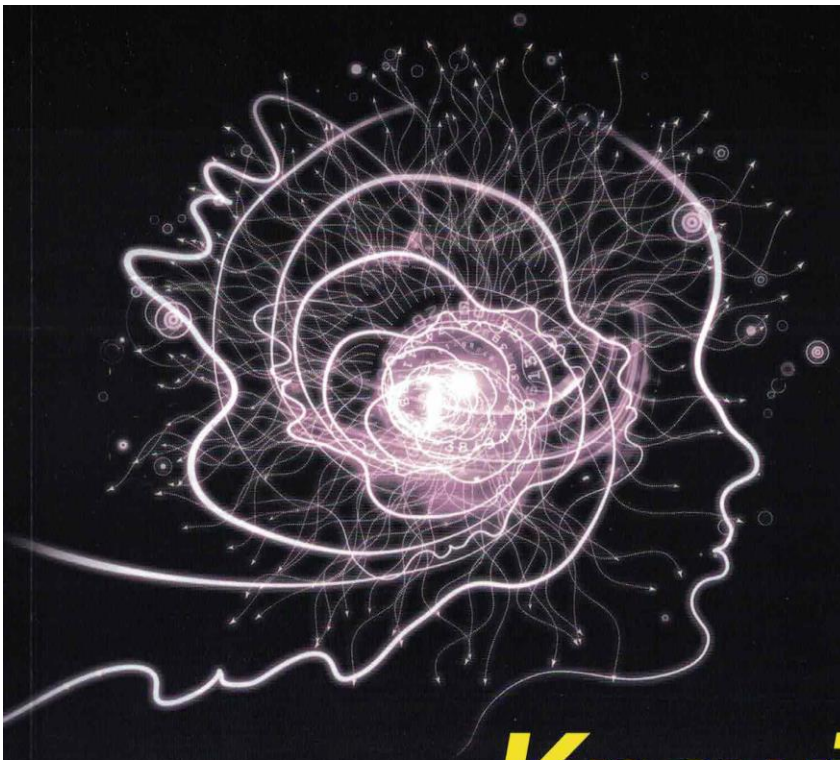

Knowing Brain Healing Brain

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P-1057

Lipocalin-2 is associated with multiple indices of neuropathy in streptozotocin-induced diabetic mice

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Neuropathy is a common complication of uncontrolled diabetes. Metabolic abnormalities and inflammatory process have been associated with diabetic neuropathy. Lipocalin-2 (LCN2) is an acute phase protein known to promote neuroinflammation via the recruitment of inflammatory cells and the induction of pro-inflammatory mediators in diverse neurological disorders. Previously, our study demonstrated that LCN2 contributes to the development of pain hypersensitivity following peripheral nerve injury via proalgesic chemokine expression. Here, we explore the role of LCN2 in multiple aspects of neuropathy in streptozotocin-induced mouse model of diabetes. In this study, we show that induction of diabetes increased the expression of LCN2 in the multiple regions of the both central and peripheral nervous systems including hippocampus, dorsal root ganglion, and sciatic nerve. Genetic deficiency of Lcn2 in mice significantly improved diabetes-induced cognitive impairment, which was accompanied by the reduced glial activation in the hippocampus. Lcn2 deficiency also attenuated diabetes-induced sciatic nerve damages as determined by nerve conduction velocity and density of intra-epidermal nerve fibers. Elevated immune cells and cytokine levels in different nervous tissues were the indicative of a detrimental outcome from diabetes following LCN2 expression. Taken together, our findings highlight the critical role of LCN2 in the pathogenesis of diabetic neuropathy.

Key Words: Lipocalin-2, Diabetes, Neuroinflammation, Intradermal nerve fiber density, Neuropathy

P-1058

Aquilariae Lignum extract attenuates glutamate-induced neuroexcitotoxicity in HT22 hippocampal cells

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An imbalance between excitatory and inhibitory neurotransmitters is known to induce neuronal excitotoxicity which is a major cause of neurodegenerative disorders. Excessive glutamate concentration leads to the neuronal death by increasing oxidative stress and affecting the apoptotic signaling pathway. We investigated the anti-excitotoxic effects and associated working mechanisms of 30% ethanol extract of Aquilariae Lignum (ALE) against hippocampal neuronal death by glutamate. HT22 cells were treated with glutamate (20 mM) for 24h following pretreatment with ALE (5, 10, 25 μg/mL). Cell viability, biochemical analysis, flow chemistry, and Western blotting assays were performed.
Glutamate treatment substantially increased the intracellular level of reactive oxygen species (ROS) and Ca2+ influx into the cell, which were followed by apoptosis. ALE pretreatment, however, significantly attenuated these excitotoxicity-related features according to the results of Annexin V analysis and the lactate dehydrogenase assay, in which the calpain pathway (in a caspase 3-independent manner) may be involved. ALE pretreatment also significantly attenuated the glutamate-induced activation of both inflammation-associated molecules (extracellular signal-regulated kinase, c-Jun N-terminal kinases and p38) and death-related molecules (p53, apoptosis-inducing factor). The inactivation of brain-derived neurotrophic factor (BDNF) was restored by ALE pretreatment.
Our results verified that A. Lignum has potential neuroprotective effects on glutamate-induced excitotoxicity in hippocampal neuron cells, and its underlying mechanism may involve the regulation of ROS-mediated cell death pathways.

Key Words: Aquilariae lignum, Excitotoxicity, Calpain-dependent, Calcium overload, Apoptosis

P-1059

Axonal neuropathy in Charcot-Marie-Tooth disease with stop loss and translational elongations of the 3' UTR in the neurofilament-heavy polypeptide gene

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Previously reported a cryptic amyloidgenic element (CAE) in the 3' UTR of the neurofilament-heavy polypeptide (NEFH) gene as the underlying cause of axonal Charcot-Marie-Tooth neuropathy type 2CC (CMT2CC). Two frame shift variants (p.Asp1004Ginfs*58) and (p.Pro1008Alafs*56) in NEFH in CMT2 families result in stop loss and translation of a CAE encoded by the 3' UTR. This study identified a de novo c.3015_3027dup predicting p.Lys1010Glnfs*57 in NEFH from a Korean CMT2 family with an atypical clinical symptom of prominent proximal weakness. The patient showed atypical clinical manifestations compared to the other CMT patients with axonal neuropathy. There was proximal weakness of the deltoid and hip muscles. Electromyography (EMG) revealed proximal and distal chronic neurogenic changes in a non-length-dependent pattern and additional myopathic features in proximal muscles. Lower limb MRI revealed marked hyperintense signal changes in the thigh muscles compared to those in the calf muscles. In this study, we suggest that stop loss and translational elongations by the 3' UTR of NEFH mutations are frequent genetic cause of axonal Charcot-Marie-Tooth neuropathy harboring the characteristics of proximal dominant weakness.

Key Words: Neurofilament-heavy polypeptide, NEFH, CMT2CC, Axonal neuropathy

P-1060

Effect of inhibitory spike-timing-dependent plasticity on burst synchronization in a scale-free neuronal network

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We consider the Barabási-Albert scale-free network (SFN) composed of inhibitory bursting Hindmarsh-Rose neurons. This inhibitory neuronal population has adaptive dynamic synaptic strengths governed by the inhibitory spike-timing-dependent plasticity (iSTDP). In previous works without iSTDP, burst synchronization (BS) was found to appear in a range of noise intensities for fixed synaptic inhibition strengths. Here, we investigate the effect of iSTDP on BS by varying the noise intensity. We employ an anti-Hebbian time window for the iSTDP update rule, in contrast to the Hebbian time window for the excitatory STDP. A Matthew effect in inhibitory synaptic plasticity is thus found to occur; good BS (with higher bursting measure) gets better via long-term depression (LTD), while bad BS (with lower bursting measure) gets worse via long-term potentiation (LTP). This kind of Matthew effect is in contrast to that in excitatory synaptic plasticity where good (bad) synchronization gets better (worse) via LTP (LTD). Furthermore, emergences of LTD and LTP of synaptic inhibition strengths are intensively investigated via a microscopic method based on the distributions of time delays between the pre- and the post-synaptic burst onset times. Finally, in the presence of iSTDP we investigate the effects of network architecture on BS by varying the symmetric attachment degree l^* and the asymmetry parameter Δl in the SFN, and Matthew effects in inhibitory synaptic plasticity are also found to occur by varying l^* and Δl.

Key Words: Inhibitory spike-timing-dependent plasticity, Burst synchronization, Scale-free network, Bursting neurons