to continue working on their impairments within their home environment. This essentially became a six-month study to measure feasibility and preliminary effectiveness in two individuals with a history of severe TBI and their caregivers over time.

Additionally, they also volunteered in the Café when feasible. The remaining two participants showed a desire to volunteer but could not due to transportation issues and family commitments. *Therefore, not only did the study answer the research question but also boosted the morale of the TBI families to seek further options through jobs and installing a harness at home.*

Future Directions

The next step consists of conducting a randomized pilot study with the recommended changes mentioned in Chapter 3. Since this is a feasibility study, data cannot be used for estimation of sample size. Effect size calculated (Table 10) for some measures may be used in future studies. However, the values should be used with caution given the small sample size of the feasibility study. An interesting outcome to consider for the next study is the GCS score of all the participants. Severe TBI is typically associated with significant functional impairments which disrupt the quality of life. In this study, all participants had a GCS score below 6 (severe TBI). This breakthrough can be significant as long-term deficits are known to persist and increase over time in individuals with severe TBI. Thus, by providing community-settings equipped with the novel BWSS, it may be possible to establish new guidelines and environments to set eligibility criteria's and determine potential effectiveness of the intervention.

Table 11 The effective size of outcome measures which reported a maximum change

Outcome Measure	Cohens d	Effect size
10 Meter Walk Test	0.64	Medium
Timed Up and Go Test	1.15	Large
Trail Making Test B	0.6	Medium
Jebsen Hand Taylor Function Test	0.83	Large
6 Minute Walk Test	0.58	Medium

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Appendix A

HEALTH HISTORY FORM

Today's Date: _____

Date of Neurologic Injury/Diagnosis: _____

The following is a list of common health problems. In the first column please indicate if you currently or have ever had any of the problems in the past. In the second column please indicate if you are currently receiving treatment for the problem. In the last, please indicate if the problem currently limits any of your daily activities.

	Do you or have you had the problem?		Do you currently receive treatment for this problem?		Does this problem limit your daily activities?	
	Y	N	Y	N	Y	N
Heart Disease	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Heart Attack	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
High Blood Pressure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Low Blood Pressure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lung Disease/Asthma	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Diabetes	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Ulcer or Stomach Disease	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Eye, Ear, Nose, Throat Problems	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Nausea/Vomiting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Hernia or intestine problem	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Kidney Problem	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Liver/Gall Bladder problems	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Drug or alcohol use	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Anemia or blood condition	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Vascular condition	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Ringing in the ears	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Cancer	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Sexual dysfunction	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Anxiety/Depression	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Seizures	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fainting/Headache	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

HEALTH HISTORY FORM (Page 2)

	Do you or have you had the problem?		Do you currently receive treatment for this problem?		Does this problem limit your daily activities?	
	Y	N	Y	N	Y	N
Dizziness/Vertigo	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Nerve disease/disorder	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Muscle disease/disorder	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Immune disease/disorder	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Hearing loss	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Vision loss	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Arthritis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Speech/Communication	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Allergies	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Skin Disorder	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Are you pregnant?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Smoking/Tobacco use	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Bowel/Bladder irregularities	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Menstrual irregularities	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Recent unexplained weight loss or gain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Stroke	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Osteoporosis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Numbness or tingling	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Shortness of breath	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Surgeries with corresponding dates: _____

Appendix B

MONTREAL COGNITIVE ASSESSMENT (MOCA) SCALE

MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

VISUOSPATIAL / EXECUTIVE		Copy cube		Draw CLOCK (Ten past eleven) (3 points)		POINTS	
				<input type="checkbox"/> Contour <input type="checkbox"/> Numbers <input type="checkbox"/> Hands		___/5	
NAMING							
						___/3	
MEMORY							
Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.		FACE	VELVET	CHURCH	DAISY	RED	No points
1st trial							
2nd trial							
ATTENTION							
Read list of digits (1 digit/ sec.).		Subject has to repeat them in the forward order [] 2 1 8 5 4				___/2	
		Subject has to repeat them in the backward order [] 7 4 2					
Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors		[] FBACMNAAJKLBAFAKDEAAAJAMOFAB				___/1	
Serial 7 subtraction starting at 100 [] 93		[] 86	[] 79	[] 72	[] 65	___/3	
		4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt					
LANGUAGE							
Repeat : I only know that John is the one to help today. []						___/2	
The cat always hid under the couch when dogs were in the room. []							
Fluency / Name maximum number of words in one minute that begin with the letter F [] _____ (N ≥ 11 words)						___/1	
ABSTRACTION							
Similarity between e.g. banana - orange = fruit [] train - bicycle [] watch - ruler						___/2	
DELAYED RECALL							
Has to recall words WITH NO CUE	FACE []	VELVET []	CHURCH []	DAISY []	RED []	Points for UNCUE recall only	
Category cue							
Multiple choice cue							
Optional							
ORIENTATION							
[] Date	[] Month	[] Year	[] Day	[] Place	[] City	___/6	
© Z.Nasreddine MD		www.mocatest.org		Normal ≥ 26 / 30		TOTAL ___/30	
Administered by: _____						Add 1 point if ≤ 12 yr edu	

Appendix C

TRAIL MAKING TEST A AND B

Trail Making Test (TMT) Parts A & B

Instructions:

Both parts of the Trail Making Test consist of 25 circles distributed over a sheet of paper. In Part A, the circles are numbered 1 – 25, and the patient should draw lines to connect the numbers in ascending order. In Part B, the circles include both numbers (1 – 13) and letters (A – L); as in Part A, the patient draws lines to connect the circles in an ascending pattern, but with the added task of alternating between the numbers and letters (i.e., 1-A-2-B-3-C, etc.). The patient should be instructed to connect the circles as quickly as possible, without lifting the pen or pencil from the paper. Time the patient as he or she connects the "trail." If the patient makes an error, point it out immediately and allow the patient to correct it. Errors affect the patient's score only in that the correction of errors is included in the completion time for the task. It is unnecessary to continue the test if the patient has not completed both parts after five minutes have elapsed.

- Step 1: Give the patient a copy of the Trail Making Test Part A worksheet and a pen or pencil.
- Step 2: Demonstrate the test to the patient using the sample sheet (Trail Making Part A – SAMPLE).
- Step 3: Time the patient as he or she follows the "trail" made by the numbers on the test.
- Step 4: Record the time.
- Step 5: Repeat the procedure for Trail Making Test Part B.

Scoring:

Results for both TMT A and B are reported as the number of seconds required to complete the task; therefore, higher scores reveal greater impairment.

	Average	Deficient	Rule of Thumb
Trail A	29 seconds	> 78 seconds	Most in 90 seconds
Trail B	75 seconds	> 273 seconds	Most in 3 minutes

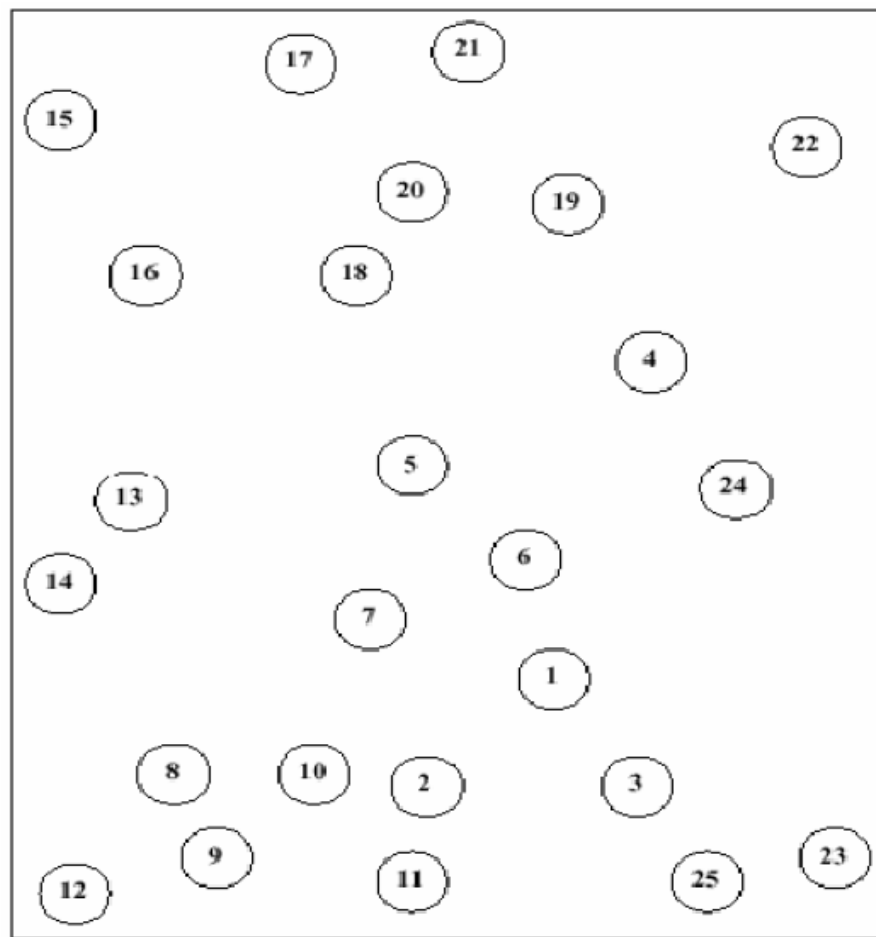
Sources:

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Trail Making Test Part A

Subject ID: _____

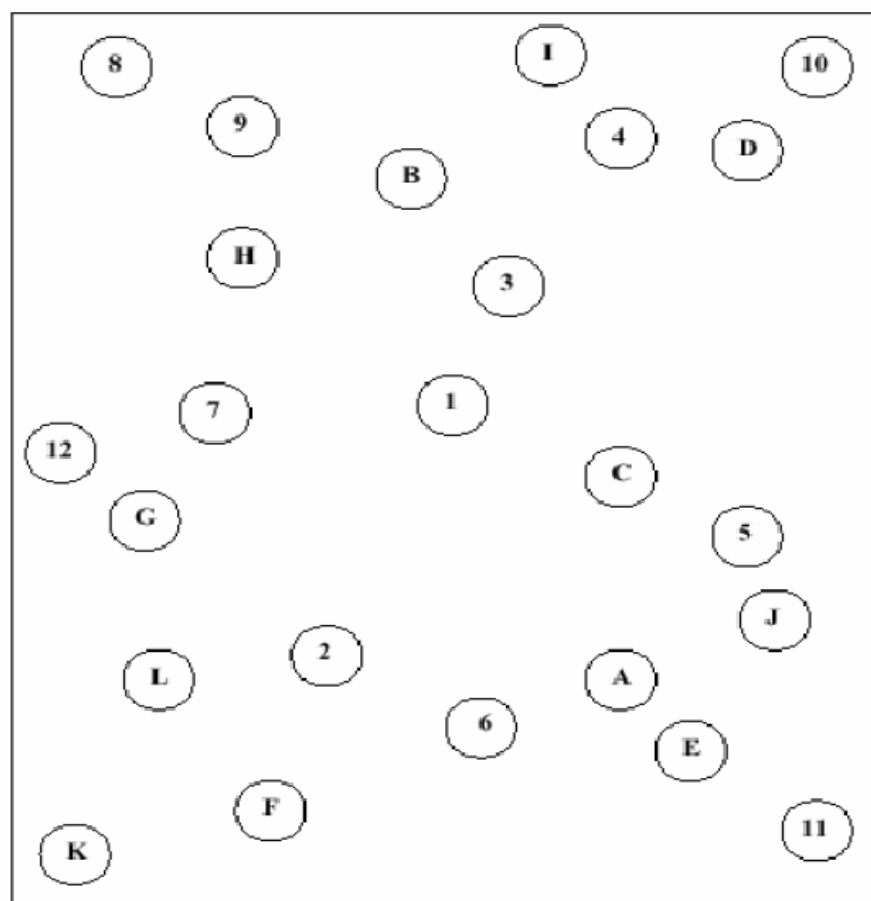
Date: _____



Trail Making Test Part B

Subject ID: _____

Date: _____



Appendix D

6 MINUTE WALK TEST

6 Minute Walk Test

Items Needed: stop watch, cones, chair or bench, device to measure distance

Instructions:

This test is one of endurance. I am going to ask you to walk continuously at a comfortable pace for 6 minutes; however, if you need to sit and rest, you can do so at any time. You can stop and rest or sit and rest. [You can use your assistive device] As talking can affect your performance, we're only going to talk if you have any questions or you want to tell me how you're feeling. Your goal when you are finished is to state that you covered as much distance as you could, and you could not have walked any farther. I will be walking with you. I'll start the time when I say "Go". Are you ready?

Subjects will walk as far as possible around a 42 meter rectangular path until the 6 minute time has elapsed. Chairs/benches will be positioned at intervals in the course.

At 1 minute intervals, tell subject that they are doing well and how much time has elapsed. If subject has requested a rest break, let them know that they can take as much time as necessary. Continue to provide them with a time elapsed statement at 1 minute intervals.

Appendix E

10 METER WALK TEST

10 Meter Walk Test

Set-Up:

- Mark a course that is 10 meters in length and place an additional mark 6 meters from the finish line. This will allow subjects an opportunity to achieve a leisurely pace by the time you start the test

Instructions:

Test A:

- 1) This test will tell us the time it takes you to leisurely walk 6 meters.
- 2) Start at this point and when I say "Go" walk at a pace like you were going to get a drink from the refrigerator.
- 3) Experimenter will say "Stop" when your foot crosses the line.
- 4) Repeat 3 times and take the average score

Test B:

- 5) This test will tell us the time it takes you to quickly walk 6 meters.
- 6) Start at this point and when I say "Go" walk as quickly as you can to the finish line
- 7) Experimenter will say "Stop" when your foot crosses the line.
- 8) Repeat 3 times and take the average score

Appendix F

TIMED UP AND GO TEST (TUG)

Timed “Up and Go”*

Directions

The timed “Up and Go” test measures, in seconds, the time taken by an individual to stand up from a standard arm chair (approximate seat height of 46 cm [18in], arm height 65 cm [25.6 in]), walk a distance of 3 meters (118 inches, approximately 10 feet), turn, walk back to the chair, and sit down. The subject wears their regular footwear and uses their customary walking aid (none, cane, walker). No physical assistance is given. They start with their back against the chair, their arms resting on the armrests, and their walking aid at hand. They are instructed that, on the word “go” they are to get up and walk at a comfortable and safe pace to a line on the floor 3 meters away, turn, return to the chair and sit down again. The subject walks through the test once before being timed in order to become familiar with the test. Either a stopwatch or a wristwatch with a second hand can be used to time the trial.

Instructions to the patient

“When I say ‘go’ I want you to stand up and walk to the line, turn and then walk back to the chair and sit down again. Walk at your normal pace.”

Variations

You may have the patient walk at a fast pace to see how quickly they can ambulate. Also you could have them turn to the left and to the right to test any differences.

*Podsiadlo D, Richardson S. The timed “up and go”: a test of basic functional mobility for frail elderly persons. *JAGS* 1991; 39: 142-148.

Scoring

Time for ‘Up and Go’ test _____ sec.

Unstable on turning?

Walking aid used?

Appendix G

JEBSEN HAND FUNCTION TEST

Jebson Hand Test of Hand Function

Description: The *Jebson* was designed to provide a short, objective test of hand functions commonly used in activities of daily living. The test was developed for health professionals working in restoration of hand function. The test items include a range of fine motor, weighted and non-weighted hand function activities which are timed: (1) writing (copying) a 24-letter sentence, (2) turning over 3 x 5" cards, (3) picking up small common objects such as a paper clip, bottle cap and coin (4) simulated feeding using a teaspoon and five kidney beans, (5) stacking checkers, (6) picking up large light objects (empty tin can) and (7) picking up large heavy objects (full tin can x 1 lb). There is a choice of 4 pre-written sentences for the writing subtest so that a different sentence can be selected for each re-test with the same client.

Administration: The test is conducted according to the instructions published in *Jebson et al. (1969)*. This original paper includes specific instructions for test construction and administration as well as operational definitions for all items used. The test is therapist administered and timed. No training is required. The nondominant hand is tested first, then the dominant hand, providing a score for each hand.

Research by *Rider et al., (1988)* confirmed the need to use the *Jebson* strictly as prescribed by the authors, as variation in administration may bias the test results and reduce test validity. That research confirmed a significant difference in performance if plastic checkers (which are more readily available) were used instead of wooden checkers. The Australian norms provided by *Agnew and Maas (1982)*, were based on testing using wooden checkers, as originally intended by *Jebson et al. (1969)*.

Administration time: The test takes approximately 15 minutes to complete, but can take up to 45 minutes with slower clients.

Scoring and Interpretation:

The time taken to complete each of the tasks is recorded during test administration, thus no separate scoring time is required. Comparison with normative data can take up to 15 minutes.

Normative data are available for males and females in the 20-60 year age range, for both the dominant and non-dominant hand (*Jebson et al., 1969*). *Hackel and colleagues (1992)* provide normative values for people aged 60-90. Percentile norms for the Australian population are provided by *Agnew and Maas (1982)*. Less stable test-retest results have been reported for the subtests of writing and simulated feeding; these subtest results should be interpreted more cautiously (*Stern, 1992*).

Population Groups: Adults with neurological or musculo-skeletal conditions involving hand disabilities. There is research published for clients with spinal cord injury, mild to moderate stroke, arthritis, acquired neurological disorders. The test has been used with children from 8 years (*Mazur, Menelaus, Hudson, & Stillwell, 1986; Noronha, Bundy, & Groll, 1989*).

Languages: Available in English only. The *Jebson* may be inappropriate for people with speech/language disorders or those from culturally and linguistically diverse communities (CALD), due to the dependency on language for instruction (*Hill et al. 2005*).

References:

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Appendix H

ACTION RESEARCH ARM TEST (ARAT)

ACTION RESEARCH ARM TEST

Subject ID: _____
Rater Name: _____
Date: _____

Instructions

There are four subtests: Grasp, Grip, Pinch, Gross Movement. Items in each are ordered so that:

- if the subject passes the first, no more need to be administered and he scores top marks for that subtest;
- if the subject fails the first *and* fails the second, he scores zero, and again no more tests need to be performed in that subtest;
- otherwise he needs to complete all tasks within the subtest

<u>Activity</u>	<u>Score</u>
Grasp	
1. Block, wood, 10 cm cube (If score = 3, total = 18 and to Grip) Pick up a 10 cm block	_____
2. Block, wood, 2.5 cm cube (If score = 0, total = 0 and go to Grip) Pick up 2.5 cm block	_____
3. Block, wood, 5 cm cube	_____
4. Block, wood, 7.5 cm cube	_____
5. Ball (Cricket), 7.5 cm diameter	_____
6. Stone 10 x 2.5 x 1 cm	_____
Coefficient of reproducibility = 0.98	
Coefficient of scalability = 0.94	
Grip	
1. Pour water from glass to glass (If score = 3, total = 12, and go to Pinch)	_____
2. Tube 2.25 cm (If score = 0, total = 0 and go to Pinch)	_____
3. Tube 1 x 16 cm	_____
4. Washer (3.5 cm diameter) over bolt	_____
Coefficient of reproducibility = 0.99	
Coefficient of scalability = 0.98	
Pinch	
1. Ball bearing, 6 mm, 3 rd finger and thumb (If score = 3, total = 18 and go to Gross movement)	_____
2. Marble, 1.5 cm, index finger and thumb (If score = 0, total = 0 and go to Gross movement)	_____
3. Ball bearing 2 nd finger and thumb	_____
4. Ball bearing 1 st finger and thumb	_____
5. Marble 3 rd finger and thumb	_____
6. Marble 2 nd finger and thumb	_____

Coefficient of reproducibility = 0.99

Coefficient of scalability = 0.98

Gross Movement (GM)

1. Place hand behind head (If score = 3, total = 9 and finish)

2. (If score = 0, total = 0 and finish)

3. Place hand on top of head

4. Hand to mouth

Coefficient of reproducibility = 0.98

Coefficient of scalability = 0.97

References

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De Weerd WJG, Harrison MA. "Measuring recovery of arm-hand function in stroke patients: a comparison of the Brunnstrom-Fugl-Meyer test and the Action Research Arm test." *Physiotherapy Canada*. 1985;37:65-70.

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Appendix I

FUNCTIONAL GAIT ASSESSMENT

Functional Gait Assessment

Subject ID: _____

Requirements: A marked 6-m (20 ft.) walkway that is marked with a 30.48-cm (12-in.) width.

1. Gait Level Surface

Instructions: Walk at your normal speed from here to the next mark (6 m (20 ft))

Grading: Mark the highest category that applies.

- (3) Normal – Walks 6 m (20 ft) in less than 5.5 seconds, no assistive devices, good speed, no evidence for imbalance, normal gait pattern, deviates no more than 15.24 cm (6 in) outside of the 30.48 (12-in) walkway width.
- (2) Mild Impairment – Walks 6 m (20 ft) in less than 7 seconds but greater than 5.5 seconds, uses assistive device, slower speed, mild gait deviations, or deviates 15.24-25.4 cm (6-10 in) outside of the 30.48 cm (12-in) walkway width.
- (1) Moderate impairment – Walks 6 m (20 ft), slow speed, abnormal gait pattern, evidence for imbalance, or deviates 25.4-38.1 cm (10-15 in) outside of the 30.48 (12-in) walkway width. Requires more than 7 seconds to ambulate 6 m (20 ft).
- (0) Severe impairment – Cannot walk 6 m (20 ft) without assistance, severe gait deviations or imbalance, deviates greater than 38.1 cm (15 in) outside of the 30.48 cm (12 in) walkway width or reaches and touches the wall.

2. Change in Gait Speed.

Instructions: Begin walking at your normal pace (for 1.5 m (5 ft)). When I tell you “go,” walk as fast as you can (for 1.5 m (5 ft)). When I tell you “slow,” walk as slowly as you can (for 1.5 m (5 ft)).

Grading: Mark the highest category that applies.

- (3) Normal – Able to smoothly change walking speed without loss of balance or gait deviation. Shows a significant difference in walking speeds between normal, fast, and slow speeds. Deviates no more than 15.24 cm (6 in) outside of the 30.48 cm (12 in) walkway width.
- (2) Mild impairment – Is able to change speed but demonstrates mild gait deviations, deviates 15.24-25.4 cm (6-10 in) outside of the 30.48 cm (12 in) walkway width, or no gait deviations but unable to achieve a significant change in velocity, or uses an assistive device.
- (1) Moderate impairment – Makes only minor adjustments to walking speed, or accomplishes a change in speed with significant gait deviations, deviates 25.4-38.1 cm (10-15 in) outside the 30.48 (12 in) walkway width, or changes speed but loses balance but is able to recover and continue walking.
- (0) Severe impairment – Cannot change speeds, deviates greater than 38.1 cm (15 in) outside 30.48 cm (12 in) walkway width, or loses balance as has to reach for wall or be caught.

3. Gait with Horizontal Head Turns

Instructions: walk from here to the next mark 6m (20 ft) away. Begin walking at your normal pace. Keep walking straight; after 3 steps, turn your head to the right and keep walking straight while looking to the right. After 3 more steps, turn your head to the left and keep walking straight while looking left. Continue alternating looking right and left every 3 steps until you have completed 2 repetitions in each direction.

Grading: Mark the highest category that applies.

- (3) Normal – Performs head turns smoothly with no change in gait. Deviates no more than 15.24 cm (6 in) outside 30.48 cm (12 in) walkway width.
- (2) Mild impairment – Performs head turns smoothly with slight change in gait velocity (eg, minor disruption to smooth gait path), deviates 15.24-25.4 cm (6-10 in) outside 30.48-cm (12 in) walkway width, or uses an assistive device.
- (1) Moderate impairment – Performs head turns with moderate change in gait velocity, slows down, deviates 25.4-38.1 cm (10-15 in) outside 30.48 cm (12 in) walkway width but recovers, can continue to walk.
- (0) Severe impairment – Performs task with severe disruption of gait (eg, staggers 38.1 cm (15 in) outside 30.48 cm (12 in) walkway width, loses balance, stops, or reaches for wall).

4. Gait with vertical head turns.

Instructions: Walk from here to the next mark (6 m (20 ft)). Begin walking at your normal pace. Keep walking straight; after 3 steps, tip your head up and keep walking straight while looking up. After 3 more steps, tip your head down, keep walking straight while looking down. Continue alternating looking up and down every 3 steps until you have completed 2 repetitions in each direction.

Grading: Mark the highest category that applies.

- (3) Normal – Performs head turns with no change in gait. Deviates no more than 15.24 cm (6 in) outside 30.48 cm (12 in) walkway width.
 - (2) Mild impairment – Performs task with slight change in gait velocity (eg, minor disruption to smooth gait path), deviates 15.24-25.4 cm (6-10 in) outside the 30.48 cm (12 in) walkway width or uses assistive device.
 - (1) Moderate impairment – Performs task with moderate change in gait velocity, slows down, deviates 25.4-38.1 cm (10-15 in) outside the 30.48 cm (12 in) walkway width but recovers, can continue to walk.
 - (0) Severe impairment – Performs task with severe disruption of gait (eg, staggers 38.1 cm (15 in) outside 30.48 cm (12 in) walkway width, loses balance, stops, reaches for wall).
5. **Gait and Pivot Turn**
Instructions: Begin with walking at your normal pace. When I tell you, “turn and stop,” turn as quickly as you can to face the opposite direction and stop.
Grading: Mark the highest category that applies.
- (3) Normal – Pivot turns safely within 3 seconds and stops quickly with no loss of balance.
 - (2) Mild impairment – Pivot turns safely in > 3 seconds and stops with no loss of balance, or pivot turns safely within 3 seconds and stops with mild imbalance, requires small steps to catch balance.
 - (1) Moderate impairment – Turns slowly, requires verbal cueing, or requires several small steps to catch balance following turn and stop.
 - (0) Severe impairment – Cannot turn safely, requires assistance to turn and stop.
6. **Step over Obstacle**
Instructions: Begin walking at your normal speed. When you come to the show box, step over it, not around it, and keep walking.
Grading: Mark the highest category that applies.
- (3) Normal – Is able to step over 2 stacked shoe boxes taped together (22.86 cm (9 in) total height) without changing gait speed; no evidence of imbalance.
 - (2) Mild Impairment – Is able to step over one show box (11.43 cm (4.5 in) total height) without changing gait speed; no evidence of imbalance.
 - (1) Moderate impairment – Is able to step over one show box (11.43 cm (4.5 in) total height) but must slow down and adjust steps to clear box safely. May require verbal cueing.
 - (0) Severe impairment – Cannot perform without assistance.
7. **Gait with narrow base of support**
Instructions: Walk on the floor with arms folded across the chest, feet aligned heel to toe in tandem for a distance of 3.6 m (12 ft). The number of steps taken in a straight line are counted from a maximum of 10 steps.
Grading: Mark the highest category that applies.
- (3) Normal – Is able to ambulate for 10 steps heel to toe with no staggering.
 - (2) Mild Impairment – Ambulates 7-9 steps.
 - (1) Moderate Impairment – Ambulates 4-7 steps.
 - (0) Severe Impairment – Ambulates less than 4 steps heel to toe or cannot perform without assistance.
8. **Gait with Eyes Closed**
Instructions: Walk at your normal speed from here to the next mark (6 m (20 ft)) with your eyes closed.
Grading: Mark the highest category that applies.
- (3) Normal – Walks 6 m (20 ft), no assistive devices, good speed, no evidence of imbalance, normal gait pattern, deviates no more than 15.24 cm (6 in) outside 30.48 (12 in) walkway width. Ambulates 6 m (20 ft) in less than 7 seconds.
 - (2) Mild Impairment – Walks 6 m (20 ft), uses assistive device, slower speed, mild gait deviations, deviates 15.24-25.4 cm (6-10 in) outside 30.48 cm (12 in) walkway width. Ambulates 6 m (20 ft) in less than 9 seconds but greater than 7 seconds.
 - (1) Moderate Impairment – Walks 6 m (20 ft), slow speed, abnormal gait pattern, evidence for imbalance, deviates 25.4-38.1 cm (12 in) walkway width. Requires more than 9 seconds to ambulate 6 m (20 ft).
 - (0) Severe Impairment- Cannot walk 6 m (20 ft) without assistance, severe gait deviations or imbalance, deviates greater than 38.1 cm (15 in) outside 30.48 (12 in) walkway width or will not attempt task.
9. **Ambulating backwards**
Instructions: Walk backwards until I tell you to stop.
Grading: Mark the highest category that applies.

- (3) Normal – Walks 6 m (20 ft), no assistive devices, good speed, no evidence for imbalance, normal gait pattern, deviates no more than 15.24 cm (6 in) outside the 30.48 cm (12 in) walkway width.
- (2) Mild Impairment – Walks 6 m (20 ft), uses assistive device, slower speed, mild gait deviations, deviates 15.24-25.4 cm (6-10 in) outside 30.48 cm (12 in) walkway width.
- (1) Moderate Impairment – Walks 6 m (20 ft), slow speed, abnormal gait pattern, evidence for imbalance, deviates 25.4-38.1 cm (10-15 in) outside 30.48 cm (12 in) walkway width.
- (0) Severe Impairment – Cannot walk 6 m (20 ft) without assistance, severe gait deviations or imbalance, deviates greater than 38.1 cm (15 in) outside 30.48 cm (12 in) walkway width or will not attempt task.

10. Steps

Instructions: Walk up these stairs as you would at home (ie. Using the rail if necessary). At the top turn around and walk down.

Grading: Mark the highest category that applies.

- (3) Normal – Alternating feet, no rail.
- (2) Mild Impairment – Alternating feet, must use rail.
- (1) Moderate Impairment – Two feet to a stair; must use rail.
- (0) Severe Impairment – Cannot do safely.

Total Score: _____ Maximum Score 30

Appendix J

FOUR SQUARE STEP TEST

Modified Four Square Step Test

Subject ID _____

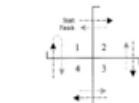


Figure 1. 2002 set-up. The subject starts in square 1, facing square 2. The subject must step over the square 1, sideways to square 2, backward to square 3, sideways to square 4, sideways to square 1, forward to square 2, sideways to square 3, and backward to square 4.

Adapted from: Kohn, 2002, November 2002

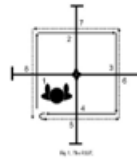


Fig. 1. 2002 set-up

Set-Up

Place tape on the floor as shown above and place 4 canes on top of the tape. **Condition**

I:

Part I: Canes:

Instructions:

"You need to face forward as you step over the canes in a clockwise and counter clockwise direction (demonstration). Both feet must **make contact** with the floor in each square before going to the next square. You can take as many steps in a box as you like. You don't want to hit the canes. You want to do this test as fast as possible, but you want to make sure that you complete the test. I'll start the clock as soon as I say the work Step."

Standing in Square 1 and facing Square 2, step FORWARD into Square 2 Step
SIDEWAYS into Square 3

Step BACKWARDS into Square 4 Step
SIDEWAYS to Square 1

Step SIDEWAYS to Square 4

Step FORWARD to Square 3 Step

SIDEWAYS to Square 2

Step BACKWARD to Square 1

Subject given practice attempt.

Subject completes sequence 2 times. If person is unable to complete: place N/A next to the attempt.

Score: Attempt 1 _____ Attempt 2 _____ Part

II: Tape:

"Now you are going to repeat the test but do not step on the tape. You need to face forward as you step over the tape. I'll start the clock as soon as I say the work Step."

Score: Attempt 1 _____ Attempt 2 _____

Condition 2:

Part I: Canes:

Instructions:

"Now, we are going to repeat the test with an additional instruction. You need to face forward as you step over the canes while keeping your hips forward & not touching the canes. I'll start the clock as soon as I say the work Step." Score: Attempt 1 _____ Attempt 2 _____

Part II: Tape Instructions:

"For this last part, you need to face forward, keep your hips forward, & not step on the tape. I'll start the clock as soon as I say the work Step."

Score: Attempt 1 _____ Attempt 2 _____

Appendix K

NEURO – QOL

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English

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March 6, 2014

Neuro-QOL Item Bank v1.0 – Ability to Participate in Social Roles and Activities – Short Form

Ability to Participate in Social Roles and Activities – Short Form

Please respond to each question or statement by marking one box per row.

In the past 7 days...		Never	Rarely	Sometimes	Often	Always
NQPRF01	I can keep up with my family responsibilities.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPRF03	I am able to do all of my regular family activities.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPRF08	I am able to socialize with my friends.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPRF09	I am able to do all of my regular activities with friends.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPRF17	I can keep up with my social commitments.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPRF26	I am able to participate in leisure activities.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPRF32	I am able to perform my daily routines....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPRF34	I can keep up with my work responsibilities (include work at home).	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

English

Page 1 of 1

March 6, 2014

Neuro-QOL Item Bank v1.0 –Anxiety – Short Form

Anxiety – Short Form

Please respond to each question or statement by marking one box per row.

In the past 7 days...		Never	Rarely	Sometimes	Often	Always
NOA1026	I felt uneasy.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NOA1022	I felt nervous.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NOA1023	Many situations made me worry.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NOA1020	My worries overwhelmed me.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NOA1027	I felt tense.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NOA1028	I had difficulty calming down.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NOA1029	I had sudden feelings of panic.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NOA1027	I felt nervous when my normal routine was disturbed.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

English

Page 1 of 1

March 6, 2014

Neuro-QOL Item Bank v1.0 – Depression – Short Form

Depression – Short Form

Please respond to each question or statement by marking one box per row.

In the past 7 days...		Never	Rarely	Sometimes	Often	Always
NODEP13	I felt depressed.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NODEP23	I felt hopeless.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NODEP27	I felt that nothing could cheer me up.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NODEP27	I felt that my life was empty.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NODEP02	I felt worthless.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NODEP19	I felt unhappy.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NODEP21	I felt I had no reason for living.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NODEP24	I felt that nothing was interesting.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

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Neuro-QOL Item Bank v1.0 – Ability to Participate in Social Roles and Activities – Short Form

Ability to Participate in Social Roles and Activities – Short Form

Please respond to each question or statement by marking one box per row.

In the past 7 days...		Never	Rarely	Sometimes	Often	Always
NQPRF01	I can keep up with my family responsibilities.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPRF02	I am able to do all of my regular family activities.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPRF08	I am able to socialize with my friends.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPRF09	I am able to do all of my regular activities with friends.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPRF17	I can keep up with my social commitments.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPRF26	I am able to participate in leisure activities.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPRF32	I am able to perform my daily routines....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPRF34	I can keep up with my work responsibilities (include work at home).	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

Neuro-QOL Item Bank v1.0 – Emotional and Behavioral Dyscontrol – Short Form

Emotional and Behavioral Dyscontrol – Short Form

Please respond to each question or statement by marking one box per row.

	In the past 7 days...	Never	Rarely	Sometimes	Often	Always
NOPER02	I had trouble controlling my temper.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NOPER05	It was hard to control my behavior.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NOPER06	I said or did things without thinking....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NOPER07	I got impatient with other people.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NOPER11	I was irritable around other people.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NOPER12	I was bothered by little things.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NOPER17	I became easily upset.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NOPER19	I was in conflict with others.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

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Neuro-QOL Item Bank v1.0 –Fatigue – Short Form

Fatigue – Short Form

Please respond to each question or statement by marking one box per row.

In the past 7 days...		Never	Rarely	Sometimes	Often	Always
NQFTG13	I felt exhausted.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQFTG11	I felt that I had no energy.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQFTG15	I felt fatigued.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQFTG08	I was too tired to do my household chores.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQFTG07	I was too tired to leave the house.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQFTG10	I was frustrated by being too tired to do the things I wanted to do.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQFTG14	I felt tired.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQFTG02	I had to limit my social activity because I was tired.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

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Neuro-QOL Item Bank v1.0 – Sleep Disturbance – Short Form

Sleep Disturbance – Short Form

Please respond to each question or statement by marking one box per row.

In the past 7 days...		Never	Rarely	Sometimes	Often	Always
NQBLP02	I had to force myself to get up in the morning.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQBLP03	I had trouble stopping my thoughts at bedtime.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQBLP04	I was sleepy during the daytime.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQBLP05	I had trouble sleeping because of bad dreams.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQBLP07	I had trouble falling asleep.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQBLP12	Pain woke me up.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQBLP13	I avoided or cancelled activities with my friends because I was tired from having a bad night's sleep.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQBLP18	I felt physically tense during the middle of the night or early morning hours.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

Neuro-QOL Item Bank v1.0 – Positive Affect and Well-Being – Short Form

Positive Affect and Well-Being – Short Form

Please respond to each question or statement by marking one box per row.

	Lately... Never	Rarely	Sometimes	Often	Always	
NQPPF14	I had a sense of well-being.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPPF12	I felt hopeful.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPPF15	My life was satisfying.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPPF20	My life had purpose.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPPF17	My life had meaning.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPPF22	I felt cheerful.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPPF19	My life was worth living.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPPF16	I had a sense of balance in my life.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQPPF07	Many areas of my life were interesting to me.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

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Neuro-QOL Item Bank v1.0 -Stigma-Short Form

Stigma-Short Form

Please respond to each question or statement by marking one box per row.

	Lately... Never	Rarely	Sometimes	Often	Always	
NQ8TG02	Because of my illness, some people avoided me.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQ8TG04	Because of my illness, I felt left out of things.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQ8TG 08	Because of my illness, people avoided looking at me.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQ8TG 16	I felt embarrassed about my illness.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQ8TG 01	Because of my illness, some people seemed uncomfortable with me.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQ8TG 17	I felt embarrassed because of my physical limitations.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQ8TG05	Because of my illness, people were unkind to me	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQ8TG21	Some people acted as though it was my fault I have this illness	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

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Neuro-QOL Item Bank v1.1 –Satisfaction with Social Roles and Activities- Short Form

Satisfaction with Social Roles and Activities – Short Form

Please respond to each question or statement by marking one box per row.

In the past 7 days...		Not at all	A little bit	Somewhat	Quite a bit	Very much
NQBAT 03	I am bothered by my limitations in regular family activities	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQBAT 23	I am disappointed in my ability to socialize with my family.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQBAT14	I am bothered by limitations in my regular activities with friends.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQBAT11	I am disappointed in my ability to meet the needs of my friends	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1

In the past 7 days...		Not at all	A little bit	Somewhat	Quite a bit	Very much
NQBAT33	I am satisfied with my ability to do things for fun outside my home.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQBAT32	I am satisfied with the amount of time I spend doing leisure activities.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQBAT47	I am satisfied with how much of my work I can do (include work at home).....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
NQBAT 46	I am satisfied with my ability to do household chores or tasks.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

Cognition Function– Short Form

Please respond to each question or statement by marking one box per row.

In the past 7 days...		Never	Rarely (once)	Sometimes (2-3 times)	Often (once a day)	Very often (several times a day)
NQCOG54H1	I had to read something several times to understand it.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQCOG75H1	My thinking was slow.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQCOG77H1	I had to work really hard to pay attention or I would make a mistake.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQCOG80H1	I had trouble concentrating.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1

How much DIFFICULTY do you currently have...

	None	A little	Somewhat	A lot	Cannot do	
NQCOG22H1	reading and following complex instructions (e.g., directions for a new medication)?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQCOG24H1	planning for and keeping appointments that are not part of your weekly routine, (e.g., a therapy or doctor appointment, or a social gathering with friends and family)?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQCOG25H1	managing your time to do most of your daily activities?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQCOG40H1	learning new tasks or instructions?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1

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Neuro-QOL Item Bank v1.0 – Lower Extremity Function (Mobility) – Short Form

Lower Extremity Function (Mobility) – Short Form

Please respond to each question or statement by marking one box per row.

		Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
NQMOR37	Are you able to get on and off the toilet?...	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQMOR30	Are you able to step up and down curbs?...	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQMOR26	Are you able to get in and out of a car?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQMOR32	Are you able to get out of bed into a chair?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQMOR25	Are you able to push open a heavy door?..	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQMOR33	Are you able to run errands and shop?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQMOR31	Are you able to get up off the floor from lying on your back without help?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NQMOR28	Are you able to go for a walk of at least 15 minutes?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1

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Neuro-QOL Item Bank v1.0 – Upper Extremity Function (Fine Motor, ADL) – Short Form

Upper Extremity Function (Fine Motor, ADL) – Short Form

Please respond to each question or statement by marking one box per row.

		Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
NOUEX29	Are you able to turn a key in a lock?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NOUEX20	Are you able to brush your teeth?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NOUEX44	Are you able to make a phone call using a touch tone key-pad?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NOUEX36	Are you able to pick up coins from a table top?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NOUEX30	Are you able to write with a pen or pencil?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NOUEX28	Are you able to open and close a zipper?...	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NOUEX33	Are you able to wash and dry your body?..	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
NOUEX37	Are you able to shampoo your hair?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1

Appendix L

IRB PHOTO/VIDEO CONSENT FORM



Permission for Video Recordings and Photography

Date _____

Study title: Use of an immersive environment to promote recovery

I hereby give consent to allow a videotape or photograph to be taken of me to be used for educational or research purposes only. This includes use in presentations, in courses taught to students and in publications. I understand that I do not have to allow video to be recorded or photos to be taken in order to participate in the rest of the study.

I understand that during presentation of these video materials, my face will be blocked out so that I am not identifiable to others. All video materials will be stored electronically on password-protected machines. The original video data with my identity will be stored electronically for up to 10 years after the end of the study and then destroyed by wiping all files from hard drives and servers. The video data that has my identity hidden will be kept with other study materials indefinitely.

Subject Name _____

Subject Signature _____

Witness _____

Appendix M

IRB APPROVED CONSENT FORM

UD IRB Approval from 02/01/2018 to 01/29/2019

University of Delaware
Informed Consent Form

Title of Project: Use of an Immersive Environment to Promote Recovery

Principal Investigators: Cole Galloway, PT, PhD and Devina Kumar, PT

You are being asked to participate in a research study. This form tells you about the study including its purpose, what you will be asked to do if you decide to participate, and any risks and benefits of being in the study. Please read the information below and ask the research team questions about anything we have not made clear before you decide whether to participate. Your participation is voluntary and you can refuse to participate or withdraw at any time without penalty or loss of benefits to which you are otherwise entitled. If you decide to participate, you will be asked to sign this form and a copy will be given to you to keep for your reference.

WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this study is to determine whether rehabilitation therapy for people with neurologic impairments can be done in an "immersive environment". "Immersive" means that the therapy is done in a real-world setting and not in the clinic. "Immersive" also means that the therapy is meant to work on physical, mental and social impairments all at the same time. The immersive environment that is the focus of this study is the Go Baby Go Café on the STAR campus. The Go Baby Go Café serves both as a fully functioning business (sales of ice cream and other food and beverages) run by the UD Creamery as well as a place for patients and research subjects to participate in multiple forms of therapy under the direction of a rehabilitation professional in a safe but real world setting as Café employees. In some participants, we will also test the feasibility of using non-invasive brain stimulation within the immersive environment. We will use the approach called transcranial direct current stimulation (tDCS). tDCS is a safe procedure that causes certain areas of the brain to temporarily become more active (i.e., "excitable") that we think helps people learn and perform skills more easily. We think that combining tDCS with the immersive training may provide a powerful stimulus for enhancing physical, mental and social performance in patients with neurological impairments.

We anticipate enrolling 20 individuals in this study. You are being asked to take part in this study because you have a neurologic injury or disease and are able to stand and/or walk. We have also reviewed with you the full study Inclusion and Exclusion Criteria Checklist and you preliminarily appear to be eligible. If you are currently receiving traditional therapy (PT, OT and SLP) for up to 6 hours you may continue to do so and will be in the control group where you will not be exposed to the immersive environment. If you are NOT receiving traditional therapy, you may be eligible to participate in the

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Participant Initials

café and be exposed to the immersive environment. There are a few remaining requirements we must check before we can make a final determination whether or not you can participate. These will be reviewed with you in detail if you agree to participate.

WHAT WILL YOU BE ASKED TO DO?

Clinical Testing and Initial Evaluation Items

There will be two Evaluation sessions within two weeks of each other which will take place on the ground floor of the Health Sciences building on the STAR campus and will take approximately 2-3 hours to complete the functional measures and questionnaires. First, we will make a final determination whether or not you may be eligible to participate in the full study. You will complete two short tests that measure your thinking, memory and communicating abilities and your mood and emotional well-being. If you are not eligible, you will be notified at that time and your participation will end. If you are eligible to participate in at least a portion of the activities, we will continue. If you are eligible to participate in the tDCS portion of the study, you will next be asked to decide whether or not you wish to do so. We think that combining tDCS with the immersive training may provide an enhanced training environment, but you are not required to complete this component if you prefer not to do so.

Next, you will complete several standard clinical tests examining your walking, balance, thinking, memory and other related skills. We will also ask you questions about how your neurologic disease or injury has impacted your daily life. At the end of this evaluation session, you will be asked to wear a Fitbit for the next 7 days during waking hours while you perform your daily routine at home and in the community. The Fitbit is a small, lightweight device that tracks the numbers of steps you take. You will wear the Fitbit around your ankle and bring it back to us to obtain the recorded data.

After this Initial Evaluation and Fitbit recordings are completed, the full study can begin. The study involves testing and training components for those receiving training in the enriched environment. If you are undergoing therapy currently, you will only come for the testing component.

Testing Sessions

In testing sessions, you will return to the STAR campus and repeat many of the same test items you completed at the Initial Evaluation. You may also be asked to wear the

Fitbit again at home. After every two weeks of training sessions, a test session will be done, in which the tests completed during the Initial Evaluation session will be repeated. In addition, you may also be asked to complete a self made measure called "Memory Recall Test" Depending on your progress and interest, you will continue with Café sessions for another 2 weeks, when evaluations will again be completed. This process may be repeated until a maximum of 12 weeks of Café sessions are finished, at which point a final evaluation (using evaluations described under Initial Evaluation section) will be completed. Thus, you may attend up to 6 evaluation sessions lasting 2-3 hours each and up to 36 sessions in the Café lasting up to two hours each.

Upon completion of the intervention, if eligible, you may also be asked to come for a follow up testing session at 1, 3, 6 and 12 months. At the follow up, you will be tested on the same measures that you were tested on at the baseline and during the intervention. The follow up testing session would last about 2-3 hours and would be done at the STAR campus at University of Delaware. This is to see the lasting effect of the intervention. Your participation for the follow up is entirely voluntary and will not affect their participation in the current or future studies.

Training Sessions

All training sessions will take place in the Go Baby Go Café on the STAR campus. The Go Baby Go Café is a free-standing approximately 10'x10' structure that is both a fully functioning small business and a site for patients and research participants to practice physical, mental and social activities under the direction of a rehabilitation therapist in a safe but real-world scenario as Café employees.

It is important to note that the immersive environment makes this project very different from other studies. You will not only be a research participant, but you will also be working as a Go Baby Go Café (unpaid) employee. As such, you will regularly interaction not only with members of the research team, but also with other (non-research) Go Baby Go Café employees and managers, and with the public, who may be customers and/or passers-by.

After the initial testing session, you will participate in the training at the Café 2-3 times per week for 1-2 hours per session, depending on your tolerance. You and the Physical Therapist or individuals trained by the Physical Therapist (who will be considered as part of the research team) will set 1-2 goals each week that will guide the exact activities you will be doing in the sessions. Every Friday, the Physical Therapist will assess the achievement of your weekly goals using the "cueing guidelines" of the Executive Function Performance Test. Your therapy will be intermingled ("immersion")

with your real-world role as Café staff, working alongside paid staff from UD Creamery to serve ice cream and snacks to the public.

Depending on your goals and abilities, Café activities will range from standing at the counter and greeting customers, to taking orders and filling an order for a customer. A member of the Research Team is present at all sessions to help ensure your safety and progression toward goals. While you are in the Café you will wear a harness that is connected to an overhead support system that allows free movement around the Café, but will prevent you from falling if you lose your balance.

If you are eligible, you may also receive brain stimulation (tDCS) at the start of each Café session. Even if eligible, you may choose not to have brain stimulation. Whether you are not eligible or not interested in receiving brain stimulation will in no way exclude you from the study. For participants receiving brain stimulation, we will place electrodes over certain locations on your head and secure them with elastic bands. The electrodes will deliver a direct current stimulation. The stimulation may produce a slight tingling, tickling or itching sensation under the electrodes, but many people do not feel anything at all or only feel something for the first few seconds. The stimulation will last for the first 20 minutes of your Café training sessions. Often during the stimulation, we will ask you how you are feeling. If you report feeling pain, soreness, fatigue or anxiety beyond your level of comfort, we will stop the procedures.

During Café sessions, your heart rate, your Rate of Perceived Exertion (a measure of how hard you feel you are working), and number of steps taken recorded via the Fitbit, will be tracked.

If you permit, you may also be video-taped or photographed so that later we can go back and evaluate certain activities. Whether or not you agree to have video recordings made of you, you may still participate in the other components of the study

At the end of the study, you may be asked to complete a short survey asking you about your experience of this novel intervention in an enriched environment. This is not mandatory and will not affect your future participation in any future studies at the University of Delaware.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Physical risks include loss of balance, fall, small cuts, bruises or fatigue during testing or during Café sessions. For those participating in the tDCS, many people do not feel the tDCS at all, but there is a risk you may feel a tingling, burning, or itching sensation under the electrode, which is usually described as annoying but not uncomfortable or painful. If it occurs, it typically subsides very quickly.

Psychological risks include possible discomfort, frustration, anxiety and/or embarrassment during testing or training sessions because some activities may be difficult to perform. There may be added anxiety or embarrassment during Café training sessions because these (deliberately) take place in public in a highly visible and highly trafficked location. In addition, it is important to realize that the research team does not control who comes in and out of the building and who may pass by or speak to you at the Café. Although it is not anticipated, there may be unexpected, or potentially negative, interactions with members of the public, just as you might encounter in your everyday life. Your privacy is not guaranteed in this public training environment.

To minimize risks of loss of balance, fall or fatigue, all movement testing is completed by a Physical Therapist and you will be appropriately guarded at all times using standard clinical safety procedures (e.g.-use of a gait belt and/or over-ground harness system when needed). During Café sessions, you will wear a harness connected to an overhead support to minimize the risk of falls. A member of the research team will attend all Café sessions to help ensure your safety and to intervene if you become overly frustrated or tired. To minimize the risks of cuts, burns and bruises associated with handling hot drinks or the coffee machine, a research team member will make sure all appropriate precautionary measures are taken. You can always request to end a session early due to fatigue, frustration etc. For subjects completing tDCS, we use well established parameters that have been demonstrated to be safe and effective for human brain stimulation for over 10 years. To minimize itching or burning sensations, we slowly ramp up and ramp down the delivery of electrical current, which makes it only mildly uncomfortable, if it is perceived at all.

To minimize risks of frustration, anxiety or embarrassment, we will fully explain to you and give you examples of the kinds of encounters we expect you will have and also some examples of potentially negative encounters you might have so that you can be aware and informed. In addition, members of the research team can intervene if any particularly difficult situation arises, which might include ending the session early. Again, you can always request to end a session early for any reason.

WHAT ARE THE POTENTIAL BENEFITS?

There may be no direct benefits to you for participating. However, it is possible that you may increase your balance and/or daily physical activity, improve your communication and/or feel more confident in your abilities. The future benefit to others from this study is an understanding of the pros and cons of using this type of immersive environment to work on a variety of impairments to improve recovery from neurologic injury/disease.

HOW WILL CONFIDENTIALITY BE MAINTAINED?

Your participation in this study and the follow up requires us to collect some personal information from you. Any information you provide that could identify who you are (e.g., your name, your date of birth, etc.) will be stored in paper format in a locked file cabinet or electronically on encrypted and password-protected computers or servers.

You may be asked to be videotaped or photographed during this research. If you agree to this, the videotape or photograph will be used for educational or research purposes only. This includes use in presentations, in courses taught to students and in publications

The major outcomes of this study are the data we collect at the Initial Evaluation followed by every other week up to 12 weeks of sessions. These data, and all other information we collect will be de-identified, meaning that we will replace your personal information with a numerical code. The key linking subject code numbers with individual names will be maintained on an encrypted and password-protected computer.

No identifying information will be used in any presentations or publications that result from this study. De-identified data may be presented in abstract, poster, presentation, or published manuscript format. Data with identifying information will be saved for 10 years after the project is complete or the data are published, whichever comes first. Once the study is completed, all identifying information will be destroyed through shredding and wiping files from hard drives and servers. De-identified data will be stored indefinitely and may be used in future related studies by members of the research team. Data will not be shared with outside teams of researchers.

Your research records may be viewed by the University of Delaware Institutional Review Board, but the confidentiality of your records will be protected to the extent permitted by law.

Please note that because the training is performed in a fully public environment, the research team cannot prevent you from being identified or possibly recorded by Café customers or any other passers-by during Café sessions.

WILL THERE BE ANY COSTS RELATED TO THE RESEARCH?

There are no costs associated with your participation in this research.

WILL THERE BE ANY COMPENSATION FOR PARTICIPATION?

Yes. For your time and participation, you will be given a \$100 gift card of a local store upon completion of the study.

WHAT IF YOU ARE INJURED DURING YOUR PARTICIPATION IN THE STUDY?

If you are injured during research procedures, you will be offered first aid at no cost to you. If you need additional medical treatment, the cost of this treatment will be your responsibility or that of your third-party payer (for example, your health insurance). By signing this document you are not waiving any rights that you may have if injury was the result of negligence of the university or its investigators.

DO YOU HAVE TO TAKE PART IN THIS STUDY?

Taking part in this research study and the follow up is entirely voluntary. You do not have to participate in this research. If you choose to take part, you have the right to stop at any time. If you decide not to participate or if you decide to stop taking part in the research at a later date, there will be no penalty or loss of benefits to which you are otherwise entitled. Your refusal will not influence current or future relationships with the University of Delaware.

You may choose not to participate in the tDCS component of the study and this will not affect your ability to participate in other aspects of the study. Please initial at the appropriate location below to indicate whether or not you wish to have tDCS:

_____ I DO want to do the
part of the study
(subject initials)

_____ I DO NOT want to do the tDCS
part of the study
(subject initials)

_____ Subject IS eligible for tDCS
(researcher initials)

_____ Subject IS NOT eligible for tDCS
(researcher initials)

You can also choose not to undergo video recording and/or photography, also without affecting your ability to participate in other aspects of the study. You can indicate your desire to participate in video by signing a separate video/photography release form.

Your participation in the study could be terminated by the investigators if we deem it inappropriate for you to continue, if your status changes such that we think you fail to meet all inclusion/exclusion criteria, if your participating may place you at risk medically or psychologically, and/or if we experience technical problems with data collection that prevent collection of useable data.

WHO SHOULD YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

If you have any questions about this study, please contact one of the Principal Investigators, Cole Galloway or Devina Kumar at (302)831 3697 or (215) 512-1323. If you have any questions or concerns about your rights as a research participant, you may contact the University of Delaware Institutional Review Board at 302-831-2137.

Your signature below indicates that you are voluntarily agreeing to take part in this research study. You have been informed about the study's purpose, procedures, possible risks and benefits. You have been given the opportunity to ask questions about the research and those questions have been answered. You will be given a copy of this consent form to keep.

Signature of Participant

Date

Printed Name of Participant

Page 8 of 8
Participant Initials

Appendix N

PARENTAL GUARDIAN PERMISSION FORM

UD IRB Approval from 02/01/2018 to 01/29/2019

University of Delaware
Parental Permission Form

Title of Project:

Use of an Immersive Environment to Promote Recovery

Principal Investigators: Cole Galloway, PT, PhD and Devina Kumar, PT

Your child or ward is being asked to participate in a research study. This form tells you about the study including its purpose, what participants will be asked to do if you allow them to participate, and any risks and benefits of being in the study. Please read the information below and ask the research team questions about anything we have not made clear before you decide whether your child or ward can participate. His or her participation is voluntary and you can refuse to allow them to participate or request to withdrawal at any time without penalty or loss of benefits to which you are otherwise entitled. If you decide to let your child or ward participate, you will be asked to sign this form and a copy will be given to you to keep for your reference. For the rest of the form, your child or ward may be referred to as a "participant".

WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this study is to determine whether rehabilitation therapy for people with neurologic impairments can be done in an "immersive environment". "Immersive" means that the therapy is done in a real-world setting and not in the clinic. "Immersive" also means that the therapy is meant to work on physical, mental and social impairments all at the same time. The immersive environment that is the focus of this study is the Go Baby Go Café on the STAR campus. The Go Baby Go Café serves both as a fully functioning business (sales of ice cream and other food and beverages) run by the UD Creamery as well as a place for patients and research subjects to participate in multiple forms of therapy under the direction of a rehabilitation professional in a safe but real world setting as Café employees. In some participants, we will also test the feasibility of using non-invasive brain stimulation within the immersive environment. We will use the approach called transcranial direct current stimulation (tDCS). tDCS is a safe procedure that causes certain areas of the brain to temporarily become more active (i.e., "excitable") that we think helps people learn and perform skills more easily. We think that combining tDCS with the immersive training may provide a powerful stimulus for enhancing physical, mental and social performance in patients with neurological impairments.

We anticipate enrolling 20 individuals in this study. Your child or ward is being asked to take part in this study because he/she a neurologic injury or disease and are able to stand and/or walk. We have also reviewed with you the full study Inclusion and Exclusion Criteria Checklist and the participant preliminarily appears to be eligible. If you child or ward is currently receiving traditional therapy (PT, OT and SLP) for up to 6 hours he may continue to do so. He/she will be in the control group where he/she will not be exposed to the immersive environment. If your child or ward is NOT receiving traditional therapy, he/she may be eligible to participate in the café and be exposed to the immersive environment. There are a few remaining requirements we must check before we can make a final determination regarding eligibility for participation. These will be reviewed with you in detail if you agree to allow your child or ward to participate.

WHAT WILL PARTICIPANTS BE ASKED TO DO?

Clinical Testing and Initial Evaluation Items

There will be two Evaluation sessions within two weeks of each other which will take place on the ground floor of the Health Sciences building on the STAR campus and will take approximately 2-3hours to complete the functional measures and questionnaires. First, we will make a final determination whether or not the participant may be eligible to participate in the full study. The participant will complete two short tests that measure thinking, memory and communicating abilities, mood and emotional well-being. If the participant is not eligible, you will be notified at that time and his/her participation will end. If the participant is eligible to participate in at least a portion of the activities, we will continue. If the participant is eligible to participate in the tDCS portion of the study, he/she will next be asked to decide whether or not they wish to do so. We think that combining tDCS with the immersive training may provide an enhanced training environment, but he/she is not required to complete this component if you prefer them not to do so.

Next, the participant will complete several standard clinical tests examining walking, balance, thinking, memory and other related skills. We will also ask questions about how the neurologic disease or injury has impacted his/her daily life. At the end of this evaluation session, the participant will be asked to wear a Fitbit for the next 7 days during waking hours while performing daily routine at home and in the community. The Fitbit is a small, lightweight device that tracks the numbers of steps one take. He/she will wear the Fitbit around their ankle and bring it back to us to obtain the recorded data.

After this Initial Evaluation and Fitbit recordings are completed, the full study can begin. The study involves testing and training components for those receiving training in the enriched environment. If you child or ward is undergoing therapy currently, he/she will only come for the testing component.

Testing Sessions

In testing sessions, you will return to the STAR campus with them and we will repeat many of the same test items the participant completed at the Initial Evaluation. The participant may also be asked to wear the Fitbit again at home. After every two weeks of training sessions, a test session will be done, in which the tests completed during the Initial Evaluation session will be repeated. In addition, the participant may also be asked to complete a self made measure called "Memory Recall Test". Depending on his/her progress and interest, the participant will continue with Café sessions for another 2 weeks, when evaluations will again be completed. This process may be repeated until a maximum of 12 weeks of Café sessions are finished, at which point a final evaluation (using evaluations described under Initial Evaluation section) will be completed. Thus, the participant may attend up to 6 evaluation sessions lasting 2-3 hours each and up to 36 sessions in the Café lasting up to two hours each.

Upon completion of the intervention, if eligible, the participant may also be asked to come for a follow up testing session at 1, 3, 6 and 12 months. At the follow up, the will be tested on the same measures that they were tested on at the baseline and during the intervention. The follow up testing session would last about 2-3 hours and would be done at the STAR campus at University of Delaware. This is to see the lasting effect of the intervention. Their participation for the follow up is entirely voluntary and will not affect their participation in the current or future studies.

Training Sessions

All training sessions will take place in the Go Baby Go Café on the STAR campus. The Go Baby Go Café is a free-standing approximately 10'x10' structure that is both a fully functioning small business and a site for patients and research participants to practice physical, mental and social activities under the direction of a rehabilitation therapist in a safe but real-world scenario as Café employees.

It is important to note that the immersive environment makes this project very different from other studies. The participant will not only be a research participant, but will also be working as a Go Baby Go Café (unpaid) employee. As such, the participant will regularly interaction not only with members of the research team, but also with other (non-research) Go Baby Go Café employees and managers, and with the general public, who may be customers and/or passers-by.

After the initial testing session, the participant will participate in the training at the Café 2-3 times per week for 1-2 hours per session, depending on his/her tolerance. You or a personal assistant will have to attend all the training sessions with the participant. The participant and the Physical Therapist or individuals trained by the Physical Therapist (who will be considered as part of the research team) will set 1-2 goals each week that will guide the exact activities the participant will be doing in the sessions. Every Friday, the Physical Therapist will assess the achievement of the participant's weekly goals using the "cueing guidelines" of the Executive Function Performance Test. His/her

therapy will be intermingled ("immersion") with your real-world role as Café staff, working alongside paid staff from UD Creamery to serve ice cream and snacks to the public.

Depending on the participant goals and abilities, Café activities will range from standing at the counter and greeting customers, to taking orders and filling an order for a customer. A member of the Research Team is present at all sessions to help ensure the participant safety and progression toward goals. While you are in the Café the participant will wear a harness that is connected to an overhead support system that allows free movement around the Café, but will prevent the participant from falling if he/she loses balance.

If the participant are eligible, he/she may also receive brain stimulation (tDCS) at the start of each Café session. Even if eligible, you may choose for them to not to have brain stimulation. Whether the participant are not eligible or not interested in receiving brain stimulation will in no way exclude the participant from the study. For participants receiving brain stimulation, we will place electrodes over certain locations on your head and secure them with elastic bands. The electrodes will deliver a direct current stimulation. The stimulation may produce a slight tingling, tickling or itching sensation under the electrodes, but many people do not feel anything at all or only feel something for the first few seconds. The stimulation will last for the first 20 minutes of their Café training sessions. Often during the stimulation, we will ask the participant how he/she is feeling. If the participant report feeling pain, soreness, fatigue or anxiety beyond his/her level of comfort, we will stop the procedures.

During Café sessions, the participants heart rate, your Rate of Perceived Exertion (a measure of how hard you feel you are working), and number of steps taken recorded via the Fitbit, will be tracked.

If you permit, he/she may also be video-taped or photographed so that later we can go back and evaluate certain activities. Whether or not you agree to have video recordings made of the participant, he/she may still participate in the other components of the study

At the end of the study, the participant may be asked to complete a short survey asking him/her about their experience of this novel intervention in an enriched environment. This is not mandatory and will not affect their future participation in any future studies at the University of Delaware

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Physical risks include loss of balance, fall, small cuts, bruises or fatigue during testing or during Café sessions. For those participating in the tDCS, many people do not feel the tDCS at all, but there is a risk the participant may feel a tingling, burning, or itching

sensation under the electrode, which is usually described as annoying but not uncomfortable or painful. If it occurs, it typically subsides very quickly.

Psychological risks include possible discomfort, frustration, anxiety and/or embarrassment during testing or training sessions because some activities may be difficult to perform. There may be added anxiety or embarrassment during Café training sessions because these (deliberately) take place in public in a highly visible and highly trafficked location. In addition, it is important to realize that the research team does not control who comes in and out of the building and who may pass by or speak to the participant at the Café. Although it is not anticipated, there may be unexpected, or potentially negative, interactions with members of the public, just as the participant might encounter in his/her the participant everyday life. The participant's privacy is not guaranteed in this public training environment.

To minimize risks of loss of balance, fall or fatigue, all movement testing is completed by a Physical Therapist and the participant will be appropriately guarded at all times using standard clinical safety procedures (e.g.-use of a gait belt and/or over-ground harness system when needed). During Café sessions, the participant will wear a harness connected to an overhead support to minimize the risk of falls. A member of the research team will attend all Café sessions to help ensure his/her safety and to intervene if he/she become overly frustrated or tired. In such cases, sufficient rest breaks/decrease in task frequency or termination of that session would be allowed. To minimize the risks of cuts, burns and bruises associated with handling hot drinks or the coffee machine, a research team member will make sure all appropriate precautionary measures are taken. The participant can always request to end a session early due to fatigue, frustration etc. For subjects completing tDCS, we use well established parameters that have been demonstrated to be safe and effective for human brain stimulation for over 10 years. To minimize itching or burning sensations, we slowly ramp up and ramp down the delivery of electrical current, which makes it only mildly uncomfortable, if it is perceived at all.

To minimize risks of frustration, anxiety or embarrassment, we will fully explain to the participant and give you examples of the kinds of encounters we expect him/her to have and also some examples of potentially negative encounters they might have so that they can be aware and informed. You or the participant's personal assistant will also assist us in identifying these psychological issues early on. In addition, members of the research team can intervene if any particularly difficult situation arises, which might include ending the session early. Again, the participant can always request to end a session early for any reason.

WHAT ARE THE POTENTIAL BENEFITS?

There may be no direct benefits to your child or wards participation in this study. However, it is possible that the participant may have an increase in balance and/or daily physical activity, improved communication and/or feel more confident in his/her abilities. The future benefit to others from this study is an understanding of the pros and cons of using this type of immersive environment to work on a variety of impairments to improve recovery from neurologic injury/disease.

HOW WILL CONFIDENTIALITY BE MAINTAINED?

Your child or wards participation in this study and the follow up requires us to collect some personal information from you. Any information you provide that could identify who they are (e.g.name, your date of birth, etc.) will be stored in paper format in a locked file cabinet or electronically on encrypted and password-protected computers or servers.

You may be asked if they can be videotaped or photographed during this research. If you agree to this, the videotape or photograph will be used for educational or research purposes only. This includes use in presentations, in courses taught to students and in publications

The major outcomes of this study are the data we collect at the Initial Evaluation followed by every other week up to 12 weeks of sessions. These data, and all other information we collect will be de-identified, meaning that we will replace their personal information with a numerical code. The key linking subject code numbers with individual names will be maintained on an encrypted and password-protected computer.

No identifying information will be used in any presentations or publications that result from this study. De-identified data may be presented in abstract, poster, presentation, or published manuscript format. Data with identifying information will be saved for 10 years after the project is complete or the data are published, whichever comes first. Once the study is completed, all identifying information will be destroyed through shredding and wiping files from hard drives and servers. De-identified data will be stored indefinitely and may be used in future related studies by members of the research team. Data will not be shared with outside teams of researchers.

Your research records may be viewed by the University of Delaware Institutional Review Board, but the confidentiality of your records will be protected to the extent permitted by law.

Please note that because the training is performed in a fully public environment, the research team cannot prevent you from being identified or possibly recorded by Café customers or any other passers-by during Café sessions.

WILL THERE BE ANY COSTS RELATED TO THE RESEARCH?

There are no costs associated with your child or wards participation in this research.

WILL THERE BE ANY COMPENSATION FOR PARTICIPATION?

Yes. For you time and participation in this project, you will be provided with a gift card of \$100. This would be given upon completion of the study.

WHAT IF THE PARTICIPANT IS INJURED DURING PARTICIPATION IN THE STUDY?

If the participant is injured during research procedures, he/she will be offered first aid at no cost to you. If he/she needs additional medical treatment, the cost of this treatment will be your responsibility or that of your third-party payer (for example, your health insurance). By signing this document you are not waiving any rights that your child or ward may have if injury was the result of negligence of the university or its investigators.

DOES THE PARTICIPANT HAVE TO TAKE PART IN THIS STUDY?

Taking part in this research study and the follow up is entirely voluntary. Your child or ward does not have to participate in this research. If you choose to let them take part, you have the right to stop at any time. If you decide not to let him/her participate or if you decide to stop him/her from taking part in the research at a later date, there will be no penalty or loss of benefits to which you are otherwise entitled. Your refusal will not influence current or future relationships with the University of Delaware.

You may choose to not let your child or ward participate in the tDCS component of the study and this will not affect his/her ability to participate in other aspects of the study. Please initial at the appropriate location below to indicate whether or not you wish for them to have tDCS:

_____ I DO want my child/ward to do the _____ I DO NOT want my child/ward
(Subject initials) tDCS part of the study (Subject initials) to do tDCS part of the study

_____ Subject IS eligible for tDCS
(Researcher initials)

_____ Subject IS NOT eligible for tDCS
(Researcher initials)

You can also choose to not allow video recording and/or photography, also without affecting his/her ability to participate in other aspects of the study. You can indicate your desire to his/her participation in video by signing a separate video/photography release form.

Your child or ward's participation in the study could be terminated by the investigators if we deem it inappropriate for him/her to continue, if your status changes such that we think he/she fail to meet all inclusion/exclusion criteria, if his/her participating may place them at risk medically or psychologically, and/or if we experience technical problems with data collection that prevent collection of useable data.

WHO SHOULD YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

If you have any questions about this study, please contact one of the Principal Investigators, Cole Galloway or Devina Kumar at (302)831 3697 or (215) 512-1323. If you have any questions or concerns about your rights as a family member /guardian, you may contact the University of Delaware Institutional Review Board at 302-831-2137.

Your signature below indicates that you are voluntarily agreeing to take part in this research study. You have been informed about the study's purpose, procedures, possible risks and benefits. You have been given the opportunity to ask questions about the research and those questions have been answered. You will be given a copy of this consent form to keep.

Signature of family member/guardian

Date

Printed Name of family member/guardian

Appendix O

ASSENT FORM

UD IRB Approval from 02/01/2018 to 01/29/2019

ASSENT TO PARTICIPATE IN RESEARCH

Title of Project: Use of an Immersive Environment to Promote Recovery

Investigator(s): Cole Galloway, PT, PhD and Devina Kumar, PT

I am asking if you want to be part of a research study. This form tells you what the study is about, what you will be asked to do if you want to be in the study, and the possible bad and good things about this study. Please read this paper and ask us any questions you have.

WHAT IS THE PURPOSE OF THIS STUDY?

This study is to learn whether working as a volunteer in the Go Baby Go Café on the STAR campus helps people with brain injuries.

Some people who are in the study will wear a cap that includes a brain stimulator while they work in the café. The stimulator uses magnets to cause certain parts of the brain to become more active for a short time. We think that combining stimulation and working in the café may help more than working in the café without stimulation.

You are being asked because you have a brain injury and are able to stand and/or walk. If you want to be in the study, we have a few other questions and activities for you to do to see if the study is right for you.

WHAT WILL YOU BE ASKED TO DO?

Measuring what you can do for the first time

There will be two visits over two weeks. Each visit will be 3 hours or less. These sessions are at the University of Delaware. Each visit you will answer questions and do activities to show your abilities. These questions and activities will let you show us how you think and move. After the two sessions, we can tell you whether the study is right for you.

Measuring what you can do every two weeks

After you start the study, we will repeat the same questions and activities that we did before you started the study. This is to see if working in the café or traditional therapy is helping you.

Measuring what you can do after you complete the study

After you complete the study, you may come back after a few months to do the same tests you did before. This is to see if the changes seen during the café or while getting traditional therapy remained even after the study was over.

Working in the Café

If you are working in the café, it should be fun and challenging. Every time you are working you will have a helper in the café with you as well as your family/guardian sitting beside the café. You will also work with other people working in the café to serve the customers.

What will you do during your work time? Depending on your abilities, Café activities will range from standing at the counter and greeting customers, to taking orders and filling an order for a customer. A member of the Research Team is with you to help you working towards your goals. While you are in the Café you will wear a harness that is connected to an overhead support system that allows you to move around the Café.

If you are eligible, you may also receive brain stimulation (tDCS) at the start of each Café session. Even if eligible, you may choose not to have brain stimulation. We will place electrodes on your head and secure them with elastic bands. The electrodes will cause a slight tingling, tickling or itching sensation under the electrodes, but many people do not feel anything. The stimulation will last for the first 20 minutes of your Café training sessions. Often during the stimulation, we will ask you how you are feeling. If you report feeling pain, soreness, fatigue or anxiety, we will stop.

During Café sessions, your heart rate, how hard you feel you are working, and the number of steps will be tracked.

If you permit, you may also be video-taped or photographed so that later we can go back and review your activities in the café.

If you are getting traditional therapy, then you do not need to come to the café. We will only meet every two weeks for measuring your ability to do different things.

WHAT ARE THE POSSIBLE BAD THINGS ABOUT THIS RESEARCH?

Some of risks include loss of balance, fall, small cuts, bruises or fatigue during testing or during Café sessions. For those participating in the tDCS, many people do not feel the tDCS at all, but there is a risk you may feel a tingling, burning, or itching sensation under the electrode, which is usually described as annoying but not uncomfortable or painful. If it occurs, it typically stops very quickly. You might also have discomfort, anxiety and/or embarrassment during testing or training sessions because some activities may be difficult to perform.

To minimize risks of loss of balance, fall or fatigue, testing is completed by a trained researcher and you will be guarded at all times using a gait belt and/or a harness system when needed.

During Café sessions, you will wear a harness connected to an overhead support to minimize the risk of falls. A member of the research team will attend all Café sessions to help ensure your safety and to intervene if you become overly frustrated or tired. In such cases, sufficient rest breaks/decrease in task frequency or ending of that session would be allowed.

To reduce the chances that you will get hurt with hot drinks or the coffee machine one of our research team members will check on you. You can always tell us you want to stop at any time if you get tired or frustrated. For subjects completing tDCS, we use guidelines that have been shown to be safe and effective for human brain stimulation for over 10 years. To minimize itching or burning sensations, we slowly ramp up and ramp down the delivery of electrical current, which makes it only mildly uncomfortable, if it is felt at all.

To decrease risks of frustration, anxiety or embarrassment, we will fully explain to you and give you examples of the kinds of activities you will perform and also examples of possible encounters you might have. Your family member/guardian and/or personal assistant will also assist us in situations that may be stressful. A researcher will intervene if a difficult situation arises, which might include ending the session early if you would like. Again, you can always request to end a session early for any reason.

WHAT ARE THE POTENTIAL GOOD THINGS ABOUT IT?

There may be no direct benefits to you for participating. However, it is possible that you may increase your balance and/or daily activity, improve your communication and/or feel more confident in your abilities.

The future benefit to others from this study is an understanding of the benefits of using the café for others.

WHO MAY KNOW THAT YOU PARTICIPATED IN THIS RESEARCH?

We will have to collect some personal information from you. Any information you provide that could identify who you are (e.g., your name, your date of birth, etc.) will be stored in paper format in a locked file cabinet or electronically on password-protected computers or servers.

All data will be de-identified, meaning that we will replace your personal information with a numerical code. De-identified data may be presented in abstract, poster, presentation, or published manuscript format. Data with identifying information will be saved for 10 years after the project is complete or the data are published, whichever comes first.

We may also if you can be videotaped or photographed. If you agree to this, the videotape or photograph will be used for educational or research purposes, in classes taught to students and in publications. No information that can identify you will be used in any presentations or publications that result from this study.

Please note that because the training is performed in a fully public environment, the research team cannot prevent you from being identified or possibly recorded by Café customers or any other passers-by during Café sessions.

WILL YOU RECEIVE ANY COMPENSATION FOR PARTICIPATION?

Yes, you will get \$100 gift card from a local store. This for your time and participation in the study.

CAN YOU CHANGE YOUR MIND ABOUT BEING IN THE STUDY?

You do not have to participate in this study or come back for testing once it's over. Taking part in this research study or coming back for the testing again is up to you. If you choose to take part, you can change your mind and stop at any time. If you decide not to participate or if you decide to stop taking part in the research later, there is no penalty. If, at any time, you decide to stop please let us know by telling one of the researchers.

You may choose not to participate in the tDCS component of the study and this will not affect your ability to participate in other aspects of the study. Please initial at the appropriate location below to indicate whether or not you wish to have tDCS:

_____ I DO want to do the tDCS part of the study the study (subject initials)	_____ I DO NOT want to do the tDCS part of (subject initials)
_____ Subject IS eligible for tDCS (researcher initials)	_____ Subject IS NOT eligible for tDCS (researcher initials)

You can also choose not to undergo video recording and/or photography, also without affecting your ability to participate in other aspects of the study. You can indicate your desire to participate in video by signing a separate video/photography release form.

Your participation in the study could be terminated by the investigators if we deem it inappropriate for you to continue, if your status changes such that we think you fail to meet all inclusion/exclusion criteria, if your participating may place you at risk medically or psychologically, and/or if we experience technical problems with data collection that prevent collection of useable data.

WHO SHOULD YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

If you have any questions about this study, please tell Dr. Cole Galloway (PI) at (302)831 3697 or Devina Kumar at (215) 512-1323

If you have any questions or concerns about your rights as a research participant, you may contact the University of Delaware Institutional Review Board at hsrb-research@udel.edu or (302) 831-2137.

If you want to participate, and we have answered all of your questions about it, please sign below.

Printed Name of Participant

Signature of Participant

Date

Person Obtaining Consent
(PRINTED NAME)

Person Obtaining Consent
(SIGNATURE)

Date

Appendix P

SURVEY QUESTIONNAIRE

SURVEY QUESTIONS FOR GO BABY GO CAFÉ RESEARCH STUDY

1. On a scale of 1 – 10 with 10 being the most positive, how satisfied were you with your previous outpatient rehabilitation?

☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10

Very negative > Barely Positive > Somewhat Positive > Mostly Positive > Very Positive

2. On a scale of 1 – 10 with 10 being the most positive, how satisfied were you with the rehabilitation intervention at the Go Baby Go Café?

☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10

Very negative > Barely Positive > Somewhat Positive > Mostly Positive > Very Positive

3. On a scale of 1 – 10 with 10 being the most positive, how likely are you to prefer this over conventional therapy?

☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10

Very negative > Barely Positive > Somewhat Positive > Mostly Positive > Very Positive

4. On a scale of 1 – 10 with 10 being the most positive, how would likely are you to continue volunteering at the Go Baby Go Café?

☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10

Very negative > Barely Positive > Somewhat Positive > Mostly Positive > Very Positive

5. On a scale of 1 – 10 with 10 being the most positive, how would you describe the approach of rehabilitation at the Go Baby Go Café? (address social, cognitive, physical and communication impairments at the same time in a real world enriched environment)

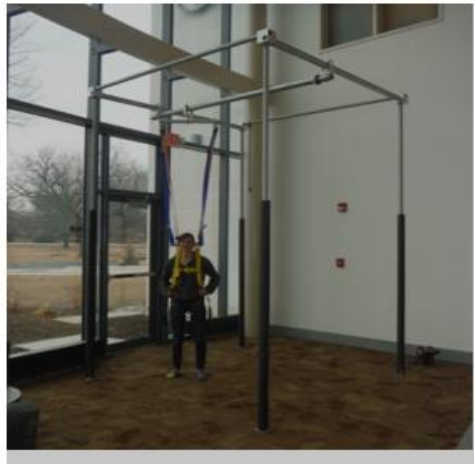
☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10

Very negative > Barely Positive > Somewhat Positive > Mostly Positive > Very Positive

Appendix Q

OASUS

ENLITEN OASUS Open Area Support System



The Enliten OASUS system provides fall limit support over an area while allowing the user the freedom to engage in general activity with no limitations and no fear of falling. The free-standing unit can be custom fitted to any area up to 12 by 20 feet. Larger areas can be accommodated with additional intermediate support legs. All these units are engineered for users up to 300 pounds, but they can be custom designed to meet any patient weight. Set-up takes about an hour and then you are ready to go... literally. No modifications are needed to the building and nothing is attached to the surroundings. Use it for a room at home, a small business, a physical therapy clinic or even a sales kiosk. The four support legs can be positioned to reduce intrusion within the building giving open access to the entire area within the system footprint. Price is based on size and options but starts at around \$3,000. Isn't it time you started moving safely?

The OASUS has three primary components: the frame, the harness support and the harness. Each portion can be customized to fit your particular needs. Frame areas typically range from 6 by 6 foot squares up to 12 foot by greater than 20 foot rectangles. Leg height is typically 8 or 9 feet. The frame and associated support hardware are designed for users up to 350 pounds. Connecting the frame to the harness is the harness support. For fall arrest, it can be as simple as a spreader bar with two adjustable vertical straps. By changing out the spreader bar for an "H"-shaped spreader frame and adding four elastic supports, biased body weight support can be achieved to give the user a lift at every step. Any harness with connection points at the shoulders can be used. Standard

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units use a commercial rescue harness that is adjustable to fit users from 5 feet to 6 feet 4 inches tall weighing between 140 and 300 pounds.

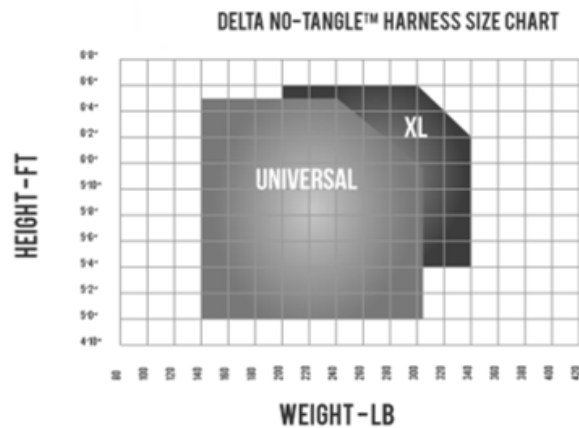
Standard Harness:

The standard harness supplied with an OASUS system is a Delta No Tangle Vest Style Harness with Stand Up Rear D-ring, Shoulder Retrieval D-rings and Tongue Buckle Leg Straps. It is shown below.



This harness features:

- Exclusive No-Tangle design
- Spring-loaded stand-up back D-ring
- Quick adjust shoulder straps with ratchet windup
- Adjustable non-slip chest strap with easy to use quick connect buckle
- Two shoulder retrieval D-rings to connect to the support frame
- Polyester webbing construction
- Easy adjust, tongue buckle leg straps



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