Presentations

Serotonin and depression: Challenges of studies in animal models

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Career

Naoyuki Hironaka received his bachelor's and master's degrees in Psychology from the University of Tokyo and a doctorate in Physiology from Saitama Medical University. He has been engaged in preclinical studies of CNS drugs at the Central Institute for Experimental Animals and other research institutes for more than 40 years, and has studied the neuroscience of drug addiction at the Japan Science and Technology Agency. He is currently a councilor with the Japanese Pharmacological Society, the Society of Neuropsychopharmacology, and the Japanese Medical Society of Alcohol and Addiction Studies.

Abstract

Historically, antidepressant drug development has focused on the brain monoaminergic systems, including serotonin and noradrenaline, as targets for pharmacological intervention. Behavioral testing methods, the forced swimming and tail-suspension tests, have since become standard pharmacological evaluation methods, and the classical monoamine hypothesis has been refined. With these advances in basic research, new animal models and antidepressant drugs have been introduced, through which the existence of treatment-resistant patients has been revealed. New hypotheses about depression have emerged that focus on hypothalmic-pituitary-adrenal-axis dysfunction or brain inflammation; however, monoamines remain relevant to these new hypotheses as classical antidepressants are still effective in animal models built on these concepts. Consequently, we can speculate that neural mechanisms of depression have a multi-layer structure. At the foundational level, neural plasticity regulated by neurotrophins might be relevant; the monoamines (especially serotonin), mediated by the function of multiple uncharacterized intermediate layers, are relevant to the surface layer of observable characteristics. Clinical signs of depression also have multiple layers. Some signs, like a depressed mood or loss of pleasure, are overtly apparent; however, these might reflect implicit agitation caused by various incompatible motivations. Our next challenge of animal model study is to incorporate this structuralist view of depression.