

Oral Communications

OC01

Methanandamide Ameliorates Mast Cell-Mediated Neurogenic Inflammation.

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Aim: Mast cell (MC) degranulation play key role in migraine pathophysiology by inducing dural neurogenic inflammation. It was reported that endocannabinoids could prevent neurogenic inflammation but related mechanisms have not yet been clarified. We aimed to investigate effects of methanandamide and cannabinoid receptors on mast cell degranulation mediated-neurogenic inflammation induced by MC secretagogue compound-48/80.

Methods: In-vivo and ex-vivo rat groups (n=7) were intraperitoneally and topically administered saline, compound-48/80 (2 mg/kg), methanandamide (20 mg/kg), cromolyn (50 mg/kg) + compound-48/80, methanandamide + compound-48/80, rimonabant (2 mg/kg) + methanandamide + compound-48/80, capsazepine (10 mg/kg) + methanandamide + compound-48/80. Neurogenic inflammation markers including calcitonin gene-related peptide (CGRP) and substance-P(SP) levels in plasma, brainstem and brain samples were measured using ELISA. Ex-vivo dural MC numbers and degranulations were determined. Data were analyzed with One-Way ANOVA.

Results: Compound-48/80 increased CGRP and SP levels in plasma, brainstem and brain (p<0.05), these increasements were prevented by cromolyn and methanandamide (p<0.05). Rimobabant blocked effect of methanandamide (p<0.05) but capsazepine had no effect. Methanandamide decreased MC degranulation induced by compound-48/80 in ex-vivo group (p<0.05).

Conclusions: MC degranulation causes neurogenic inflammation by inducing CGRP and SP release in plasma, brainstem and brain. Methanandamide ameliorates neurogenic inflammation by stabilizing dural MCs, as well as by attenuating CGRP and SP release through cannabinoid-1 receptors in brainstem and brain. Endocannabinoids and their receptors may be new targets for migraine treatment. Grant-number: 2016.08.02.1095 (AIBU-BAP).

OC02

Astaxanthin's Free-Radical Scavenging Activity in an Experimental Cerulein-Induced Acute Pancreatitis

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Aim: We investigated astaxanthin (ATX)'s thereupatic effects and underlying antiinflammatory mechanisms in a cerulein-induced acute pancreatitis rat model.

Methods: After ethical approval (76.2017mar), female Wistar rats (n=18) were injected twice with cerulein (50 µg/kg/hr intraperitoneally), with an hour in between (Acute pancreatitis; AP); while control group had vehicle injections (n=6). AP rats were treated with saline, astaxanthin (ATX; 20 mg/kg), astaxanthin + Peroxisome proliferator-activated receptor (PPAR)-alpha antagonist GW6471 (ATX+GW;1 mg/kg). Vehicle, astaxanthin or astaxanthin+GW6471 (ATX+GW) were injected after the first cerulein injection. At the 7th h following the last injection, rats were sacrificed with cardiac puncture under anesthesia. The pancreas was removed and samples were stored for the determination of malondialdehyde (MDA), glutathione (GSH), superoxide dismutase (SOD) and catalase levels, myeloperoxidase activity, luminol-lucigenin chemiluminescence levels. One-Way ANOVA and post-hoc Tukey was performed to analyze data in Graphpad Prism v.7.

Results: In all AP groups GSH was reduced, MDA, MPO and luminol CL were increased (p<0.01). ATX reversed these changes (p<0.01). In contrast to ATX group, elevations in the ATX+GW were not significant. While luminol was decreased in ATX group, lucigenin, SOD, catalase remained unchanged in all groups.

Conclusions: Astaxanthin, probably due to its free-radical scavenging activity, protected pancreatic tissue.

OC03

Effects of Bmal1 on Akt Signal Pathway After Oxygen Glucose Deprivation

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Aim: Circadian rhythm plays an important role in pathophysiological processes. Bmal1 which is involved in the regulator of biological rhythm, is an important contributor to the formation of neuronal damage after brain injury. In this study, we aimed to examine the effects of Bmal1 on cellular damage mechanisms after in-vitro oxygen-glucose deprivation (OGD).

Methods: Cell survival were investigated using OGD in lentivirus mediated Bmal1 overexpression or Bmal1 silencing in N2A cells. Both groups were treated with 1µM melatonin or vehicle at the beginning of reperfusion. To determine effect of Bmal1 on intracellular signalling, targeted proteomics (IP-MS) and pathscan analysis were performed. In addition, the effects of Bmal1 on Akt signalling pathway were demonstrated using in-vitro OGD and in-vivo cerebral ischemia model.

Results: Cell survival were increased in Bmal1 overexpressing cells, while it was decreased in Bmal1 knockdown cells. It was demonstrated that Bmal1 enhanced the level of Akt, Erk-1/-2 and Bad proteins. In addition, it has been shown that Bmal1 effects on Akt signal pathway following in-vitro and in-vivo ischemia.

Conclusions: Results showed that Bmal1 increased cellular survival after ischemic injury via the Akt signal pathway. These results may contribute to the determination of new target molecules for pharmacological therapy.