ANALYSIS OF CHANGES IN C-FOS IMMUNOREACTIVITY INDUCED BY TRAUMATIC BRAIN INJURY IN RAT BRAIN STRUCTURES RELEVANT TO MICTURITION

The present study was undertaken to test the hypothesis that dysregulation of signal transmission contributes to altered bladder function in an animal model of traumatic brain injury (TBI). Control and lateral fluid-percussion TBI animals were examined. TBI induced a significant increase in c-Fos-like immunoreactivity (IR) in the locus coeruleus - Barrington nucleus (LC-BN) complex (66.5±10.3 neurons versus 5.5±3.2 neurons, $p<0.001$) and the pontine nucleus incertus (NI), both in pars compacta (NIc) (78.25±8.53 neurons versus 11.33±1.54 neurons, $p<0.001$) and pars dissipata (NId) (16.0±5.5 neurons versus 1.7±2.4 neurons, $p<0.001$). TBI also induced a decrease in c-fos immunoreactivity in the ventrolateral periaqueductal grey matter (vlPAG) (18.8±10.8 neurons versus 48.0±19.1 neurons, $p<0.001$) and an increase in the dorsal raphe PAG (DR) (27.3±12.3 neurons versus 12.0±6.0 neurons, $p<0.001$). The injury-induced changes were coupled to urinary retention followed by prolonged bladder filling and overdistention. These results provide immunohistochemical evidence for TBI-induced alterations in neuronal activity in central micturition regulating circuits and show that LC-BN, DR and NI activation is associated with an inhibition of voiding behavior. It suggests for the first time that TBI-induced dysregulation in neuronal activity may alter information-processing about bladder fullness, possibly through modulation of the LC-NE response to afferent bladder impulses. Chemical coding of the associated brain neuronal circuitry activated by TBI and discrimination between the injury stress- and bladder afferent-activated stimuli remain to be elucidated.