A631 - Early, single-dose estrogen increases levels of brain-derived neurotrophic factor (BDNF), a neurotrophin for neuronal survival and neurogenesis following indirect brain inflammation caused by severe torso burns

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Introduction:
Prior studies have found that patients with severe burns may suffer significant neurocognitive changes. While frequently attributed to psycho-social issues, we have found a substantial, rapid and sustained (30 min - 45 day) increase in rat brain inflammatory markers (for example, IL-6) following remote torso burns that is blunted by a single post-burn dose of estrogen. Brain-derived neurotrophic factor (BDNF), one of the most active neurotrophins, protects existing neurons and encourages the growth and differentiation of new neurons and synapses. As estrogens not only blunt inflammation but also exert an influence on CNS growth factors, we hypothesized that 17β-estradiol (E2) might affect levels of BDNF in the post-burn rat brain.

Methods:
Male rats (n = 44) were assigned randomly into three groups: controls/no burn (n = 4); burn/placebo (n = 20); and burn/E2 (n = 20). Burned rats received a 40% 3° TBSA dorsal burn, fluid resuscitation and one dose of E2 or placebo (0.5 mg/kg intraperitoneally) 15 minutes post-burn. Eight animals from each of the two burn groups (burn/placebo and burn/E2) were sacrificed at 24 hours and at 7 days, respectively (sham group at 7 days only), with four each of the two burn groups sacrificed at 45 days. Brain tissue samples were analyzed by ELISA for BDNF.

Results:
Mean levels of BDNF were significantly elevated within 24 hours and continued to increase up to 45 days post-injury in burned animals receiving the 17β-estradiol (>300 pg/mg) as compared with the placebo-treated burned animals (<160 pg/mg) and controls (<120. pg/mg). See Figure 1.

Conclusion:
Early, single-dose estrogen administration following remote severe burn injury significantly elevated levels of BDNF in brain tissue. This finding may represent an extremely novel and important pathway to enhance both neuroprotection and neuroregeneration in burn patients.
BDNF Levels (pg/mg) in the Brain

- CONTROL
- BURN + 17-β ESTRADIOL
- BURN + VEHICLE

TIME POST BURN INJURY:
- 24 HR
- 7 DAY
- 45 DAY

BDNF RAT BRAIN TISSUE (pg/mg)