

新しい血管作動物質の中樞神経系における 産生・分泌・受容機構に関する組織化学的研究

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平成元年より2年間「新しい血管作動物質の中樞神経系における産生・分泌・受容機構に関する組織化学的研究」という課題で科学研究費(一般C)を交付していただき、研究をおこなった。

近年、心房性ナトリウム利尿ペプチド(ANP)とそのファミリー(BNP, CNP)、エンドセリン、内因性ジギタリス様物質(EDLS)など、水・電解質代謝と血圧を調節する液性因子が次々に発見され、その化学構造が決定されてきた。これら血管作動物質は中樞神経系での産生・分泌や作用について注目されている。ラット、イヌ、日本ザルの脳を用いて、上記物質について組織化学的に解析を行なった。今回の研究進行中にもCNPやEDLSの化学構造決定の報告がなされ、それに対応するため当初の研究計画より若干の手直しが余儀なくされた。しかし、その意味ではこれらの物質の組織化学的解析に関して先駆的役割をはたしたことになり、この研究を発展させることにより今後さらに大きな成果が得られるものと思われる。

研究組織

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研究成果の概要

Recently, some humoral agents which play a role in water-balance, electrolyte metabolism and blood pressure control, i.e. ANP/BNP/CNP family (ANPs), endothelin (ET) and endogenous digitalis-like substance(EDLS) were identified and their chemical structure were determined. In this research, we analyzed these vasoactive substances with histocytochemical technique using the central nervous system of rat, pig, dog and macaque.

The nerve terminals of ANP- and BNP-neurons were observed in the posterior horn of spinal cord of rat and pig. The BNP-neurons were seen in the pig hypothalamus, but were not found in the rat brain except the spinal cord. These results were confirmed biochemical and physiological reports, which proposed that BNP existed mainly in mammalian heart but not in the brain; and CNP, a new peptide of ANPs is found in mammalian brain.

ET-immunoreactivities were not recognized in the mammalian central nervous system. The central nervous tissues have 10^2 pg/g of ET, which level of bioactive substance cannot be detected with immunohistochemistry, though there were some immunohistochemical reports using mammalian brain. In those reports, the researcher used the antibody, the epitope of which had high homology to other bioactive substances. We made ontogenetical study on this neuropeptide, i.e. ET in rat with immunohistochemical and molecular biological technique. ET was first detected on the day 19 of gestation in rat salivary gland. Because ET is also considered to be a cell-proliferation factor, ET is possible to be the secondary discovered NGF (nerve growth factor).

EDLS were histochemically studied using anti-digoxin and anti-ouabain antibodies which have high-affinity to EDLS. EDLS-neurons were distributed in the magnocellular nuclei of mammalian hypothalamus. Recent biochemical study shows EDLS resembles to ouabain, *cis-trans-cis* type steroid of plant origin. It is thought that *cis-trans-cis* type steroid exists in the mammalian brain as a neurohormone.