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Nitric oxide and interlukin-6 levels in intellectual disability adults with epilepsy

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ABSTRACT

Nitric oxide (NO) and interlukin-6 (IL-6) are highly reactive mediators that have been shown to play different roles in a variety of different biological process. The role of NO and IL-6 in the neuropathogenesis of brain seizures is still questionable. In order to evaluate the role of NO and IL-6 in neurological disorders such as seizures, we investigated 19 adults with intellectual disability (ID) who suffer from epilepsy and treated for convulsions. NO metabolites (NOx) and IL-6 levels in serum obtained after night-sleep were significantly high among ID individuals diagnosed with epilepsy versus ID people without epilepsy. These results indicated that NOx and IL-6 may have a pathophysiological role in convulsions. Consequently, we suggest that professionals consider chemical inhibitors that might be helpful against the function of NO and IL-6.

Treating patients with chronic neurological diseases is becoming increasingly complex for a variety of reasons, such as the presence of dual neurological diagnoses (i.e., intellectual disability (ID) and epilepsy; Down syndrome and Alzheimer; and schizophrenia and ID), existence of several comorbid conditions, increased age, and psychological barriers such as lack of motivation, anxiety and depression. As a result, careful monitoring and assessment is essential. Laboratory testing can

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improve the assessment and accordingly influence treatment planning. Biochemical measurements should form baseline for the initial assessment of clinical characteristics in healthy and non-healthy adults (Flanagan, Melillo, Abdallah, & Remington, 2007). In the current study, we aimed to evaluate the role of nitric oxide (NO) and interlukin-6 (IL-6) in ID adults who are also diagnosed with epilepsy.

Nitric oxide is an inflammatory mediator that is an important free radical serving as a second messenger in processes including neurotransmission, maintenance of vasodilator tone, elicits the activation of neurotransmission in CNS, and arterial pressure and it has been suggested that cytokine-mediated circulatory shock is caused by activation of the inducible isoform (type II) of NOS (Czapski, Cakala, Chalimoniuk, Gajkowska, & Strosznajder, 2007). In biological systems, nitric oxide decomposes to nitrite and nitrate, and the cytokine-mediated increases in concentrations of nitrite/nitrate. NO is constitutively synthesized by endothelial NO synthetase (eNOS) and inducible neuronal iNOS, respectively. In CNS, excessive amounts of NO produced by neurons induce limbic seizures and delayed hippocampus neuronal damage due to the enhancement of glutamate release by neuronal NO (Jelenkovic et al., 2002). Excessive iNOS levels in the brain have been detected in epileptogenetic mice (Murashima, Yoshii, & Suzuki, 2002). NO may be related to the cytokine levels in animals with epilepsy indicating an inflammatory condition, since not only reactive oxygen species (ROS) and reactive nitrogen species (RNS) are involved in oxidative stress and brain damage, but also pro-inflammatory cytokine such as IL-6 (Hamano, Noguchi, Fukui, Issiki, & Watanabe, 2002; Miura, Miyamoto, Nakamura, & Watanabe, 2002; Stover, Schoning, Sakowitz, Woiciechowsky, & Unterberg, 2001). Thus, increases of NO and IL-6 production in the serum may reflect inflammatory conditions in brain tissue. Therefore, the aim of this study was to investigate the serum level of NO and IL-6 in adults with intellectual disability diagnosed also with epilepsy.

1. Methods

1.1. Participants

The sample consisted of permanent residents who lived in residential care center. After being referred to the study by the institutional health-care medical doctor, only candidates that answer the three inclusion criteria were used in the experimental group: (1) mild intellectual deficiency, as diagnosed within 1–3 years after birth by IQ-scores defined by the Wechsler Abbreviated Scale of Intelligence (Harcourt Assessment Inc., San Antonio); (Hays, Reas, & Shaw, 2002). (2) Epilepsy, diagnosed due to a presence of recurrent, unprovoked seizures, and as such the diagnosis was made based on the medical history and measurement technology of electroencephalography (EEG). The participants were either presenting short (>5 min) or long time (>20 min) convulsions. All participants in the experimental group were treated with anticonvulsant medications such as Teril CR (TARO™) 100–400 mg, Depalet® 500 mg, or combination of the two. (3) Participants lived in the care center for at least 5 years prior to being tested. Candidates were excluded if they had a clinical history of neurological disease (e.g., Parkinson's disease, stroke, Alzheimer's disease, neuropathy or brain surgery), or in the case of any peripheral neurological sign. None of the participants received narcotic medications at the time of the experiment. To eliminate the factors which might affect free radicals and inflammatory condition we also excluded all individuals with one of the following conditions: pulmonary disease, type II diabetes mellitus, chronic or acute heart failure, smoking, alcohol drinking, or taking dopamine or lithium. From a sample population of 118 permanent residents with ID only 35 were also diagnosed with having mild ID and epilepsy. Nineteen participants were randomly selected to participate in the experimental group (10 females and 9 males; mean age = 51.5 with standard deviation (S.D.) of ±7.32 years; range 44–65 years). The control group (n = 10) was age and gender and medical history matched including the exclusion criteria, were ID individuals without epilepsy. The study received prior approval by the Institutional Ethic Committee of Residential Care Centers under the administrative control of the Israeli Ministry of Welfare. Oral consent was obtained from participants as well as a written consent from their parents or guardians. A total of 7 mL of venous blood samples were collected overnight fasting and were drawn into 'vacutainer' 10 mL tubes for metabolites assay which did not contain any additives.