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Topographical study of the distribution of GABA in the human substantia nigra

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In 1971, Precht & Yoshida first proposed the hypothesis that striatonigral fibres release GABA as a transmitter. Since then, interest has been focussed on the high concentrations of GABA which occur in the substantia nigra of most mammals and man (Perry, Hansen & Kloster, 1973). Since GABA, glutamic acid decarboxylase and the high affinity uptake of GABA appear to be specifically located in the nerve terminals of certain inhibitory neurons, it has been proposed that GABA in the substantia nigra may well be exclusively localized in nerve terminals. The main cellular components of the human substantia nigra are the melanin-rich cells which send their axons to the striatum and are believed to be dopaminergic in function. It would be of interest, therefore, to know the morphological distribution of GABA in the substantia nigra and its relationship to the dopaminergic neurons. In addition it now appears that a knowledge of the distribution of GABA in the substantia nigra could be of clinical value since a decreased level of GABA in the substantia nigra appears to be a feature of Huntingdon's chorea.

The midbrain from a neurologically normal 28-year-old male was obtained at autopsy within four hours of death. Using the method of Miyata & Otsuka (1972), transverse sections (150 μm thickness) of the rostral, middle and caudal substantia nigra were placed in a cold box (-20°C) and cut under a binocular microscope into 500 x 500 μm square blocks with a razor blade. The map of GABA distribution in each level of the substantia nigra was obtained by superimposing photographs taken before and after cutting the sections into square blocks.

In the rostral substantia nigra, the GABA distribution was markedly uneven, and the highest concentrations (more than 11.0 mM) were found in the pars reticulata. In the middle and caudal substantia nigra the GABA distribution was again uneven and the highest GABA levels were equally divided between the pars reticulata and the pars compacta. More detailed analysis of the results also supported the view that in the substantia nigra the highest concentrations of GABA are due to the presence of striato-nigral nerve terminals as they synapse with the dendrites of the nigral dopaminergic neurons whose cell bodies are located in the pars compacta (Rinvik & Grofova, 1970). In the cat more than half the synapses in the pars reticulata undergo degeneration following lesions of the ipsilateral caudate nucleus (Grofova & Rinvik, 1970) and the same kind of lesion in the rat is accompanied with a reduction in the GABA concentration of the substantia nigra.

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