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MEETING ABSTRACT

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Traumatic brain injury-induced cognitive decline: mechanisms and treatment options

Liga ZVEJNIECE[1,*], Edijs VAVERS[1], Baiba SVALBE[1], Lasma LAUBERTE[1], Gundega VIKMANE[1] and Maija DAMBROVA[1,2]

[1]Laboraory of Pharmaceutical Pharmacology, Latvian Institute of Organic Synthesis, Riga, Latvia; [2]Rīga Stradiņš University, Riga, Latvia

Traumatic brain injury (TBI) is the leading cause of disability and death in Europe among young adults and children and an increasing problem in the elderly. In the past decades, tremendous clinical and pre-clinical efforts were undertaken to understand the acute, life-threatening pathophysiological events occurring acutely after TBI. The first aim was to develop therapeutic procedures able to reduce the formation of brain edema, intracranial hypertension, cerebral ischemia, and secondary loss of brain tissue in order to save the patient's live. In the past few years, it became more recognized that also weeks, months or even years after the initial event additional morbidity may occur, which significantly contributes to the overall burden of head injury. These long-lasting sequels of TBI range from sleep disorders, fatigue syndrome, depression, neuro-endocrine deficits, epilepsy, and psychiatric disorders to chronic neurodegeneration leading to parkinsonism, cognitive decline and dementia. Across all levels of TBI severity, attention, processing speed, episodic memory, and executive function are the most commonly affected. Data from the few available human studies suggest that chronic TBI is associated with brain atrophy and long-lasting neuroinflammation for up to 18 years after TBI. These findings were corroborated by longitudinal experimental studies in mice and rats showing progressive brain atrophy after TBI for up to one year after injury and long-lasting activation of microglia, and invaded monocyte invasion from 24 hours up to 1.5 years after the experimental TBI. The important role for neuroinflammation in TBI is further supported by a reduced lesion volume and improved behavioral outcome upon neutralization of IL-1β, a pro-inflammatory cytokine which may lead to changes on the synaptic level. The paradox of neuroprotection in TBI is that, despite a long list of potential neuroprotective agents active under experimental conditions, no compound has demonstrated protection in clinical trials. The ultimate aim of the CnsAflame project is to determine the underlying causes of chronic TBI to facilitate the development of an effective cure and run a multi centre preclinical trial of a drug candidate.

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Keywords: traumatic brain injury – drug discovery and development – pharmacotherapy

**Corresponding author: Liga Zvejniece, Laboratory of Pharmaceutical Pharmacology, Latvian Institute of Organic Synthesis, 21 Aizkraukles Str., LV-1006, Riga, Latvia. E-mail: liga@farm.osi.lv*