Migration influences autonomic regulation of response to sensory stimuli in children

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Background: Regulation of response towards sensory stimuli is integral towards adaptive functions in children. Autonomic activity between the parasympathetic and sympathetic nervous systems has been suggested to support such regulatory mechanisms. The environment has long been implicated on its ability to influence the autonomic functions of children. However, the influence of migration in influencing autonomic activity is yet to be fully understood. **Aim**: In this research we explore how migration can influence autonomic regulation in the face of sensory stimuli among migrant children compared to their peers between children from their host and origin country. **Methods**: 113 typically-developing children (31 Chinese children in Hong Kong; 28 Filipino children in Hong Kong; and 54 Filipino children in the Philippines) ages 7-12 years old, were subjected to a sensory laboratory paradigm (SLP) while consecutively measuring heart rate variability and electrodermal activity. The SLP comprised of a resting baseline, auditory sensory stimulation and recovery conditions. **Results**: MANOVA results suggest that autonomic regulation of response to sensory stimuli are: 1) significantly different for children inhabiting different countries (p= 0.002-0.005) across conditions; 2) significantly different between migrant children and children from their country of origin (p= 0.002- 0.039) except for recovery conditions; and 3) not significantly different between migrant children and children from their host country across conditions. **Conclusions**: Migration to a new environment influences autonomic activity and has the ability to override ethnicity effects among children in their ability to regulate responses to sensory stimuli. The findings of this study have implications on further understanding the impact of migration on children's health and functioning.

The role of the physical environment on the resting autonomic functions of children

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Background: The experiences at a particular living environment may be different from that at another. Previous research looked at how the physical environment influences behaviours. Resting autonomic functions have been implicated to serve as underlying mechanism for behaviours. Nevertheless, the role of the physical environment on the resting autonomic is rarely examined. **Aim**: The aim of this research is to examine the role of the physical environment on the resting autonomic functions of children. **Methods**: Data from 52 urban and rural-dwelling male children with typical development were analysed for group differences on the multivariate autonomic measures of heart rate variability (HRV) and electrodermal activity (EDA) at resting baseline. The normalized unit of high-frequency band of HRV was used to index parasympathetic activity, while the HRV normalized unit of low-frequency bands and EDA skin conductance level for sympathetic activity during a 3-minute autonomic resting state laboratory paradigm. **Results**: The results of our study suggest significant differences in the resting autonomic functions between children living in different physical environments using a critical α= 0.05 (V= 0.25, F(3,47)= 5.26, p= <0.00, d= 1.16). Our data supports the theory on allostasis, which earlier proposed the mediating role of individual differences in physical living environments on physiological responses. **Conclusion**: The physical environment has the capacity to significantly influence resting autonomic functions. The findings may suggest autonomic mechanisms underlying previously reported behavioural differences influenced by the child's environment.

Cardiac sympathetic nerve activity increase mediated by mechanical pressure stimulation is exaggerated in acutely inflamed muscles

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Inflammation is an influential factor on homeostatic mechanisms. Experimentally-induced myositis reportedly affects withdrawal motor response. In contrast, the influence of myositis on autonomic responses to muscle stimulation has been little studied. Recently, we reported that mechanical pressure stimulation of calf muscles changes cardiac sympathetic nerve activity (CSNA) and heart rate (HR). We aimed to examine the influence of myositis on CSNA changes in response to muscle pressure stimulation. Experiments were performed on isoflurane-anesthetized rats. Respiration was controlled with a ventilator. HR was calculated from arterial pressure waveforms obtained through a catheter implanted in the carotid artery. Mass discharges of CSNA was recorded with bipolar hook electrodes. Mechanical pressure stimulation (10 N/cm^2 for 30 sec) was applied perpendicularly to the calf. To inflame calf muscles, 3% λ-carrageenan solution was injected in a calf on the day before the experiment. Saline was injected to the contralateral calf as control. CSNA increased or decreased in response to mechanical pressure stimulation of inflamed and non-inflamed calves, in parallel with HR. CSNA changes were negatively correlated with pre-stimulus CSNA levels. At the lower level of pre-stimulus CSNA, inflamed calf stimulation consistently increased CSNA and such a change was significantly greater than that of non-inflamed calf stimulation (by 67% and 18% of pre-stimulus level, respectively). In contrast, at the higher level of pre-stimulus CSNA, changes did not differ between non-inflamed and inflamed calf stimulation. The present study results showed that acute myositis exaggerated CSNA increase in response to muscle pressure stimulation.

Cardiovascular pressor effects of orexins in the dorsomedial hypothalamus

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Orexins are important regulators of cardiovascular functions. The dorsomedial hypothalamus (DMH) is an essential mediator of cardiovascular responses to stress and contains dense orexinergic fibers and receptors. In the present study, cardiovascular effects of orexins in the DMH were examined. A unilateral injection of orexin A (30 pmol) in the DMH produced elevation of arterial pressure and heart rate. The sites at which orexin A produced cardiovascular effects were located within or immediately adjacent to the DMH and larger responses were induced at the compact part of the dorsomedial hypothalamic nucleus. Intra-DMH pretreatment of an orexin receptor 1 (OX1R) antagonist, SB-334867 (15 nmol) attenuated orexin A-induced responses (17.7±2.8 vs. 5.2±1.0 mmHg; 54.6±10.0 vs. 22.8±7.4 beats/min). Intra-DMH injection of [Ala^{11},D-Leu^{15}]-orexin B (300 pmol), an orexin receptor 2 (OX2R) agonist, elicited cardiovascular responses mimicking the responses of orexin A, except for a smaller pressor response (7.4±1.7 vs. 16.4±1.8 mmHg). To examine the distribution of OX1R and OX2R that involved in cardiovascular regulation, effects of orexin B (100 pmol) and then orexin A (30 pmol), were examined at a same site. Two patterns of responses were observed: (1) both orexin A and B, and (2) only orexin A induced cardiovascular responses, respectively suggesting OX1R/OX2R-mediated and OX1R-predominant mechanisms. Therefore, orexins regulated cardiovascular functions through OX1R/OX2R- or OX1R-mediated mechanisms at different locations in the DMH.

KNOCKDOWN OF OREXIN IN THE MEDIAL HYPOTHALAMUS REDUCES BLOOD PRESSURE IN ADULT SPONTANEOUSLY HYPERTENSIVE RATS (SHR).

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BACKGROUND: The neuropeptide orexin activates the sympathetic nervous system and contributes to the regulation of blood pressure as part of its role in the control of arousal during wakefulness and motivated behaviour. Recent work suggests that an upregulation of orexin in neurons of the medial hypothalamus contributes to the hypertensive phenotype of the spontaneously hypertensive rat (SHR). AIM: Determine the extent to which a knockdown of orexin in neurons of the medial hypothalamus reduces blood pressure in the SHR. METHODS: SHR (10-14 weeks old, n=15, 145 mmHg average) and normotensive Wistar Kyoto rats (WKY, n=15, 104 mmHg average) were implanted with telemetric probes and bilaterally injected in the medial hypothalamus with an adeno-associated virus (AAV) expressing an shRNA against prepro-orexin. Mean blood pressure (MAP) was recorded day and night weekly for 1 month. RESULTS: A significant interaction between strain and treatment ($p < 0.045$) was found for the change in average MAP one month after the virus injection, when compared to rats with missed injections. This was consistently observed day and night. In the SHR, MAP was significantly decreased (-11.1 mmHg [day] and -11.09 mmHg [night], $p<0.05$) while in the WKY it remained the same (+2.86 mmHg [day] and -0.33 mmHg [night], neither statistically significant). Immunostaining for orexin and NeuN confirmed a reduction in medial hypothalamus orexin expression without sign of neuronal damage. CONCLUSION: The results support the idea that an upregulation of orexin in neurons of the medial hypothalamus contributes to the elevated blood pressure in the SHR.

Prefrontal hemodynamic changes measured using near-infrared spectroscopy during Valsalva maneuver in patients with orthostatic intolerance

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Valsalva maneuver (VM) with beat-to-beat blood pressure (BP) and heart rate monitoring has been used to evaluate autonomic dysfunction including orthostatic intolerance (OI). However, the sensitivity is not enough to detect the cerebral hemodynamic change, which is suspected as the most possible cause in developing symptoms. To investigate cerebral hemodynamics in OI, patients with OI and normal healthy subjects were recruited. VM was performed with beat-to-beat BP monitoring and a NIRS probe on the forehead to investigate the cerebral hemodynamics. Patients were sub-grouped according to VM: patients with normal VM and with abnormal VM. NIRS signals as oxyhemoglobin, deoxyhemoglobin, and total hemoglobin were measured at four different source-detector distances (SD) (15 mm, 30 mm, 36 mm, and 45mm) and estimated for the following parameters; latency, amplitude, duration, and integrated total signal. Those NIRS parameters were compared among the normal healthy control group and the two OI patient sub-groups. We found that the latency of oxyhemoglobin increment at 30 mm SD in healthy control group, normal VM group, and abnormal VM group were as follows: 0.39 ± 0.23 seconds, 2.79 ± 0.36 seconds, and 8.14 ± 0.55 seconds, respectively ($p<0.05$). The healthy group showed a statistically significant sustained blood volume change during VM compared to those of abnormal VM group. Among the four parameters, the latency of oxyhemoglobin increment could be the best marker to detect pathologic status of the OI. Based on our findings, NIRS is a reliable tool to evaluate cerebral hemodynamics evoked by autonomic reflex during VM.

Rapamycin ameliorates the portal hypertension, cardiovascular autonomic dysfunction, and alterations in the excitability of sympathetic and parasympathetic cardiac neurons in cirrhotic rats

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Cardiovascular autonomic dysfunction (CAD) is prevalent irrespective of etiology and contributes to the increased morbidity and mortality in patients with cirrhosis. Recently, we have observed that cirrhosis and portal hypertension-induced CAD is attributable to an imbalance of excitability between sympathetic and parasympathetic cardiac neurons. A previous study has shown that rapamycin improves liver function by limiting inflammation, fibrosis, and portal pressure in the early phase of cirrhotic portal hypertension. Thus, we examined whether rapamycin ameliorates development of the portal hypertension, the CAD, and the functional plasticity of the cardiac autonomic neurons in cirrhotic rats. Biliary cirrhotic rats were generated via common bile duct ligation (CBDL). From the first day of CBDL, rats orally received 0.5 mg/kg/day for 2 weeks. Picrosirius red and Masson staining showed that rapamycin inhibited heavy collagen deposition, as verified by broad fibrotic septa surrounding abnormal nodules. In accordance with the histological examination, rapamycin significantly inhibited CBDL-induced increase in the transcripts that encode alpha-smooth muscle actin, TGF-beta, and type I collagen. Development of the portal hypertension was prevented in the rapamycin-treated CBDL rats. More importantly, rapamycin inhibited the CBDL-induced decreases in the BRS and HRV. Using the gramicidin-perforated patch-clamp technique, cell excitability was recorded in sympathetic stellate ganglion (STG) and parasympathetic intracardiac ganglion (ICG) neurons. Rapamycin inhibited the CBDL-induced increase and decrease in the frequency of action potential discharge in the STG and ICG neurons, respectively. Taken together, these results suggest that cirrhotic portal hypertension is associated with CAD and functional plasticity of the cardiac autonomic neurons.

Bowel movement frequency in patients with idiopathic REM sleep behavior disorder

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Background: Some patients with idiopathic rapid eye movement sleep behavior disorder (RBD) eventually develop Parkinson's disease and may represent premotor Parkinson's disease. Abbott et al. (2007) reported that constipation could be one of the earliest markers of the beginning of the Parkinson's disease process. **Aim**: To examine the association between late-life bowel movement frequency and idiopathic RBD. **Methods**: Information on the frequency of bowel movements was collected using a validated questionnaire (Constipation Assessment Scale) in 63 men aged 53–79 years with video polysomnography-confirmed idiopathic RBD. **Results**: In 23 (36.5%) idiopathic RBD patients, bowel movements occurred once a day or more, but in 40 (63.5%) patients, defecation was less than once a day. Fifty-one (81.0%) patients complained of difficulty with defecation. Nineteen (30.2%) patients used laxatives more than 1–2 times a month. **Conclusions**: These findings provide evidence that constipation is observed frequently in middle-aged and elderly patients with RBD.

Cerebral blood flow during infusion of dobutamine

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We used dobutamine and examined the effect of changes in heart rate and cardiac contractility, and corresponding increases cardiac output and blood pressure on cerebral blood flow (CBF) regulation in humans. Twelve healthy subjects participated in the study, control values of cardiac output and CBF at the internal carotid artery (ICA) and the external carotid artery (ECA) were measured during resting in a supine position. Subjects next received two steady-state infusions of dobutamine (low dose; 5μg/kg/min and high dose; 15μg/kg/min) for 6 min of each dose and the same measurements were repeated. Dobutamine increased cardiac output, via enhanced cardiac contractility and heart rate, as well as arterial blood pressure. Neither dose of dobutamine increased ICA blood flow, while both doses significantly increased ECA blood flow (ICA; -5% and -8%, ECA; +21% and +58%, $P<0.05$, low and high dose). These findings suggest that increase in ECA blood flow under influence of regulated ICA blood flow via cerebral autoregulation may protect over-perfusion of intracranial blood flow during elevations in cardiac output and accompanying increases in blood pressure.

Study of short term heart rate variability in patients with transient ischemic attack

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Background: Cardiac autonomic dysfunction is commonly observed in stroke patients. However little is known about the status of autonomic functions in patients with transient ischemic attack (TIA). Given the similarities in the pathogenesis of stroke and TIA, we hypothesized that the abnormal autonomic functions would be more common, and more frequently impaired, in patients with TIA when compared with controls. **Aim**: The study aimed to investigate cardiac autonomic functions in terms of heart rate variability (HRV) in TIA patients and compare it with normal controls. **Methods**: 20 TIA patients and 20 age and sex matched controls were included. Patients were recruited from Neurology OPD of VMMC and Safdarjung Hospital. Control participants were either family members, friends of recruited patients or were those attending OPD for minor complaints. The study was launched after getting ethical clearance from Institutional ethical committee of VMMC and Safdarjung Hospital, New Delhi. In time domain we measured standard deviation of normal R-R interval (SDNN), root mean square of successive R-R intervals (RMSSD). In the frequency domain we measured high frequency power (HF), low frequency power (LF) and LF/HF ratio. **Results**: Compared with controls, HRV components including SDNN, RMSSD, Total spectral power, HF spectral power were reduced and LF/HF significantly increased in patients with transient ischemic attack. **Conclusion**: Our study provides a good evidence about presence of autonomic dysfunction in TIA patients. Though, both sympathetic and parasympathetic nervous system was found to be affected, more affection was of parasympathetic division.

Influence of interaction among the elderly through amusement on their salivary amylase and autonomic nervous system activity: One-month introduction at a day care service center for the elderly

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Background: Prevention of nursing through amusement devices has recently been attracting attention. Matsukuma et al. was suggested that amusement increases motivation and positiveness, promotes activeness, and produces new communication [1, 2]. However, no study on the physiological function demonstrating 'pleasant stimulation' by interaction through amusement has been performed. **Objective:** Amusement was introduced for one month and interaction among the elderly and its influence on their salivary amylase, autonomic nervous system activity were investigated. **Methods:** The subjects were 9 elderly females (age: 89.0±4.7 years old) who periodically visited a day care service center for the elderly. The survey was performed between October 2015 and December 2015. For the amusement, Blackjack was introduced. The survey period was comprised of 3 amusement introduction periods: pre-amusement, and one week and one month after amusement introduction. In each period, sympathetic nerve activity (CSI), and parasympathetic nerve activity (CVI) were measured during amusement, and the difference in the salivary amylase level between before and after amusement was determined. Repeated measures one-way ANOVA was performed regarding the survey period as a factor and CSI, CVI, and difference in the amylase level as dependent variables. **Results:** Significant amusement-induced changes were noted in the CVI and salivary amylase level. These were significantly lower at one month after amusement introduction than those in pre-amusement. **Conclusion:** Amusement-induced laughing and regret or interaction through the amusement influenced their autonomic nerve system and they may have felt comfortable.

References

[1] Matsuguma H, Fujioka S, Nakajima A, Kaneko K, Kajiwara J, Hayashida K, et al. Research and Development of Serious Games to Support Stand-up Rehabilitation Exercises (in Japanese). Information Processing Society of Japan journal. 2012; 53(3): 1041-1049.
[2] Matsuguma H, Fujioka S, Nakamura N, Harada H, Hyakutake E, Uchinoura M, et al. Introduction of The Serious Game into Long-Term Care Health Facility to Support Stand up-Sit down Exercise for Rehabilitation (in Japanese). Institute of Electronics, Information, and Communication Engineers Technical Report, Multimedia and Virtual Environment. 2012; 112(25): 13-17.

Effect of Low-Frequency Electroacupuncture Stimulation into the Sacral Region on the Heart Rate and Defecation Function

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Decrease in defecation function significantly reduces QOL. So far, it is reported that there are about 750,000 people with constipation in Japan per 10 million people, and there are still many. Therefore, the discovery of other treatments is urgent. So this study aimed to clarify in the effect of low-frequency electroacupuncture (EA) stimulation into the sacral region on the heart rate (HR) and defecation function. We conducted a randomized-controlled crossover study. Subjects were ten subjects who were evaluated as constipation tendency by the Japanese version constipation measure (CAS-J). Initially, the participants were randomly assigned to one of the two following groups: sham group and EA group. The intervention was conducted for 5 days. After 5 minutes resting, the subjects received 15 minutes sham stimulation or EA stimulation, during which, with the HR were measured. The CAS-J score was measured again after the completion of the intervention. In the EA group, bilateral sites between the first and second sacral foramina were stimulated at a frequency of 2 Hz. In the sham group was tapped to the skin at the same sites using an acupuncture tube. The EA group was decreased HR and CAS-J score better than the sham group. Therefore, it was suggested that EA stimulation to the sacral region may decrease HR and promote defecation function.

Evaluation of cardiac autonomic functions and C-reactive protein in patients of first myocardial infarction with and without type 2 diabetes mellitus

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Background: Diabetic subjects are more likely to experience a myocardial infarction(MI) and have worse outcomes compared to non-diabetics. However, underlying mechanisms are not clear. Recent observations point to the role of autonomic dysfunction and inflammation in pathogenesis of diabetes mellitus(DM) as well as MI.Despite a close association between DMand MI, there is absence of comprehensive study on the impact of diabetes on autonomic functions along with inflammatory marker i.e. high sensitivity C-Reactive protein(hsCRP)in MI patients. **AIM**: To study the impact of type 2 DM on cardiac autonomic functions and inflammatorystatus of MI patients. **Methods**: 60 diagnosed patients of first MIof either sex (age range 45-65 years),30 with type 2 DM(group I) and 30 without diabetes(group II) were selected between 4-6 weeks of acute episode of MI.The cardiac autonomic functions included short term heart rate variability and standard battery of cardiac reflex tests. Fasting blood sample was taken for hs-CRP levels. **Results**: HRV parameters such as Standard deviation of normal to normal RR interval(SDNN),Square root of mean squared differences of successive RR intervals(RMSSD), total power, low frequency(LF)and high frequency(HF)and parasympathetic reactivity tests(Deep breathing test, 30:15 ratio)were reducedin diabetics as compared to non diabetic MI patients. CRP levels were similar but associations of level of inflammation with autonomic tests was found in both groups. **Conclusion**: Cardiac autonomic tests are worsened bypresence of diabetes in MI patients and inflammation also has an impact on these tests.

Aortic baroreceptor activity in relation to the rheological properties of the atherosclerotic aorta in KHC rabbits

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Pathohistological alteration of the arterial wall due to atherosclerosis could affect baroreceptor activity. We investigated change in aortic nerve activity (ANA) due to administration of vasoactive drugs in relation to the rheological properties of the wall in eight normal and Kurosawa and Kusanagi-hypercholesterolemic (KHC) rabbits aged 10-12 months under pentobarbital and butorphanol anesthesia. Changes in arterial pressure (AP) at the ascending aorta and left ANA in response to intravenous injections of phenylephrine and sodium nitroprusside were recorded simultaneously. Circumferential wall strips were excised for mechanical tensile test from the ascending aorta and from the region between bifurcation of the brachiocepharic and left subclavian arteries where aortic baroreceptors exist closely. The threshold of baroreceptors in the KHC rabbit group was significantly high compared with that in the normal rabbit group. Maximal ANA during a rise in AP reduced markedly in the KHC rabbit group. The sensitivity of the baroreceptors was significantly lower in the KHC rabbit group than in the normal rabbit group. Wall tension in the ascending aorta at high strain was significantly greater in the KHC rabbit group than in the normal rabbit group whereas there was no significant difference in wall tension between the two rabbit strains at any strain. Wall stress and incremental elastic modulus in the baroreceptor region were significantly smaller in the KHC rabbit group than in the normal rabbit group. We can conclude that the reduced transducer activity of the aortic baroreceptors was mainly caused by pathohistological alteration of the wall due to atherosclerosis.

Effect for autonomic nerves activity and psychological condition by the combination of nitrous oxide inhalation sedation and listening to music

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Background: Nitrous oxide (N_2O) inhalation sedation or listening to music has been widely accepted as a relaxation method during dental treatment. However, it is unclear the effect of the combination of N_2O inhalation sedation and listening to music on human's body and mind. Aim: We analyzed the heart rate variability (HRV), Modified Dental Anxiety scale (MDAS), modified visual analog scale (modified VAS), and State-Trait Anxiety Inventory (STAI) scores to clarify the effect for autonomic nerves activity and psychological condition by the combination of N_2O inhalation sedation and listening to music. Methods: Forty healthy volunteers were randomized into four groups: air inhalation group (control group), N_2O inhalation group (N_2O group), listening to music group (music group), and N_2O inhalation and listening to music group (N_2O and music group). HRV was recorded during the experiment. MDAS, modified VAS, and STAI scores were evaluated pre and post-experiment. Results and Conclusions: When compared to the control group, low frequency/high frequency (LF/HF) was significantly increased in the music group during the intervention ($p<0.05$). The increased LF/HF seen in the music group was significantly decreased in the N_2O and music group ($p<0.05$). The anxiety score evaluated by MDAS, modified VAS and STAI-S in the N_2O and music group was the most reduced in the four groups ($p<0.05$). Our results suggested that the combination of N_2O inhalation sedation and listening to music alleviated the autonomic nerves activity and the psychological condition.

Activated brown adipose tissue shows nuclear accumulation of phosho-nuclear factor kappa B p65-like immunoreactive protein

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Brown adipose tissue (BAT) generates heat in response to sympathetic activation, and is involved in body temperature regulation and body weight control. Our previous immunohistochemical studies showed that a protein (or proteins) detected by an antibody against phosphorylated nuclear factor kappa B p65 (pNFkB) accumulated in the nucleus of activated BAT cells. In this study, to examine if the pNFkB-like protein accumulated in the nuclei of activated BAT is real NFkB, we studied its molecular weight by Western blotting (WB). ***In vivo* study**: Mice were maintained at 30°C for 18 hours, and exposed to cold (4°C) for 15, 30 or 60 min. Mice kept at 30°C were used as the control. Nuclear fraction of BAT was processed for WB. Exposing mice to 4°C significantly augmented a protein band with molecular weight 120,000. This response was evident after 15 min cold exposure and remained at similar levels after 30 and 60 min cold exposure. ***In vitro* study**: Primary culture of rat BAT cells were stimulated with a beta adrenergic agonist, isoproterenol (ISO: 1-10 μM), for 10, 30 or 60 min. The nuclear fraction was analyzed by WB. A protein band with molecular weight 45,000 was significantly augmented by ISO (1μM, 10 min). In both the *in vivo* and *in vitro* studies, we could not detect a protein band with molecular weight around 65,000 corresponding to that of NFkB p65. These results indicate that the protein that is accumulated in the nuclei of activated BAT is not NFkB p65.

Identification of neurotransmitters acting on the spinal defecation center in rats.

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Regulation of defecation reflex by the central nervous system is of particular interest, as understanding these mechanisms may shed light on the pathophysiology of some diseases such as the irritable bowel syndrome. It has been known that defecation control centers are located in the pontomedullary brainstem and lumbosacral spinal cord. However, functional roles of them, especially the roles of lumbosacral defecation center, in regulating colorectal motility remain unclear. We have previously set up an in vivo experimental system to address this issue, and demonstrated that a peptide hormone ghrelin activates the spinal defecation center, resulting in propulsive colorectal motility. In this study, we aimed to investigate neurotransmitters that control colorectal motility through acting on the spinal defecation center. Rats were anesthetized with alpha-chrolarose and ketamine. The rats were cannulated at the colorectum and changes in colorectal pressure and expelled volume were measured. We injected noradrenaline, dopamine, serotonin, histamine or somatostatin into the lumbosacral spinal cord. When histamine was injected into the spinal defecation center, there was no change on colorectal motility. In contrast, intrathecally injected noradrenaline, dopamine, serotonin or somatostatin, respectively, enhanced colorectal motility. Further investigations of the mechanism of action revealed that these neurotransmitters directly act on the spinal defecation center and the effects are transmitted thorough the pelvic nerve that is the sacral parasympathetic nerve. These findings are important to understand how the central nervous system controls defecation and would provide new insights into the pathophysiology of colorectal dysfunction in patients of the irritable bowel syndrome.

Serotonin in the lumbosacral defecation center regulates colorectal motility in rats

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Irritable bowel syndrome is stress-induced disturbed bowel habits characterized by abdominal pain and motility disorder such as diarrhea or constipation. However, a causal mechanism remains unclear. The descending inhibitory pain modulation pathway that is activated by abdominal pain in irritable bowel syndrome involves projections from the rostral ventromedial medulla, in which serotonin biosynthesis is increased by stress, to the spinal cord. We hypothesized that serotonin released from the rostral ventromedial medulla influences the lumbosacral defecation center and dysfunction of the serotonergic regulation may be related to defecation disorders. In the present study, therefore, we examined effects of stimulation of 5-HT receptors in the lumbosacral spinal cord on colorectal motility in rats. Colorectal intraluminal pressure and expelled fluid volume were recorded in anaesthetized rats. Administration of serotonin into the L6-S1 spinal cord elicited periodic increases in colorectal intraluminal pressure, being associated with increases in fluid output. Pharmacological experiments revealed that the serotonin-induced enhancement of colorectal motility is mediated by both 5-HT2 and 5-HT3 receptors. The colokinetic effect of serotonin was unaffected even after disconnection of the defecation center from supraspinal regions by severing the T8 spinal cord, while transection of the pelvic nerves prevented the effect of serotonin. Simultaneous administration of sub-effective doses of serotonin, dopamine and noradrenaline, neurotransmitters of descending pain inhibitory pathways, into the spinal cord caused propulsive colorectal motility slightly but substantially. In conclusion, serotonin acts on 5-HT2 and 5-HT3 receptors in the lumbosacral defecation center to enhance colorectal motility in cooperation with dopamine and noradrenaline.

The autonomic nerve function of patients with lower extremity lymphedema during complex decongestive physiotherapy

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Background and Aim: We investigated the autonomic nerve function (using heart rate variability [HRV]) of patients hospitalized with lower extremity lymphedema who underwent two weeks of complex decongestive physiotherapy. Subjects: The two healthy patients included a 56-year-old woman and a 62-year-old woman who had undergone hysterectomy and inguinal lymphadenectomy, respectively. Methods: Compression was performed for two weeks using the device and bandage. And they did rehabilitation during compression. The subjects performed a standing 6-minute walk tests twice (before and after therapy). In the standing test, the subject sat for 5 min, stood for 10 min, then sat again for 5 min. During the standing test, blood pressure, heart rate, bilateral frontal head oxygen saturation (SaO_2,HbI)) and the autonomic nervous function (by evaluating heart rate variability [LF,HF,L/H]) were chronologically measured. Results: The patients showed a smaller thigh circumference and longer the distance of 6-minute walk test. At the start of the study, the heart rate and blood pressure variability during the standing test was greater than at the end. The absolute autonomic nerve function values at the start were higher than at the end. The autonomic nerve function values during the standing test were higher at the start of the study period and normal at the end. Discussion and Conclusion: The exercise tolerance and swelling of the patients improved. We hypothesize that the autonomic nerve function was high before complex decongestive physiotherapy, which encouraged venous return, and that the improved swelling reduced the autonomic nerve activity, correcting the peripheral circulatory function

Blockade of orexin 2 receptor in the paraventricular nucleus reduced arterial pressure in spontaneously hypertensive rats

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Numerous studies have suggested the important role of orexin (also known as hypocretin) in the regulation of cardiovascular homeostasis. Overactive orexin system may participate in the development of essential hypertension in the spontaneously hypertensive rats (SHRs). In the central nerve system, the paraventricular hypothalamic nucleus (PVN) is well known as a critical site to tonically control cardiovascular functions. Furthermore, functional studies also demonstrated that the PVN is an essential region responsible for maintaining hypertension in SHRs. Orexinergic fibers and orexin 2 receptor (OX2R) were detected at high levels in the PVN, indicating that orexin mainly actions through OX2R in the PVN. Thus, we examined the role of OX2R activity in the PVN in the regulation of hypertension. Arterial pressure and heart rate were recorded in anesthetized SHRs and Wistar-Kyoto (WKY) rats. Bilateral microinjections of a selective OX2R antagonist, TCS-OX2-29 (10 nmole), into the PVN at levels 1.4 to 2.1 mm caudal to the bregma caused long-lasting and significant reductions of mean arterial pressure (MAP) and heart rate in SHRs (35 ± 8 mmHg and 37 ± 13 beats min^{-1}, n=5) when compared with vehicle treated group (n=6). TCS-OX2-29 did not cause significant changes in either MAP or heart rate in WKY rats (n=5). This study provides evidences indicating that elevated OX2R activity in the PVN may contribute to the maintenance of hypertension in SHRs.