Increased paraoxonase and arylesterase activity in thyroiditis patients compared to healthy individuals

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Aim: The aim of this study was to assess whether there is a significant difference in paraoxonase and arylesterase activities and distribution of phenotypes in thyroiditis patients compared to healthy volunteers.

Introduction: Human serum paraoxonase 1 (PON1; EC3.1.1.2) is an antioxidant enzyme showing both paraoxonase and arylesterase activities. The PON1−192 polymorphism has two isoforms, namely PON1 Q and PON1 R. PON1 Q contains a glutamine at position 192. PON1 R contains an arginine at position 192. It shows a 6 fold higher activity towards paraoxon hydrolysis compared to Q isoform. Arylesterase activity is similar in both isoforms. The R allele shows a greater degree of stimulation of its paraoxon-hydrolyzing activity by 1 M NaCl than does the Q allele. The ratio of Salt stimulated PON 1 activity/Arylesterase activity (P/A ratio) is trimodally distributed. The three modes correspond to paraoxonase phenotypes, QQ, QR and RR.

Methods: Fifty thyroiditis patients and one hundred and thirty seven apparently healthy individuals were enrolled in this study. Serum samples of both groups were analysed for basal paraoxonase activity, salt stimulated paraoxonase activity (with 1 M NaCl) and arylesterase activity (spectrophotometrically). P/A ratio was used to assess the phenotypes (dual substrate method).

Results: Basal PON 1 activity (205.27 ± 115.00 U/l vs. 251.1 ± 129.6 U/l, p = 0.002) and arylesterase activity (159.53 ± 37.11 vs. 177.59 ± 46.90, p = 0.024) was significantly higher in thyroiditis patients compared to healthy volunteers. Percentage of QQ phenotype was significantly higher in thyroiditis patients compared to healthy individuals. Percentage of QR phenotype was significantly lower in thyroiditis patients compared to healthy individuals. There was no difference in percentage of RR phenotype in thyroiditis patients and healthy individuals.

Conclusion: Serum PON 1 activity and arylesterase activity was significantly higher in thyroiditis patients compared to healthy individuals. Percentage distribution of phenotypes in thyroiditis patients was significantly different from healthy individuals.

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PS111

The relationship between dyslipidemia and disease activity in Iranian population with systemic lupus erythematosus

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Aim: This study was designed for evaluating the relationship between dyslipidemia and diseases activity in systemic lupus erythematosus (SLE) patients.

Introduction: In spite of high prevalence of dyslipidemia in SLE patients and its role in patients’ cardiovascular events, there was scant study about the relation between dyslipidemia and disease activity in SLE patients in Iran.

Aim: This study was conducted during 2014–2016 on SLE patients who referred to the Hasheminejad hospital (Tehran – Iran). The serum levels of triglyceride, cholesterol, LDL, and HDL were measured, then dyslipidemia and correlated factors were evaluated. The activity of disease was determined by SLE disease activity index (SLEDAI).

Results: 62 out of 72 patients (87%) were female and the mean age was 34 years. The median disease duration was 1 year and 49% of patients had active disease (SLEDAI ≥ 6). Proteinuria and nephritis were observed in 18% and 24%, respectively, 62% of patients had at-least one abnormality in their lipid profile. High cholesterol (>200 mg/dL), high triglyceride (>150md/dL), high LDL (>130 mg/dL) and low HDL (<50 mg/dL in females and <40md/dL in males) levels were observed in 25%, 42%, 20% and 49% of patients, respectively. Patients with active disease had lower age and disease duration in comparison of others (P < 0.05), while there were no differences in terms of sex and weight between patients in active and inactive phases (P > 0.05). The frequency of proteinuria, nephritis and decreased level of complements were higher in active SLE patients, too. Patients with active disease had also higher levels of serum cholesterol, triglyceride and LDL and lower level of serum HDL. In logistic regression, the odds ratios of patients with high cholesterol, using more than 10 mg/day prednisolone and with low serum HDL level for having active disease were 6.6, 5.6 and 3.4, respectively (P < 0.05).

Conclusion: Our findings showed that dyslipidemia is prevalent in SLE patients especially in patients with active SLE disease. In addition, patients with high cholesterol, using more than 10 mg/day prednisolone and with low HDL had higher chance for having active disease. Hence, it seems that there is a relation between disease activity and lipid profile abnormalities in SLE patients.

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PS168

Astrocytic A2A receptors: Novel targets to manage brain disorders

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Aim: To validate astrocytic adenosine A2A receptors (A2AR) as a novel target to prevent abnormal glutamate overexcitation.

Introduction: Astrocytes are responsible for clearance of extracellular glutamate, a process controlled by A2AR, extolling

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their key role as regulators of synaptic transmission and of the abnormal glutamate overexcitation implicated in both acute and chronic brain diseases. We have previously showed that activation of astrocytic A2AR reduce astrocytic glutamate uptake under physiological and pathological conditions,1-3 and that A2AR are aberrantly up-regulated upon multiple brain insults.4-6

Methods: We incorporated EGFP reporter either alone or combined with either a small hairpin to down-regulate A2AR (shA2AR) or a control sequence (shCTR) into Mokola Lyssavirus (Mok-G) and Vesicular Stomatitis Virus (VSV-G) lentivectors and tested whether Mok-G-coated lentiviruses selectively and efficiently transduced astrocytes in primary culture or in mouse brain through stereotaxic administration of lentivectors into striatum [STR], hippocampus [HIPP] and prefrontal cortex [PFC] (compared to neurtrophic VSV-G-coated lentivirus as controls). Herein, we evaluated viral spreading and cell-type transduction through immunofluorescent colocalization of EGFP with glial (GFAP and vimentin) and neuronal (NeuN) markers.

Results: After 25 days post-infection, Mok-G,EGFP transduced 68% of cultured astrocytes (EGFP- and DAPI-positive, n = 1); 100% of GFAP-positive cells colocalized with EGFP as well as 86% cells expressing Vimentin only and 47% expressing both Vimentin and GFAP. Mok-G,shA2AR lentiviruses robustly reduced A2AR immunoreactivity compared to Mok-G,shCTR in cultured astrocytes. At 4 weeks post-brain administration, Mok-G,EGFP was expressed mainly in astrocytes (GFAP-positive cells) in both STR and HIPP, and to a lower extent in the PFC, whereas VSV-G-coated lentivirus colocalized with NeuN marker and not with GFAP in any tested brain areas.

Conclusion: These data supports the ability of Mok-G lentivectors to efficiently transduce astrocytes to control A2AR density, paving the way for their application to control pathophysiological processes involving astrocytes.


References

Introduction: The widely consumed psychoactive drug cannabis, containing cannabinoid compounds, and/or caffeine, with adenosinergic antagonizing proprieties, exert their central actions by affecting cognitive operations such as learning and memory. Indeed, endogenous adenosine and endocannabinoids (eCB) are known to interfere with physiological synaptic plasticity phenomena that represent the neuronal substrate of memory formation.

Methods: Whole-cell voltage-clamp recordings (Vh = −70 mV) were performed on hippocampal CA1 pyramidal cells of 3 to 5 weeks-old C57BL/6 mice. Slices (350 μm thick) were perfused with artificial cerebrospinal fluid (aCSF) supplemented with glutamate receptor antagonists (CNQX, 25 μM and DL-APV, 50 μM) to block glutamatergic transmission and isolate GABA-mediated responses. Inhibitory postsynaptic currents (IPSCs) were evoked every 3 s through a stimulation electrode placed in stratum radiatum. The recording electrode was filled with a CsCl-based intracellular solution and DSI was evoked through a 5 s voltage step of +80 mV. The magnitude of DSI was measured 9 s after the depolarizing step and DSI recovery was evaluated between 30 and 60 s after depolarization.

Results: When recording eCB-mediated DSI we observed a decrease in electrical-evoked IPSC amplitudes to 81.0 ± 5.4% of baseline (p < 0.01, n = 14) that fully recovered to 90.2 ± 5.4% after 30–60 s. The adenosine A1 receptor antagonist, DPCPX (100 nM), prevented DSI, recordings showing a non-significant change in IPSCs amplitude to 95.1 ± 12.0% of baseline (p = 0.3473, n = 10) that was maintained throughout the recovery period (87.1 ± 12.0%).

Conclusion: These results suggest that tonic adenosine A1 receptor activation is necessary for the occurrence of DSI. The mechanisms involved in this process remain unclear and need further investigation.1-4

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PS087
High-sucrose diet effects on the dendritic trees of developing neurons of the adolescent rat
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Aim: In the present study, we aimed to explore the effect of high-sucrose diets on the dendritic trees of immature granule cells of the adolescent male rats.

Introduction: Adolescence is a period of high susceptibility to exogenous factors as the rat brain is still developing. Evidence shows that high-sucrose diets may be more detrimental to adolescent rats, therefore we intended to study immature granule cells in the hippocampal formation of these animals. For that, we used