学 位 論 文 の 要 旨

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学　位　論　文　名　Evaluation of Autonomic Nervous System by Salivary Alpha-Amylase Level and Heart Rate Variability in Patients With Schizophrenia

発　表　雑　誌　名　European Archives of Psychiatry and Clinical Neuroscience
（巻: 初頁～終頁等, 年）　(doi: 10.1007/s00406-013-0411-6 [Epub ahead of print])

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論 文 内 容 の 要 旨

INTRODUCTION

During the onset and progression of schizophrenia, there are many signs of dysfunction of the autonomic nervous system (ANS). That suggests the possibility of an imbalance between sympathetic and parasympathetic activity. As the relative stability of internal environment depends largely on the functioning of the ANS, even a slight disorder of the ANS could induce a wide range of neuropsychophysiological disorders. Therefore, a practical method to evaluate sympatho-vagal activity would be useful in clinical sciences. Several studies have also shown alterations in ANS using electrophysiological methods such as electrodermal measures and heart rate variability (HRV). These studies have demonstrated decreasing of the ANS in patients with schizophrenia.

On the other hand, salivary alpha-amylase (sAA) has recently been considered to be a useful marker for evaluating the sympathetic-adrenal-meduallary (SAM) system. Several studies reported a significant increase in sAA following psychosocial stress, indicating the association of high stress levels with higher sAA. When sudden stressful stimuli occur, sympathetic fibers trigger the salivary glands, which secrete amylase within minutes. Therefore, sAA has the potential to be useful as a marker of autonomic activity because salivary gland secretion is regulated by both SNS and PNS. There was a study that reported that the sAA level

was increased significantly in patients with schizophrenia compared to controls and that the correlation between the sAA level and psychotic state was highly significant in patients with schizophrenia. However, there is little evidence as to which branch (sympathetic or parasympathetic) of the ANS is predominant in the increases in sAA. We investigated ANS function represented in patients with schizophrenia by measuring sAA and HRV.

MATERIALS AND METHODS

The study subjects consisted of 25 patients with schizophrenia and 25 healthy controls, who were recruited from October 2010 to March 2011. Schizophrenia symptoms were assessed using the Brief Psychiatric Rating Scale (BPRS). First, subjects were measured sAA activity by using hand-held monitor. Next, HRV was checked with a hand-held device consecutively. Five min electrocardiogram segments were obtained, and power spectra were automatically created via a fast Fourier transformation. The resulting spectrum was integrated, and areas associated with discrete frequency bands were obtained from the output of the device: low frequency (LF: 0.04-0.15 Hz) of HRV representing both SNS and PNS activity; high frequency (HF: 0.15-0.4 Hz) of HRV associated almost entirely with PNS activity; total power (TP: 0.03-0.4 Hz) representing overall ANS activity.

RESULTS AND DISCUSSION

The sAA activity in the patients was significantly higher than that in the controls ($p<0.001$). Furthermore, the correlation between sAA level and psychiatric symptoms was highly significant ($P=0.02$).

With respect to differences in the HRV between the two groups, spectral powers, which mainly reflect PNS activity, were markedly lower in the schizophrenia group than in the control group (HF, $p=0.007$). However, there were no significant differences between two groups in the spectral powers that reflected mainly SNS activity (LF/HF, $p=0.47$).

In the present study, we found that the sAA levels in patients with schizophrenia were significantly higher than those of normal healthy controls and that the sAA level increased significantly with increases in psychotic state. With respect to differences in the HRV between the two groups, spectral powers, which mainly reflect PNS activity, were markedly lower in the schizophrenia group than in the control group. However, there were no significant differences between two groups in the spectral powers that reflected mainly SNS activity. We suggest that the sAA level is increased mainly by inhibition of PNS activity and that SNS shows relatively high activity. We also consider that measurement of the sAA level may be a useful marker for assessment of the severity of schizophrenia. Further research with additional subjects is clearly necessary because the mechanism of schizophrenia, especially dysfunction of the

sympatho-parasympathetic balance, is still poorly understood.

CONCLUSION

The results of this study indicate that the reduced PNS function is characterized by increase in sAA level in patients with schizophrenia. These findings imply that PNS activity might be suppressed and the SNS shows relatively high activity in patients with schizophrenia.