Severe Remote Burn Injury Results in Early, Elevated Markers of Alzheimer’s Disease

Leyya Suleman, MSII, Joshua Gatson, PhD, David Maass, BS, Victoria Warren, RN, Steven Wolf, MD, Joseph Minei, MD, Paul Pepe, MD, Ahamed Idris, MD, Jane Wigginton, MD

Department of Surgery, Divisions of Burn, Trauma, Critical Care and Emergency Medicine, UT Southwestern Medical Center, Dallas, TX

INTRODUCTION

Prior studies have found that patients with severe burns may suffer neurocognitive decline. While these observations are frequently attributed to psycho-social causes, our lab recently reported that remote burn injury is associated with significant brain changes, including new data revealing a substantial, rapid, and sustained (30 min - 45 day) increase in rat brain inflammation following remote burns. Other acute brain injury processes, such as traumatic brain injury (TBI) and stroke have been associated with an accelerated accumulation of Aβ40, Aβ42, and Tau, and ultimately a clinical picture of early-onset Alzheimer’s disease (AD).

HYPOTHESIS

We hypothesized that AD-like processes may be triggered in the indirect brain injury following remote, severe burns, similar to that seen with direct brain injury (TBI and stroke).

METHODS

52 male rats were randomized into 2 groups:
1) sham burn (n=8)
2) burn (n=44)

Burned rats received a 40% 3° TBSA dorsal scald burn, and fluid resuscitation with Lactated Ringer’s solution. 8 animals from the burn group were sacrificed at 0.5,1,2,4,6,8,12,24 hours and 7 days, with 4 sacrificed at 45 days. Brain tissue samples were analyzed by ELISA for cytokines, Aβ 40, Aβ 42, Tau and phospho-Tau.

RESULTS

Figure 1. All measured pro-inflammatory cytokines were elevated up to 45 days in the brain after remote severe burns

Figure 2. Brain levels of Tau and phospho-Tau were elevated for up to 45 days after remote severe burns

CONCLUSION

Severe remote burn injury not only results in early, robust, and sustained neuroinflammation, but also significantly increases brain levels of Aβ40, Aβ42, and Tau. This novel finding may pave the way for future brain-preserving interventional trials in burn patients, as well as provide a more rapid and effective testing-ground for new therapies aimed at slowing and/or preventing AD.