Cognitive recovery and late worsening after severe Traumatic Brain Injury

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Traumatic brain injury (TBI) is one of the leading cause of disability due to neurologic impairment in children and young adults. Acute and chronic cerebral lesions in response to an insult may lead to acute or delayed neuronal death, apoptotic cell death, oxidative stress, B-amyloid deposition, neuronal degeneration and gliosis. Chronic neuroinflammation has been postulated as a relevant feature of the response to TBI. This raises the possibility of ongoing brain damage in long-term survivors, such that their cognitive function and motor function continues to deteriorate for months and years after the injury. Much of the disabilities results from a spectrum of cognitive impairments that in several cases get worse in time, sometimes progressing to a severe neurocognitive disorder and even to Alzheimer's Disease (AD). TBI and Alzheimer's disease have similarities as to protein and cellular responses and genetic influences. Severe TBI may hasten or even trigger the onset of AD even after many years, irrespective of age when the TBI occurred. In many cases the location and the extent of focal brain injuries does not fully explain the neurocognitive impairments. Altered neurochemistry and diffuse cellular injury (DAI) are important contributors to brain dysfunction, associated with poor outcome after TBI.
In order to explore a putative set of criteria predicting to some extent the cognitive outcome, series of clinical and neuropsychological assessments in a sample of TBI patients were correlated with neuroimaging studies and bio-umoral profiles (every 3 months for 1 year). In particular, the plasma levels of the main antioxidant/detoxifying enzymes have been evaluated together with the levels of inflammatory markers. The neuroimaging studies were performed at 2 time points (< 2 months and > 6 months) and include: (i) MR Spectroscopy (MRS) to explore brain metabolites, particularly N-Acetyl-Aspartate (NAA), Choline (Cho), Creatine (Cr); (ii) Diffusion Tensor Imaging (DTI) by Fractional Anisotropy (FA); (iii) Functional MRI (fMRI) by studying both resting state and activation in Vegetative (VS) or Minimally Conscious (MCS) states; (iv) Arterial Spin Labelling (ASL) that allows the absolute quantitative evaluation of the brain flow values.
The patients were enrolled among the subjects admitted to an acute neurorehabilitation facility in Bologna and were aging from 18 to 65. The first assessment was conducted 30 days after the trauma and the follow up lasted at least 12 months. A cohort of 15 patients is already included in the study and 12 of them had also functional neuroimaging studies. The cognitive recovery had different patterns in time: for about ¼ of the patients an early recovery was followed by progressive worsening, while about 75% of the cases show a continuous but more or less rapid recovery of consciousness and cognitive functioning. The relationship between these 2 different trends and the biochemical and neuroimaging markers will be discussed.

Supported by MIUR-FIRB project n. RBAP11HSZS