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This Week's Citation Classic™

Vogt M. The concentration of sympathin in different parts of the central nervous system under normal conditions and after the administration of drugs.
J. Physiology **123**:451-81, 1954.
[Department of Pharmacology, University of Edinburgh, Scotland]

A map of the distribution of noradrenaline (NA) and adrenaline was obtained by bioassay of extracts of about 50 freshly dissected regions of the dog's brain and spinal cord. The NA concentration ranged from 2.0 to 0.01 µg/g fresh tissue. [The *SCI*® indicates that this paper has been cited in over 995 publications since 1955.]

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"The work was done in J.H. Gaddum's laboratory at the University of Edinburgh. It took about four years to carry out (1950-1953), but the manuscript was accidentally buried on the editor's desk until I finally had the courage to enquire about its fate. It was then published with great speed and without editorial corrections.

"The fact that cholinergic neurones (identified by the presence of choline acetyltransferase) had been shown[1] to be very unevenly distributed in the brain and practically absent from large regions suggested that acetylcholine could not be the only nervous transmitter in the central nervous system. The only other transmitter known at that time (1952) in peripheral nerves was noradrenaline (NA). A small amount of this transmitter was known to occur in the brain but was assumed to be localized exclusively in nerves to the blood vessels.

"A preliminary comparison of the concentration of NA in hypothalamus and cerebellar cortex showed that the NA was so much greater in hypothalamus than in cerebellar cortex (both highly vascularized regions) that the explanation of the difference by variable vascularity could not be correct. This observation led to my undertaking a survey of concentrations of NA and adrenaline in many brain regions with a method which used paper chromatography followed by biological assay, at the time the most sensitive method available. The results could hardly be explained by assuming that vasomotor nerves were the main source of cerebral NA, and suggested a characteristic uneven distribution of noradrenergic neurones in the brain tissue itself. Fluorescence microscopy carried out soon afterward by Swedish workers showed that catecholamine fluorescence was indeed present within neurones, many of which were found in the hypothalamus, but only a few in the cerebellum.

"Since dopamine (DA) is an obligatory precursor of NA and adrenaline, it is found in all catecholamine containing neurons. However, as shown by Carlsson,[2] there are large brain regions in which DA is the final product, and where it is therefore supposed to play the role of a transmitter or 'modulator' of impulses. Three examples are the nigro-striatal pathways, the arcuate nucleus, and certain layers in some cortical areas. There is particular interest in this last site, since the clinically beneficial effect of antagonists of DA (such as chlorpromazine) in schizophrenia can hardly be expected to be due to their action on the nigro-striatal system or on the arcuate nucleus, but a site of action in the cerebral cortex is a clear possibility."

1. **Feldberg W & Vogt M**. Acetylcholine synthesis in different regions of the central nervous system. *J. Physiology* **107**:372-81, 1948. (Cited 265 times since 1955.)
2. **Carisson A**. The occurrence, distribution and physiological role of catecholamines in the nervous system. *Pharmacol Rev*. **11**:490-3, 1959 (Cited 380 times.)