Title	Neuroprotective Effects of Lycium Barbarum Polysaccharides Against Rat Hippocampal Apoptosis Induced by Chronic Intermittent Hypoxia
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Citation	Hong Kong-Taiwan Physiology Symposium 2012 and Joint Scientific Meeting of Hong Kong Society of Neurosciences (HKSN) & The Biophysical Society of Hong Kong (BPHK), The Chinese University of Hong Kong, Hong Kong, China, 14-15 June 2012, p. 65-66, abstract no. P43
Issued Date	2012
URL	http://hdl.handle.net/10722/165033
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EFFECTS OF CHRONIC FLUOXETINE TREATMENT ON HIPPOCAMPAL NEUROGENESIS IN THYROIDOCOMIZED RATS

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Thyroid hormones (TH), thyroxine (T4) and triiodothyronine (T3), produced in thyroid gland, were known to play important roles throughout prenatal and postnatal nervous system development. In rodents, T3 is required for neurogenesis in hippocampus. Additionally, disturbances of thyroid function or the adult neurogenesis might significantly affect mental status, such as depression. Recently, the thyroidectomy including partially or entirely *removal of the thyroid gland has been widely used as an animal* model for studying depression-like behavior.

Fluoxetine, a selective serotonin reuptake inhibitor (SSRIs), is commonly used for *treating depression. T*he present study was aimed *to investigate the effect of fluoxetine on* neurogenesis and depression-like behavior in thyroidectomy model. We found the thyroidecomized rats showed depression-like response in force swimming test and exhibited a significant decline in the number of immature neurons in the dentate gyrus of the hippocampus. Chronic fluoxetine treatment (by oral, 10 mg/kg) enhanced depression-like response in thyroidocomized animals. However, the neurogenesis in the dentate gyrus of thyroidecomized rats could not be recovered by chronic fluoxetine treatments. Our studies suggested that the thyroid hormone may participate in the therapeutic effect of fluoxetine.

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FUNCTIONAL ROLE OF TRPC5 CHANNELS IN AORTIC BARORECEPTOR

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TRP channels are a superfamily of non-selective cation channels that can be divided into seven subfamilies: TRPA, TRPC, TRPM, TRPML, TRPN, TRPP, and TRPV. Many TRP isoforms have been reported to be sensors for diverse source of external and/or internal stimuli. Recently, one of the isoforms, TRPC5, has been reported to be hypo-osmolarity and pressure sensitive.

Aortic baroreceptor is the mechanosensor to detect blood pressure in aortic arch. Upon changes in arterial blood pressure, the baroreceptive nerve terminal on the aortic arch adventitia will be activated, resulting in action potentials that propagate to the cardiovascular control centre in the brain. However, the molecular identity of the baroreceptor mechanosensors is not well understood.

In the present study, immunohistochemistry demonstrated the expression of TRPC5 channels in the aortic baroreceptor nerve terminal, which is located on the aortic arch, along the nerve fiber (aortic depressor nerve) and in the ganglion region (nodose ganglion). RT-PCR and immunoblot studies confirmed the expression of TRPC5 channels in the aortic baroreceptor. In Ca^{2+} imaging studies of cultured aortic baroreceptor neurons, a TRPC5 potentiator daidzein was able to potentiate the hypotonicity-induced $[Ca^{2+}]_i$ response while a TRPC5 blocking antibodies T5E3 inhibited the response. Electrophysiological studies showed that hydrostatic pressure could activate the whole-cell current in cultured baroreceptor neurons and the current displayed a double rectifying *I-V* relationship, which is typical of TRPC5. Daidzein treatment also potentiated the pressure-induced action potential firing in isolated aortic baroreceptor neurons, which could be blocked by a TRPC blocker 2-APB. Furthermore, *trpc5* knockout mice manifested a significant reduction in aortic depression nerve activity upon blood pressure elevation when compared with wild-type mice.

Taken together, our study provides the evidence that TRPC5 is involved in pressure sensing of aortic baroreceptor neuron and is participated in the aortic baroreceptor function.

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NEUROPROTECTIVE EFFECTS OF LYCIUM BARBARUM POLYSACCHARIDES AGAINST RAT HIPPOCAMPAL APOPTOSIS INDUCED BY CHRONIC INTERMITTENT HYPOXIA

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We have shown neuronal apoptosis in the hippocampus of rats exposed to chronic intermittent hypoxia mimicking severe conditions of obstructive sleep apnea (OSA) syndrome in patients [1]. Lycium barbarum polysaccharides (LBP), active biological ingredients of traditional Chinese herbal medicine Goji, have been shown to possess cytoprotective properties [2].

The aim of this study was to examine the protective effects of LBP against neuronal apoptosis in the hippocampus in a severe OSA rodent model. We hypothesized that oral administration of LBP ameliorates neuronal apoptosis in the rat hippocampus induced by chronic intermittent hypoxia.

Adult SD rats were randomly divided into 4 experimental groups, namely: (i) normoxic control (Nx); (ii) Nx treated with LBP; hypoxic groups treated with either (iii) LBP or (iv) vehicle. The hypoxic groups were kept in a normobaric chamber with inspired oxygen alternating from 21 to 5 ± 0.5% oxygen per minute for 8 hr/day for 7 days, whereas Nx groups was maintained in room air for 7 days. LBP (1mg/kg) were orally fed to the rats 2 hours prior the daily hypoxic treatment. Rats were sacrificed and the hippocampus was harvested for measurements of oxidative marker, malondialdehyde (MDA), apoptotic cell death using TUNEL assay, protein expression levels of antioxidant enzymes, and inflammatory cytokines by Western blot.

There were significantly more TUNEL positive –labeling cells in the CA regions and dentate gyrus of the hippocampus in the vehicle-treated hypoxic group than those of the Nx control and LBP-treated groups. In addition, levels of MDA and the protein expressions of cleaved caspase 3 and inflammatory cytokines were increased in the vehicle-treated hypoxic group when compared to the Nx groups and were lowered by the LBP treatment. Intriguingly, there were significantly more PCNA-labeling cells in the dentate gyrus of the hippocampus in the LBP-treated hypoxic groups than those of the other groups. Also, the protein expression of cyclin D1 was increased in the hypoxic groups when compared to the Nx groups.

In conclusion, oral administration of LBP significantly ameliorates oxidative stress, inflammation and neuronal apoptosis with enhanced proliferative activities in the hippocampus of rats exposed to chronic intermittent hypoxia. Thus, LBP may be proposed as a health supplement to mitigate neurological deficits in OSA patients, for which awaits future studies to delineate the neuroprotective mechanism of LBP. *[Studies supported by research grants (HKU 7510/06M, HKU 766110M) from RGC and funding (201007176007, SFPBR 200911159072) from HKU]*

[1] Hung, M.W., *et al*. (2008) *J Pineal Res* 44: 214-221.
[2] Chang, R.C., *et al*. (2008). *Cell Mol Neurobiol* 28: 643-652.

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THERAPEUTIC DEEP BRAIN STIMULATION IN PARKINSONIAN RATS DIRECTLY INFLUENCES MOTOR CORTEX

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Although deep brain stimulation (DBS) of the subthalamic nucleus (STN) is now a recognized therapeutic option for Parkinson's disease (PD), its exact mechanism of action is still not settled. Antidromic activation of the motor cortex from the STN has been hypothesized to contribute to the DBS effect but has not been demonstrated in freely moving hemi-Parkinson's rats and its mechanism remains obscure. Here, in the freely moving hemi-Parkinsonian rats, we identified short latency antidromic spikes in layer V corticofugal projection neurons (CxFn) during STN-DBS. Decreased success rate with increasing stimulation frequency produced the highest frequency of random antidromic spikes at 125Hz stimulation, which correlated with the optimal therapeutic efficacy. This effect was accompanied by increased firing rate, reduced pathological burst discharge and synchronization among the CxFn. Filed potential analysis revealed the renormalization of the pathological beta band oscillation and spike-field coherence during 125Hz STN-DBS. Importantly, we found evidence that the firing probability of the CxFn is modified following the occurrence of antidromic spikes, suggesting that direct interference of synchronized firing by stochastic antidromic spikes underlies the beneficial effect of STM-DBS. Our results therefore support that STN-DBS antidromically activates CxFn in the motor cortex through the cortico-subthalamic projection,