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Perioperative Research into Memory (PRiMe): Cognitive impairment following a severe burn injury and critical care admission, part 1

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ABSTRACT

Introduction: An investigation into long-term cognitive impairment and Quality of Life (QoL) after severe burns.

Methods: A proof of principle, cohort design, prospective, observational clinical study. Patients with severe burns (>15% TBSA) admitted to Burns ICU for invasive ventilation were recruited for psychocognitive assessment with a convenience sample of age and sex-matched controls. Participants completed psychological and QoL questionnaires, the Cogstate® electronic battery, Hopkins Verbal Learning, Verbal Fluency and Trail making tasks.

Results: 15 patients (11M, 4F; 41±14 years; TBSA 38.4%±18.5) and comparators (11M, 4F; 40 ±13 years) were recruited. Burns patients reported worse QoL (Neuro-QoL Short Form v2, patient 30.1±8.2, control 38.7±3.2, p=0.0004) and cognitive function (patient composite z-score 0.01, IQR −0.11 to 0.33, control 0.13, IQR 0.47–0.73, p=0.02). Compared to estimated premorbid FSIQ, patients dropped an equivalent of 8 IQ points (p=0.002). Cognitive function negatively correlated with burn severity (rBaux score, p=0.04). QoL strongly correlated with depressive symptoms (Rho=−0.67, p=0.009) but not cognitive function.

Conclusions: Severe burns injuries are associated with a significant, global, cognitive deficit. Patients also report worse QoL, depression and post-traumatic stress. Perceived QoL from cognitive impairment was more closely associated with depression than cognitive impairment.

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1. Introduction

The survival rates of patients requiring intensive care unit (ICU) admission following severe burns injuries continue to improve with advances in critical care medicine and burns management [1–5]. Admission to ICU is associated with physical, psychological and cognitive sequelae, which are in turn associated with a multi-faceted reduction in Quality of Life (QoL). This spans physical, mental and social domains, with many severe burns patients being unable to return to work within a year of discharge [6–8].

One of the most distressing problems affecting patients following discharge from ICU is that of long-term cognitive impairment (LTCI) [9–17]. This affects up to two thirds of patients [18] and can range in magnitude from subtle to major deficits in executive function and working memory. Cognitive deficits stemming from a wide range of medical conditions are known to have a significant impact on QoL [19–24]. It has been recognised after electrical injury, however there is limited research into ICU LTCI following severe general burns [25–28] and a dearth of research into any effect this may have on QoL. Patients with major burns encounter a markedly greater magnitude of inflammatory and hypermetabolic sequelae than general ICU cohorts [29,30]. In addition to this endogenous biochemical milieu, severe burns necessitate multiple surgeries and accompanying general anaesthetics to treat their injuries, and attract numerous nosocomial infections [31,32]. Anaesthesia [33–37] and pro-inflammatory states [38,39] are also known to be associated with LTCI. As such, severe burns patients admitted to ICU are a unique subgroup of patients that may be at particularly high risk of LTCI.

It is now accepted that the brain mounts an inflammatory response following local and systemic insults [30,40–42]. There is evidence suggesting that inflammatory mediators and the immune system play a significant role in adult hippocampal neurogenesis and memory formation in both health and disease, although the processes involved in immune activated neuroplasticity are not fully understood [43]. With the use of advanced neuroimaging techniques it is possible to identify surrogate markers of neuroinflammation in specific brain regions associated with memory formation in vivo [44,45].

This study has been performed in two parts due to the breadth of data collected. In part one we set out to look for long-term neurocognitive sequelae after a severe burns injury and any resulting impact on QoL. In part two, we look for any corresponding evidence of neuroinflammation with the use of multi-parametric Magnetic Resonance Imaging (MRI), including: diffusion weighted imaging, MR spectroscopy and resting-state fMRI.

2. Materials and methods

This was a proof of principle, cohort design, prospective, observational clinical study. ClinicalTrials.gov ID: NCT03242395.

2.1. Ethics approval

Ethics approval was granted by the Surrey Borders Research Ethics Committee on the 30th January 2014 (Reference 14/LO/0049). Fully informed written consent was received from all participants in accordance with the UK Good Clinical Practice code of practice.

2.2. Recruitment and demographics

All patients admitted to the Chelsea and Westminster Hospital Burns Intensive Care Unit (BICU) between 2004 and 2015 were reviewed and considered for inclusion in this trial. Patients were also recruited through burns charities such as the Katie Piper Foundation. Recruitment ran over a two-year period from April 2014 until April 2016. Collateral information gathered included: age, sex, years of education, employment history, past medical history and the date, mechanism and size of burn. Burn severity and comorbidities were quantified by use of the revised Baux (rBaux) score and the Charlson Comorbidity Index (CCI) respectively [46,47].

A convenience sample of comparators was also recruited. The patients were asked to select a family member of the same sex and similar age for the comparator group. If no suitable kin was available then comparators were recruited via poster advertisements in the burns outpatient waiting room. After initial contact via email or telephone, volunteers were invited to attend the research department. Subsequent to providing written informed consent, participants underwent neurocognitive testing and were individually matched for age, sex and National Adult Reading Test (NART) derived Full-Scale IQ (FSIQ). The closest matches were included in the analysis and went on to have MRI scans in part two of the study.

2.3. Inclusion and exclusion criteria

All adult patients admitted to a BICU within the previous ten years (at the time of testing), who had been intubated and ventilated, and with burns greater than or equal to 15% total body surface area (TBSA) were screened for inclusion in this study.

Exclusion criteria included: BICU admission for illnesses other than burns (e.g. Toxic Epidermal Necrolysis Syndrome); evidence of head trauma; known substance misuse or alcohol excess; inability to understand plain verbal or written English; those receiving formal psychiatric treatment; those held under the Mental Health Act, or if their psychological health was deemed to be at risk from inclusion in the study (as assessed by the supervising clinical psychologist). In addition, contra-indications to MRI were also contraindications to study inclusion.

2.4. Quality of Life

QoL was assessed using the Euro QoL 5 Dimensions (EQ5D) questionnaire, the Instrumental Activities of Daily Living (iADL) scale and the National Institute of Health Neuro-QoL Short Form version 2 (NIH Neuro-QoL SF v2).

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