This Week's Citation Classic ®

Jacobowitz D M & Palkovits M. Topographic atlas of catecholamine and acetylcholinesterase-containing neurons in the rat brain. I. Forebrain (telencephalon, diencephalon). II. Hindbrain (mesencephalon, rhombencephalon). *J. Comp. Neurol.* **157**:13-28; 29-42, 1974. [Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, MD]

These two publications provided the first detailed and complete stereotaxic maps for catecholaminergic and acetylcholinesterase-staining neuronal perikarya, fibers, and terminals by using coronal serial sections throughout the whole rat brain. [The *SCI*® indicates that these papers have been cited in more than 600 and 870 publications, respectively.]

The Birth of Neurochemical Maps

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In the late 1960s and early 1970s, the excitement of catecholamine-fluorescence microscopy work of the Swedish groups in Lund and Stockholm was in the air. This technique was most instrumental in the development of what was to become the explosion that led to the "Decade of the Brain." In this same time period, it was becoming progressively more convincing that norepinephrine and dopamine were acting as neurotransmitters in the central nervous system (CNS). The functions and properties of catecholamine-containing neurons were being extensively studied, in addition to numerous drugs that influenced the uptake, storage, and release of monoamines. The fluorescence histochemical technique led to rapid advances in our knowledge of the localization of catecholaminergic cell bodies, axonal pathways, and terminal fiber plexuses.[1]

We met in 1972 at the National Institutes of Health when Mickey Palkovits arrived there from Hungary. We both agreed that there was a need for a brain stereotaxic map of the discrete localization of catecholamines. A variety of neurobiologists required detailed information of the precise localization of aminergic neurons. Because of the known dual innervation of peripheral organs by the cholinergic and adrenergic nerves of the autonomic nervous system, it was of interest to also map the localization of cholinergic nerves in the brain. For this we used the acetylcholinesterase(AChE)histochemical stain of George Koelle and J.S. Friedenwald.[2] In fact, Koelle had already described the localization of brain AChE.[3] With few exceptions, this enzyme remains an excellent marker for cholinergic nerves.

Besides the side-by-side description of the topography of catecholaminergic and AChE-stained neuronal elements, our microscopic study was focused on brain regions with "dual innervation." At that time only a few, mainly incomplete, neuroanatomical maps were available. Maps for the fine topographical localization of brain stem nuclei were especially needed. We therefore pooled our expertise and entered upon a one-year journey that was both fascinating and exhausting. Both of us sat at the binocular fluorescence microscope, cheek-to-cheek, together observing the discrete localization of fluorescence varicose fibers and cell bodies, carefully placing dot formations on prepared stereotaxic schematic outlines of coronal sections of the rat brain. We prepared a complete stereotaxic atlas of the rat hindbrain by using serial sections from every 50 mm stained with luxol fast blue and cresyl violet.

The work was finally completed, resulting in two papers, which were submitted for publication. One of the two reviewers grudgingly accepted the papers "with low priority for rapid publication," stating, "I do not see that it adds a great deal to the existing literature." It is this lack of appreciation among a subpopulation of our scientists that makes it difficult for brain "cartographers" to undertake the tedium of whole brain mappings.

We ended the first paper with the hope "that these maps will provide a background for experimental approaches..." The high number of citations is a clear indication that our expectations were fulfilled. The popularity of this work is largely due to the fact that neurotransmitters in the CNS became the target of interest of many researchers. The rapid increase in the number of fine neurochemical and neuropharmacological techniques required detailed topographical knowledge of the distribution of various neuroaciive substances in the brain. After publication, we have had much feedback from colleagues who have found these maps invaluable for their own studies. This favorable reaction to our maps served as a springboard from which our laboratory went on to map a variety of new neurochemicals that appeared at the dawn of the neuropeptide era.

1. Fuxe K. Evidence for the existence of monoamine-containing neurons in the central nervous system. IV. Distribution of monoamine nerve terminals in the central nervous system. *Acta Physiol. Scand.* 64(Supp.247):37-85. 1965. (Cited 1,435 times.)

2. **Koelle G B & Friedenwald J S**. A histochemical method for localizing cholinesterase activity. *Proc. Soc. Exp. Biol. Med.* 70:617-22. 1949. (Cited 1.190 times.) [See also: **Koelle G B**. Citation Classic. (Barrett J T, ed.) ***Contemporary classics in the life sciences. Volume 2: the molecules of life.*** **Philadelphia**: ISI Press, 1986. p. 178.]

3. **Koelle G B.** The htstochemical localization of cholinesterases in the central nervous system of the rat. *J. Comp. Neurol.* 100:211-28, 1954. (Cited 505 times.)

Received June 29. 1993