

Is there activity-dependent neurotransmitter respecification in the human hypothalamic suprachiasmatic nucleus between day and night and in depression?

- A pilot study-

Wu¹, X., Bao¹, A., Swaab², D.F.

1. Department of Neurobiology; Key Laboratory of Medical Neurobiology of Ministry of Health of China; Zhejiang Province Key Laboratory of Neurobiology, Zhejiang Province Key Laboratory of Mental Disorder's Management; Zhejiang University School of Medicine, 866 Yu-Hang-Tang Road, Hangzhou 310058, China.

2. Netherlands Institute for Neuroscience, Meibergdreef 47, 1105 BA Amsterdam, the Netherlands. d.swaab@nin.knaw.nl

Research question and background

Dysfunction of neurotransmitters or neuropeptides in the hypothalamic suprachiasmatic nucleus (SCN), e.g. GABA or vasopressin (AVP), may play an important role in neuropsychiatric disorders, such as depression. Recent studies showed that activity-dependent neurotransmitter switching between dopamine and somatostatin (SST) in the hypothalamic paraventricular nucleus (PVN) and periventricular nucleus (PeVN) promoted depressive behavior in rats. Our hypothesis, based upon previous studies, is that there might be activity-dependent neurotransmitter respecification in the human SCN, PVN and PeVN between day and night and that differences may exist in depression. The present research aimed to validate this hypothesis in postmortem human brain material.

Methods and tissues used

Hypothalami was obtained from the Netherlands Brain Bank. Three depressed patients and 12 control subjects were studied in a pilot experiment. The controls were further grouped according to i) age, i.e. young (<50 years, n=6 for SCN and 7 for PeVN or PVN study) and old (>50 years, n = 6 for SCN and n=4 for PeVN or PVN study) group; ii) time of death, i.e. daytime (died between 6:30 AM and 13:50 PM, n= 6), and nighttime (died between 21:00PM and 4:00AM, 6 for SCN and n=5 for PeVN or PVN) group; and iii) gender, i.e. male (n=4 in SCN and 6 in PeVN or PVN), and female (n=8 in SCN and n=5 in PeVN or PVN) group. The density of glutamic acid decarboxylase (GAD_{65/67}) and AVP immunoreactivity (ir) was quantified in the SCN, while tyrosin hydroxylase- (TH) and SST-ir were measured in the PVN and PeVN.

Results and conclusion

In the SCN, there was an increased ratio of GAD_{65/67} /AVP-ir level (P = 0.045) in the depression group compared with controls. The density of GAD_{65/67} in the old age group was significantly higher than in the young group (P = 0.037). In addition, there was a tendency of increase in GAD_{65/67} -ir in the night- compared with the daytime death (p = 0.078), while there was no sex difference in GAD_{65/67} -ir in the SCN (P>=0.283). Moreover, there was significant increase in SST-ir (P = 0.036) but decrease in TH-ir (P = 0.036) in the PeVN, together with a tendency toward increased SST/TH-ir (P = 0.052) in the PVN in the depression group. However, in most patients TH and SST were not localized in the same area of the PVN and PeVN.

Activity-dependent neurotransmitter respecification of dopamine and SST in the human hypothalamic PVN and PeVN may not exist. Based upon the pilot study, further research is undertaken on activity-dependent neurotransmitter respecification of GABA and vasopressin in the human hypothalamic SCN between day and night and in depression.