Quantitative Assessment of Post-Concussion Syndrome following Mild Traumatic Brain Injury using Robotic Technology

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***Abstract*— Post-Concussion Syndrome (PCS) is a common sequelae of mild Traumatic Brain Injury (mTBI). Currently, there is no reliable test to determine which patients will develop PCS following an mTBI. As a result, clinicians are challenged to identify patients at high risk for subsequent PCS. Hence, there is a need to develop an objective test that can guide clinical risk stratification and predict the likelihood of PCS at the initial point of care in an Emergency Department (ED). This paper presents the results of robotic-assisted neurologic testing completed on mTBI patients in the ED and its ability to predict PCS at 3 weeks post-injury. Preliminary results show that abnormal proprioception, as measured using robotic testing is associated with higher risk of developing PCS following mTBI. In this pilot study, proprioceptive measures obtained through robotic testing had a 77% specificity (95CI: 46% - 94%) and a 64% sensitivity (95CI: 41% - 82%).**

I. Introduction

Traumatic Brain Injury (TBI) is a global health problem, annually affecting over 10 million people worldwide [1]. In the United States, about 1.7 million people sustain a TBI every year [2]. Specifically, an annual average of approximately 53,000 TBI-related deaths were reported during 1997-2007 among United States residents [3]. Thus, TBI is a major cause of mortality and morbidity in the U.S.

TBI is often classified based on the severity of the injury as mild, moderate, and severe TBI. Traditionally, clinicians use the Glasgow Coma Scale (GCS) to determine the severity of injury in TBI patients based on eye, motor, and verbal responses to stimuli. A GCS of 13-15 after head injury is considered as mild TBI (mTBI). Mild TBI is defined as an acute brain injury to the head as a result of blunt trauma, external physical forces, or rapid acceleration/deceleration [4, 5]. Mild TBI constitutes 70% to 90% of all treated TBI cases and the reported incidence rate of mTBI is around 100 to 300 per 100,000 people [4]. However, it is important to note that a significant number of mTBI cases may not be reported [6] because patients were seen in outpatient clinics or they decided not to seek medical assistance, the latter being more likely in the mTBI population. Overall, the actual overall incidence rate of mTBI may approach 600/100,000 people.

Patients sustaining an mTBI often suffer from post-concussion symptoms or post-concussive syndrome (PCS), which include a wide spectrum of emotional, physical, and psychological complaints such as headache, fatigue, cognitive impairment, depression, dizziness, irritability and sleep problems [7]. PCS is defined as the presence of three or more such symptoms, occurring in weeks or months post injury [8]. Studies have shown that post-concussion symptoms can persist for up to a year following injury [9, 10]. Currently, there are no reliable and validated tools to prospectively identify mTBI patients at high risk of developing PCS. Thus, it remains unknown who would benefit from outpatient follow up or who may be target for therapeutic interventional trials. Furthermore, post-concussive symptoms are commonly associated with other neurological disorders, making it difficult to prognosticate PCS in mTBI patients presenting to the Emergency Department (ED) [11]. One of the major goals of our research is to evaluate the utility of advanced robotic technology in the assessment of neurologic function following mTBI.

The focus of this study is to assess the prognostic value of robotic-assisted neurologic tests. Specifically, we explore the connection between diminished performance on a robotic-assisted test of proprioception (the awareness of position, orientation, and movement of one's body and its parts) obtained within 24-hours of mTBI and the prevalence of PCS, three weeks post injury. Of particular interest to our study is the position sense component of proprioception, which describes the conscious perception of relative position of different body parts [13].

II. Background

A. Apparatus

The Kinesiological Instrument for Normal and Altered Reaching Movement (KINARM®) End-Point system (BKIN Technologies, Kingston, Ontario, Canada), is a robotic device that can detect subtle injury deficits [14] by assessing multiple neurological domains (e.g. visual, cognitive, proprioception) that may not be detectable with a standard neurological exam or other traditional clinical methods. The device, as shown in Fig. 1, consists of (1) two robotic arms that subjects grasp and use while performing a series of hand and upper-extremity tests and (2) a two-dimensional virtual reality display that serves as a visual aid for the tests. The device can be configured to present a variety of tasks that

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Figure 1. KINARM End-Point Robotic Device

provide quantitative measurements of cognitive, visuomotor, and proprioceptive capabilities. The subject's performance in each task is scored against normative data and values outside the 5/95% normal range are considered abnormal.

B. Neurologic Test Battery

The KINARM test battery consists of five tasks that allow objective assessment of sensory, motor, and cognitive functions. For example, the Arm (or upper-limb) Position-Matching task provides quantitative measures of a subject's proprioceptive capabilities. In this task, the subject grasps the robotic arms as shown in Fig. 1. The robot passively moves one of the subject's arms (passive hand) to one of 9 different target locations (see Fig. 2). When the robot stops moving, the subject is required to mirror-match the spatial position using the other arm (active hand) without the benefit of visual feedback. The process is repeated several times with the target locations randomized within each block of 9 targets. This allows measurement of variability in arm position in each trial as well as lateral and distal shifts. The subject's arms are visually blocked during the task so that the subject has only sensory information of the limb position through proprioception. Thus, this test provides a quantitative assessment of proprioception, specifically

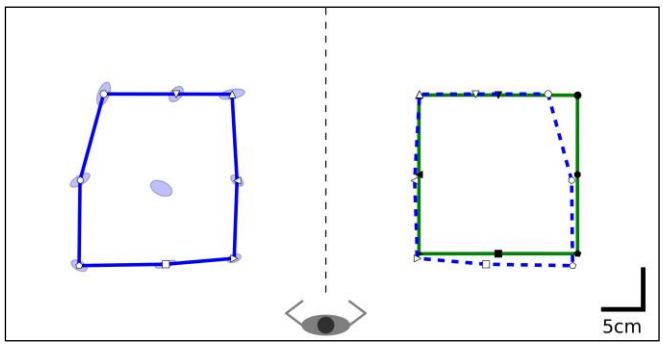

Figure 2. Arm Position-Matching Task (the green line on the right connects the mean positions of the passive hand moved by the robot and the solid blue line on the left represents the mean positions of the active hand moved by the subject)

position sense [15]. The goal of this paper is to present the association between proprioceptive measures obtained through the arm position-matching task and the prevalence of PCS three weeks post mTBI.

III. Methods

A. Technology Integration

The KINARM robotic device has a large foot print (74" by 48") and weighs approximately 800 pounds. While the device is movable, it is not easy to navigate the device in a busy setting such as the ED. Currently, the device has a dedicated testing space within the ED at the University of Cincinnati Medical Center (UCMC) and is fully integrated into the ED-based clinical research workflow. Prior to installation at UCMC, the device has never been used in an acute care setting and thus, UCMC is the first to successfully deploy this technology into active clinical research in the ED.

B. Study Design

A prospective study of mTBI patients was used to determine the association between quantitative measures of neurologic function obtained through testing on the KINARM device, and the prevalence of PCS, three weeks post injury. Clinical Study Assistants (CSAs) screened subjects for eligibility. After obtaining written informed consent, eligible subjects were enrolled and tested using the KINARM device in the ED. Subjects were contacted three weeks after enrollment in order to complete follow-up questionnaires. This study was reviewed and approved by the Institutional Review Board (IRB) at the University of Cincinnati (UC) prior to the start of subject screening.

C. Subjects

Patients presenting to the ED with a chief complaint of blunt force trauma to the head within 24 hours of injury were screened for eligibility based on the following criteria: (1) age greater than 18 years, (2) diagnosis of mTBI by the treating physician, (3) blood alcohol level (BAL) of < 100 mg/dl, (3) no focal neurologic deficit on standard neurological exam, (4) no co-morbidities such as significant acquired or baseline visual disturbance or broken wrist, that would affect test performance.

D. Testing and Follow-up

After obtaining written informed consent, subjects were enrolled and their neurologic function was assessed using a battery of tests (including the arm position-matching task) on the KINARM device. At three weeks post injury, subjects were contacted to complete the Rivermead Post Concussion Symptoms Questionnaire (RPQ) to assess the presence or absence of PCS. The RPQ consists of 16 questions, one for each symptom that could constitute PCS. The subjects were asked to rate the degree of each of the 16 PCS as compared to pre-injury levels on a scale of 0 to 4. PCS is considered to be present if the subject reports three or more questions with a score of 2 or more [16].

E. Data Analysis

The arm position-matching task generates three types of quantitative measures [15]: (1) Spatial shifts: Errors between mirrored position of the subject's arm (active hand) and the position of the arm moved by the robot (passive hand), (2) Variability: Trial-by-trial variability of active hand's position, and (3) Contraction/Expansion ratio: Ratio of the range of the spatial area covered by the active hand to the spatial area covered by the passive hand. Each of these measures is calculated in the X-direction, Y-direction, and X-Y plane, resulting in 9 parameters for each arm. Subjects performed the entire task twice, once with each arm. Hence, a total of 18 parameters were generated from this task. As mentioned earlier, each parameter score is compared to a normative database of healthy subjects, and values outside the 5/95% range are considered abnormal scores. Next, in order to define "failure" on the task, it was critical to determine the number of parameters that are identified as abnormal. It has been shown that less than 5% of the healthy subjects in the normative comparison group had four or more abnormal scores on the matching task, across both limbs [17]. Based on this limit, for the mTBI subjects in our study, we defined four or more abnormal scores as failure on the task and a positive test (or predictor) of PCS.

IV. Preliminary Results

The enrollment period of the study was March 2013 to April 2014. Fig. 3 shows the screening and enrollment process of the study. Around 1423 ED patients were screened for eligibility. Of these, 66 patients met the inclusion criteria, agreed to participate, and enrolled in the study. A total of 41 patients have completed the entire study, which includes neurological assessment on the KINARM device upon enrollment, and the follow-up Rivermead PCS questionnaire, three weeks later. Of these, 6 subjects have been excluded from analyses because of missing data such as BAL (1 case), problems during testing (1 fell asleep during testing, 2 did not complete testing due to personal time constraints, 1 subject did not understand the instructions), or comorbidity (1 case of horizontal nystagmus). A total of 35 mTBI patients (13 men, 22 women) were included in analyses of data from robotic testing and follow-up questionnaires (see Table I for subject characteristics).

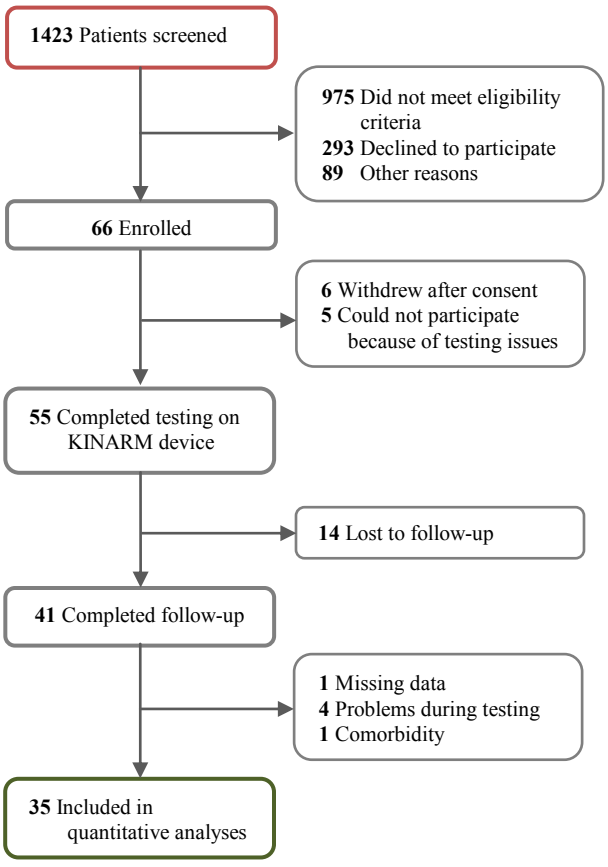

Figure 3. Flow of Study Participants

TABLE I. Characteristics of Study Participants

Characteristic		n = 35
Age – mean (min, max)		37 (19-90)
Gender	Male	13 (37.1%)
	Female	22 (62.9%)
Race	Caucasian	17 (49%)
	Non-caucasian	18 (50%)
Handedness	Right	31 (88.6%)
	Left	2 (5.7%)
	Ambidextrous	2 (5.7%)

The three types of proprioception measures, spatial shift, variability, and contraction/expansion ratio, are graphically represented for each subject in Fig. 4. The value for each parameter was normalized on a scale of -1 to 1 corresponding to the 5% to 95% reference range of the normative data. Thus, the data points in Fig. 4 represent a normalized score relative to the age- and gender-matched normative reference range (marked using two vertical black lines). As defined earlier, scores outside the reference range (-1, 1) are considered abnormal. Subjects with and without PCS are represented as two separate groups in Fig. 4. Qualitatively, it is clear from Fig. 4 that the subjects with PCS exhibited more abnormal scores than subjects without PCS.

An mTBI subject's performance on robotic testing (arm position-matching task) was assessed based on the operational definition that four or more abnormal scores is a positive test of PCS. Of the 35 subjects included in the analyses, 22 (63%, 95CI: 46%-77%) developed PCS based on analysis of RPQ survey results. 17/35 (49%, 95CI: 33%-64%) had four or more abnormal scores on the matching task; among these, 14/17 (82%, 95CI: 59%-94%) had PCS based on the RPQ results (see Table II). Thus, subjects with a positive result on the matching task (four or more abnormal scores) are at higher risk of developing PCS following mTBI (risk ratio = 1.85, 95CI: 1.06 – 3.29; Fisher's test: $p = 0.035$). The validity of the matching task as a diagnostic test of PCS is shown in Table III.

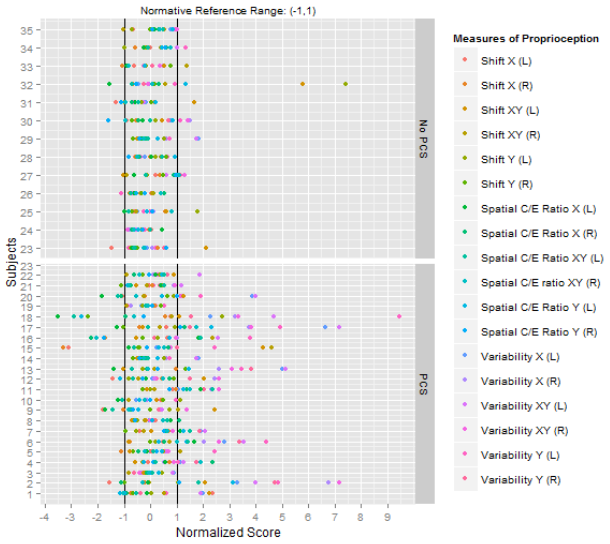

Figure 4. Proprioceptive Measures of Subjects with and without PCS

TABLE II. CONTINGENCY TABLE OF PCS PREDICTOR

Arm Position-Matching Task	Prevalence of PCS	
	PCS Present	***PCS Absent***
Positive (4 or more abnormal scores)	14	3
Negative (less than 4 abnormal scores)	8	10

TABLE III. VALIDITY OF ROBOTIC-ASSISTED MATCHING TASK

Validity Measure	**Estimate**	**95% CI**
Sensitivity	64%	41% -82%
Specificity	77%	46% - 94%
Positive Predictive Value	82%	56% - 95%
Negative Predictive Value	56%	31% - 78%
Postive Likelihood Ratio	2.76	0.97 - 7.81
Negative Likelihood Ratio	0.47	0.25 - 0.89

V. DISCUSSION

It is evident from our pilot study that robotic-assisted testing has the ability to provide detailed assessment of neurologic function in mTBI patients. Given that parameters from other tasks in the KINARM standard test battery also play a role in assessing neurologic function [18], combining the proprioceptive measures obtained through the arm position-matching task with other tasks, may be a better predictor of PCS or poor outcomes following mTBI. Further analyses, including logistic regression are underway. Examination of parameters across multiple tasks and their association to neurological deficits and/or anatomical features are a part of future analyses.

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