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EDITORIAL

Global Neurology

Ratio of naturally retained 15N to13C in rat brain regions as a unique marker for brain function

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All biogenic materials and organisms of nature consist of a mixture of stable isotopes (SIs). From differences in molecular weight, each SI molecule has its thermodynamic properties in physicochemical and biochemical reactions. As a result, small but stable retention of SI occurs during almost all chemical and biochemical processes, resulting in various isotope distributions among biogenic substances (natural abundance). Although the amount is minimal, we can detect them accurately by using mass spectrometry. Pioneering studies on isotope ecology in the twenties century have been conducted and prove that the distribution of ^{15}N and ^{13}C is applicable to a wide variety of biological studies [1,2]. However, we were unable to find any studies demonstrating the characteristics and associations between the retention of net SI to brain function. Hence, further studies are highly required [3].

The properties of neurons are different from cells distributing the other organs. They are produced in large quantities prenatally, and those incorporated into synaptic circuits survive and work for a long lifetime. Neurons placed in the specific brain region develop a large number of dendrites and form synapses on them postnatally. Every neuronal cell expresses many kinds of functional proteins such as neurotransmitter receptors, ion channels, and ion transporters on their dendrites. These functional protein molecules are renewed every moment through material metabolism. Thus, the amount of ^{15}N and ^{13}C retention in the brain regions can be expected to be somewhat higher than cells forming internal organs and skeletal muscle, which themselves are renewed in the rather short term. Thus, retention amounts of SI in those tissues may be smaller than those of brain regions.

In our study published recently [4], we obtained ^{15}N and ^{13}C from brain regions, internal organs, and skeletal muscle of the same rat and found the levels of these SIs got from each rat distribute within quite a small variation. The retention of SIs in all organs obtained from the fetus was surprisingly high but robustly decreased just after birth. The distribution of ^{15}N in the brain regions showed a characteristic increasing trend. On the other hand, the levels of ^{13}C in brain regions and the other tissues showed a minor increase after birth, and the pattern of a developmental variety of ^{13}C levels in brain regions and internal organs closely resembled each other. These data suggested that the ratio of ^{15}N to ^{13}C in each tissue may provide a better index for detecting specific biological characteristics much more clearly. The $^{15}N/^{13}C$ value in each brain region showed an apparent development-dependent increase. A developmental increase in values in the heart and skeletal muscle was observed until 20-days old, but values decreased thereafter. A very high correlation was found between voluntary wheel rotation activities and $^{15}N/^{13}C$ in the hippocampus, cerebrum, and striatum. Besides, in rats with high intelligence evaluated by radial maze learning test, $^{15}N/^{13}C$ was significantly higher in the hippocampus and striatum than ones with lower intelligence. Furthermore, we found a significant increase in ^{15}N /^{13}C of almost all brain regions examined between individuals who had received long-term maze learning and who had been raised without a task for the same period. Such differences due to free motor activity and intellectual ability were not observed in internal organs and skeletal muscles.

Our research suggests that $^{15}N/^{13}C$ is a valuable biomarker for brain functions and activities. On the other hand, by applying it to a large number of brain pathology specimens that have been stocked so far, it may provide us new clues for analyzing brain regions involved in neurological disorders.

References

1. Wada E, Ishii R, Aita MN, Ogawa NO, Kohzu A, et al. Possible ideas on carbon and nitrogen trophic fractionation of food chains: a new aspect of food-chain stable isotope analysis in Lake Biwa, Lake Baikal, and the Mongolian grasslands. *Ecol Res.* 2013; 28: 173–181.
2. Zhang Z, Tian J, Xiao H, Zheng N, Gao X, et al. A reliable compound-specific nitrogen isotope analysis of amino acids by GC-C-IRMS following derivatisation into N-pivaloyl-iso-propyl (NPIP)esters for high-resolution food webs estimation. *J Chromatogr B Analyt Technol Biomed Life Sci.* 2016; 1033-1034: 382-389.
3. Ohkouchi N, Chikaraishi Y, Close H, Fry B, Larsen T, et al. Advances in the application of amino acid nitrogen isotopic analysis in ecological and biogeochemical studies. *Organic Geochemistry.* 2017; 113: 150-174.
4. Kudo Y, Wada E. Ratio of naturally retained 15N to 13C in rat brain regions as a marker of brain function and activity. *Neurosci Res.* 2020 [Epub ahead of print]

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