ALTERATIONS OF GLUCOSE METABOLISM AFTER PILOCARPINE INDUCED STATUS EPILEPTICUS IN IMMATURE RATS

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Introduction

Perinatal hypoxia ischemic insult (HII) is a fatal paediatric neurologic condition that occurs because of the serious birth complications in new-borns [1]. In surviving infants, hypoxia-ischemia develops neurological sequelae later in the life as a long-term devastating consequence such as cerebral palsy, epilepsy, developmental delay, cognitive impairment, and behavioral disorders [2]. There are limited diagnostic and therapeutic approaches, thus it's a socio-economic burden. Altered glucose metabolism has been found in various neuropsychiatric diseases including stroke, depression, Alzheimer's disease, or ischemia [3, 4]. The aim of our study was to evaluate the cluster of metabolic biomarkers related to glucose disturbances within the physiological state in lithium-pilocarpine (Pilo) induced statuts epilepticus (SE) of immature rats.

Methods

To induce Pilo SE, male Wistar rat pups were pretreated with lithium chloride (127 mg/kg, n=11) on the 11th postnatal day. After 24 hours, the lithium pre-treated pups were administered either with Pilocarpine i.p. (35 mg /kg b.w., n=6) or saline (0,9% NaCl, n=5) in control group. On the 19th postnatal day, serum was collected [5]. The blood serum samples were analyzed by magnetic bead-based multiplex sandwich immunoassays Bio-Plex Pro Rat Diabetic Assays (Bio-Rad Laboratories, Inc., US) on the Bio-Plex 200 System instrument equipped with Bio-Plex Manager Software´s version. 6.1.0.727. The group of evaluated metabolites consisted of ghrelin, glucagon-like peptide 1 (GLP-1), glucagon, leptin and plasmino-gen activator inhibitor-1 (PAI-1). The data were statistically evaluated using Sigma plot Software. One-way analysis of variance (ANOVA) was used to evaluate the difference among all experimental groups (using the Bonferroni multiple comparison test). The level of $p < 0.05$ was considered as statistically significant difference. Data are expressed as means ± SEM.

Results and Discussion

We observed the significant changes in cluster of five metabolites measured in Pilo group vs Saline experimental group. The results are indicated in **Table 1**. There was detected significantly lower serum level of ghrelin in Pilo group compared to Saline group. Whereases, GLP-1 and Leptin serum levels were analysed significantly higher in Pilo group than Saline group. Finally, glucagon and PAI-1 serum levels were not detected in Saline group, while their serum levels witihin Pilo group were skipped up in several orders.

Table 1 The blood serum levels of analyzed biomarkers of glucose metabolism within the status epilepticus (SE) of immature rats. Saline (control group); Pilo - lithium-pilocarpine (exposed group); ND - not detected; Statistics: ANOVA One-way analysis of variance with Bonferroni multiple comparison test, compared experimental groups Pilo *vs* Saline,* $p < 0.05$ was considered as statistically significant difference, *** $p < 0.001$.

	PILO		SALINE	
	pg/mL	SEM	pg/mL	SEM
Ghrelin	633.10***	334.44	1896.09	682.72
GLP-1	5150.15***	1767.10	457.70	56.81
Glucagon	5296.98***	550.46	ND	-
Leptin	1841.80***	255.08	313.34	63.83
PAI-1	199.94***	12.15	ND	-

Our data indicates, in accordance with published data, that status epilepticus leads to significant alterations in glucose metabolism regulation in immature rats [6-10]. The role of these changes is not well understood, although several mechanisms interacting with seizures, such as anticovulsant effect of ghrelin, has been identified [11].

Conclusions

In conclusion, our data indicates an important role of systemic glucose metabolism regulation and suggests its importance in epileptogenesis. Interaction with glucose metabolism thus represents a potential pharmacological target in acquired epilepsy.

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