Reduced GAD65/67 immunoreactivity in the hypothalamic paraventricular nucleus in depression: A postmortem study
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Research question and background
Gamma-aminobutyric acid (GABA) is a major inhibitory neurotransmitter. It diminishes the activity of the hypothalamo-pituitary-adrenal (HPA) axis, which plays an important role in the pathogenesis of depression. The present study aimed at determining GABAergic input in the hypothalamic paraventricular nucleus (PVN) in depression and its correlation with the activity of corticotropin-releasing hormone (CRH) neurons.

Methods and tissues used
Brain material was obtained from the Netherlands Brain Bank (NBB, director Dr I. Huitinga) following permission for a brain autopsy and for the use of the brain material and clinical data for research purposes. The density of glutamic acid decarboxylase (GAD)(65/67)-immunoreactivity (ir) was quantified in the postmortem hypothalamic PVN of 9 major depressive (MDD) and 5 bipolar depressive (BD) patients, together with 12 matched controls, whose CRH-expressing neuron numbers had been determined in a previous study.

Results and conclusion
There was a 43% significant reduction of the density of GAD(65/67)-ir in the PVN in MDD (P=0.028) and a 20% non-significant decrease in BD patients. In addition, there was a significant negative correlation between the density of GAD(65/67)-ir and the number of CRH-ir neurons in the PVN in the depression group (Rho=-0.527, P=0.032), but not in the control group. These data suggest a diminished GABAergic input to the PVN may contribute to the activation of CRH-ir neurons in depression, most prominently in MDD, which provides a rationale for prescribing GABAergic agonists for these patients.
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