Journal of Critical Care 48 (2018) 228–236

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

Robotic technology provides objective and quantifiable metrics of neurocognitive functioning in survivors of critical illness: A feasibility study

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ARTICLE INFO

Available online xxxx
Keywords:
Critical illness
Post-intensive care syndrome
PICS
KINARM
RBANS

ABSTRACT

Purpose: To assess the feasibility of using an integrated multimodal data collection strategy to characterize the post-intensive care syndrome (PICS).
Materials and methods: Adult patients admitted to the ICU requiring invasive mechanical ventilation for >24 h and/or requiring vasopressor support were eligible for enrollment. We assessed cognitive and sensorimotor function at 3- and 12-months after ICU discharge with the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) and with the KINARM robot.
Results: At 3- and 12-months after ICU discharge, 28/70 (40%) and 22/70 (31%) returned for follow-up testing, respectively. Prominent reasons for declining testing at 3- and 12-months included: not interested (40% and 38%) and health complications (31% and 31%). The majority of returning participants completed all tasks (96%–100%) and 100% of available data was recorded. On the RBANS, 54% (3 months) and 32% (12 months) of individuals were impaired in visuospatial/constructional skills. Similarly, the KINARM assessments demonstrated that 56% of individuals had visuospatial/executive dysfunction at 3 months, and 40% had impairment at 12 months. Individual scores indicated substantial variability.
Conclusions: We demonstrated that it was feasible to quantify neurological dysfunction among participants that returned for follow-up testing. However, future investigations will need to implement multiple retention strategies.
Trial registration: This trial is registered on clinicaltrials.gov (Identifier: NCT02344043), retrospectively registered January 8, 2015.

1. Introduction

Survivors of critical illness frequently develop newly acquired long-term motor, psychological, and cognitive impairments, termed post-intensive care syndrome (PICS) [1]. In particular, the cognitive impairment typically involves memory and/or executive dysfunction [2-6]. Many of these impairments have been characterized using brief screening surveys (e.g., Montreal Cognitive Assessment [7]), subjective rating scales (e.g., Memory Assessment Clinics Self-Rating Scale [8]), or expensive and time-consuming neuropsychiatric testing. Available clinical tools may assess impairment broadly and lack detail pertaining to specific cognitive domains. As well, many clinical tests are subjective, which introduces the potential for error and inconsistent findings across study modalities.

Although current tests identify deficits among survivors of critical illness, the results obtained with various tools may not agree. Cognitive impairment rates can be highly variable (4%–62%), and incidence rates of cognitive dysfunction are higher among cohorts who had undergone comprehensive neuropsychological testing, rather than screening surveys alone [5]. The higher incidence of cognitive impairment on neuropsychological tests suggests that screening tools alone may insufficiently characterize cognitive dysfunction. Therefore, objective, comprehensive, and streamlined strategies are needed to further

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https://doi.org/10.1016/j.jcrc.2018.09.011
0883-9441/

characterize the neurocognitive impairment frequently observed among survivors of critical illness.

Robotic technology, such as the KINARM, uses real-time data monitoring to generate objective and quantitative metrics using upper limb motion to assess sensory, motor, and cognitive function, which may be essential to characterize PICS. In stroke survivors, this technology was able to identify and quantify subtle neurocognitive deficits not apparent on routine clinical assessments [9] and it has been validated in various patient populations [10-14]. Therefore, robotic technology offers the potential to objectively characterize a broad range of sensorimotor and cognitive impairments among survivors of critical illness.

The primary objective of this study was to demonstrate the feasibility of using an integrated multimodal data collection strategy to characterize PICS among survivors of critical illness using neuropsychological testing, the repeatable battery for the assessment of neuropsychological status (RBANS), as well as robotic technology, the KINARM End-Point robot.

2. Materials and methods

2.1. Study design

The Cerebral Oxygenation and Neurological outcomes FOllowing CriticAL illness (CONFOCAL) prospective observational study is registered on clinicaltrials.gov (NCT02344043) and our research protocol has been described previously [15]. Briefly, patients were recruited at an academic 33-bed general medical/surgical ICU into a study protocol approved by the local Health Sciences Research Ethics Board. Adult (≥18 years old) patients were considered eligible if they were admitted to the ICU within 24 h of having respiratory failure requiring invasive mechanical ventilation with an expected duration >24 h, and/or having shock of any etiology, as defined by the need for vasopressors at the following predefined doses: dopamine ≥7.5 μg/kg/min, dobutamine ≥5 μg/kg/min, norepinephrine ≥5 μg/min, phenylephrine ≥75 μg/min, epinephrine at any dose, milrinone at any dose (if used in conjunction with another agent), vasopressin ≥0.03 u/min if used in conjunction with another agent [15]. These inclusion criterion were adapted from the BRAIN-ICU study [6], which is currently one of the largest studies conducted to analyze cognitive impairments among critical illness survivors. Exclusion criteria included a life expectancy <24 h, an underlying diagnosis of cognitive dysfunction, a primary neurological/neurosurgical admitting diagnosis, or any reason that the subject may not participate in the follow-up assessments (e.g., limb amputation). Participants, or their surrogate decision maker, were provided details of the 3- and 12-month follow-up assessments at the time of ICU enrolment.

2.2. Data collection

Follow up assessments at 3- and 12-months after post-ICU discharge involved the administration of both the RBANS and the KINARM battery, as described below. Participants were administered tasks in the same succession to avoid potential bias (e.g., ordering effects) in our results due to varying task administration between participants. Participants could refuse to complete a task(s) at any time during the assessment. Three- and 12-month time points were chosen to increased generalizability, as large-scale studies in cognitive outcomes after critical illness frequently use similar assessment points.

2.3. Repeatable battery for the assessment of neuropsychological status (RBANS)

The RBANS was administered individually to participants by a trained researcher at 3- and 12-months after ICU discharge. This battery has alternate forms, assesses global cognition (i.e., total scale), as well as the following cognitive domains: immediate memory, visuospatial/constructional, language, attention, and delayed memory. These five indices have been described previously [16] and the RBANS has been validated previously [17-22]. Furthermore, this battery has a representative set of age-matched control data. Participant scores are converted to standardized values (i.e., index scores) in which the normative range is typically a mean of 100 ± 15 (1 SD) (i.e., approximately 68% of values fall within 1 SD from the mean), with lower scores indicating worse performance. In the current analysis, we used more stringent criteria to define impairment (i.e., a mean of 100±24.75 [1.65 SD], approximately 95% of values fall within 1.65 SD from the mean). Participants that scored >75 were not considered impaired, as these subjects had performance scores within or above the normative range. The RBANS assessment required ~20–30 min to complete.

2.4. Robotic Set-Up

Participants were seated and instructed to grasp onto handles attached to the bimanual KINARM End-Point (BKIN Technologies Ltd., Kingston, ON, Canada). These handles permit movement in a horizontal plane within a virtual reality system, which projects each task onto a horizontal reflective screen. Participants' vision of their hands and arms was occluded, and visual feedback of their hands (when provided) was represented on screen by a white circle. A trained operator described each task, using a standardized script, before it was performed by the participant. The operator visually monitored participant performance in real time to ensure that the task was completed appropriately while automated data collection and analysis software (Dexterit Version 3.6.2) measured and quantified performance. For each KINARM task, a task score was generated to provide a global performance measure. The task score is a two-sided statistic transformed to appear as a one-sided test (i.e., always positive, with higher values indicating worse performance) and sequential units are equivalent to standard deviation units away from the healthy control mean of 0. Therefore, performance was considered abnormal if the task score was outside the +1.96 range (i.e., 5th percentile). The task score has been previously described [14]. We administered 7 tasks from the KINARM Standard Tests™, visually guided reaching (VGR, see Fig. 1 A), reverse visually guided reaching (RVGR, see Fig. 1 B), arm position matching (APM, see Fig. 1 C), object hit (OH, see Fig. 1 D), object hit and avoid (OHA, see Fig. 1 E), level 1 of ball on bar (BonB, see Fig. 1 F), and spatial span (SS, see Fig. 1 G). A video representation of the KINARM tasks is available for viewing in the supplementary data (Supplementary Movie 1). Performance comparisons (intact vs. impaired) for RVGR (Supplementary Movie 2) and APM (Supplementary Movie 3) are also available. For tasks that only required a single limb, the dominant arm was chosen, and the KINARM assessment took <1 h to complete.

2.5. Feasibility

The primary outcome of our study was feasibility. We defined feasibility as the ability to conduct follow-up testing among survivors of critical illness at 3- and 12-months after ICU discharge. Assessment of feasibility for this protocol included: 1) total number of subjects that returned for follow-up testing, 2) self-reported discomfort during the procedure, and 3) the number of tasks that were successfully completed and the amount of available data recorded at follow-up. Clinical and demographic factors that may have impeded participation in follow-up assessments were also addressed. Research personnel documented by telephone the reasons participants declined follow up assessments at 3- and/or 12-months post-ICU discharge.

All graphs were generated using the ggplot2 package [23] Version 2.2.1 for R software [24] Version 3.4.1.