Brain-derived neurotrophic factor

Brain-derived neurotrophic factor (BDNF) plays an important role in promoting the growth, differentiation, survival, and synaptic stability of neurons. It is important also for neuronal survival and regeneration.

Presently, the transplantation of neural stem cells (NSCs) is known to induce neural repair to some extent after injury or disease. In as study, to investigate whether NSCs genetically modified to encode the BDNF gene (BDNF/NSCs) would further enhance synaptogenesis, BDNF/NSCs or naive NSCs were directly engrafted into lesions in a rat model of traumatic brain injury (TBI). Immunohistochemistry, western blotting and RT-PCR were performed to detect synaptic proteins, BDNF-TrkB and its downstream signaling pathways, at 1, 2, 3 or 4 weeks after transplantation. Our results showed that BDNF significantly increased the expression levels of the TrkB receptor gene and the phosphorylation of the TrkB protein in the lesions. The expression levels of Ras, phosphorylated Erk1/2 and postsynaptic density protein-95 were elevated in the BDNF/NSCs-transplanted groups compared with those in the NSCs-transplanted groups throughout the experimental period. Moreover, the nuclear factor (erythroid-derived 2)-like 2/Thioredoxin (Nrf2/Trx) axis, which is a specific therapeutic target for the treatment of injury or cell death, was upregulated by BDNF overexpression. Therefore, we determined that the increased synaptic proteins level implicated in synaptogenesis might be associated with the activation of the MAPK/Erk1/2 signaling pathway and the upregulation of the antioxidant agent Trx modified by BDNF-TrkB following the BDNF/NSCs transplantation after TBI [1)].

Korley et al. examined serum BDNF in two independent cohorts of TBI cases presenting to the emergency departments (ED) of the Johns Hopkins Hospital (JHH, n=76) and San Francisco General Hospital (SFGH, n=80), and a control group of JHH ED patients without TBI (n=150). Findings were subsequently validated in the prospective, multi-center, Transforming Research and Clinical Knowledge in TBI (TRACK-TBI) Pilot study, n=159. We investigated the association between BDNF, Glial fibrillary acidic protein (GFAP) and Ubiquitin C-terminal hydrolase -L1 (UCH-L1) and recovery from TBI at 6 months in the TRACK-TBI Pilot cohort. Incomplete recovery was defined as having either post-concussive syndrome (PCS) or a Glasgow Outcome Scale Extended (GOSE) score<8 at 6 months.

Median day-of-injury BDNF concentrations (ng/ml) were lower among TBI cases (JHH TBI: 17.5 and SFGH TBI: 13.8) than in JHH controls (60.3), p=0.0001. Among TRACK-TBI Pilot subjects, median BDNF concentrations (ng/ml) were higher in mild (8.3) than in moderate (4.3) or severe TBI (4.0), p=0.004. In the TRACK-TBI cohort, the 75 (71.4%) subjects with very low BDNF values (i.e. <the 1st percentile for non-TBI controls, <14.2 ng/ml) had higher odds of incomplete recovery than those without very low values (odds ratio: 4.0 (95% confidence interval: 1.5 - 11.0)). The area under the receiver operator curve (AUC) for discriminating complete and incomplete recovery was 0.65 (95% CI: 0.52-0.78) for BDNF; 0.61 (95% CI: 0.49-0.73) for GFAP; and 0.55 (95% CI: 0.43-0.66) for UCH-L1. Addition of GFAP/UCH-L1 to BDNF did not improve outcome prediction significantly.

Day-of-injury serum BDNF is associated with TBI diagnosis and also provides 6-month prognostic information regarding recovery from TBI. Thus, day-of-injury BDNF values may aid in TBI risk stratification [2)].

Cerebral hemorrhage significantly inhibited the spatial learning and memory ability of rats. The mechanism may be related to decreased cerebral expression of BDNF and neuroglobin (NGB).

Case series

A study of Sorri et al. from the Tampere University Hospital in Finland, included thirty patients suffering from major depressive disorder (MDD). Their serum and plasma brain derived neurotrophic factor (BDNF) levels were examined before electroconvulsive therapy (ECT) (baseline) and after the first, fifth, and last ECT session. The severity of the depression and the response to ECT were measured with Montgomery Asberg Depression Rating Scale (MADRS).

Electroconvulsive therapy caused no significant changes in serum BDNF levels. Plasma BDNF levels decreased during the fifth ECT session between the baseline and the 2-hr samples ($p = 0.019$). No associations were found between serum or plasma BDNF levels and remission. The correlations between plasma and serum BDNF levels in each measurement varied between 0.187 and 0.636.

Neither serum nor plasma BDNF levels were systematically associated with the clinical remission. However, the plasma BDNF levels somewhat varied during the ECT series. Therefore, the predictive value of BDNF for effects of ECT appears to be at least modest [3].

1)
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