Title of Project : Foundation of Synapse and Neurocircuit Pathology

Term of Project : FY2010-2014

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【Purpose of the Research Project】

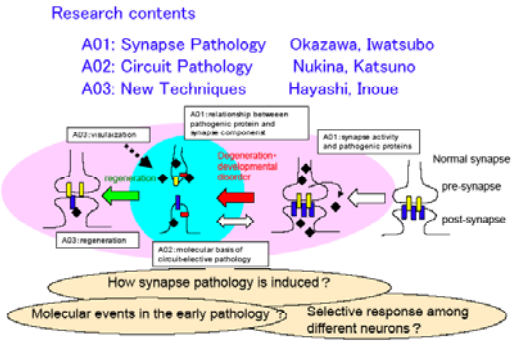
It has already been over 100 years since research on degenerative diseases began. However, it is still not possible to discover really effective treatment. It goes without saying that progress seems to be even slower for developmental disorders and mental disorders, of which identification of causative genes and elucidation of the molecular pathology lags behind. Of course, research on degenerative diseases has brought us much knowledge. The identification of causative genes accelerated understanding of the formation process of inclusion bodies and aggregate at the molecular level, beyond morphology. Furthermore, this knowledge contributes to the development of new diagnostic techniques, such as amyloid imaging.

On the other hand, however, we have realized that in cases of progressed lesions, we cannot expect recovery from symptoms even if aggregates are removed. We should now focus on various dysfunctions of neurons, and the background to these phenomena, as new problems to solve. Equally, the process from dysfunction to cell death has not yet been clarified. Since the brain is a circuit in which a neuron functions as a device, it is evident that the vulnerability of the circuit and the synapses which are in charge of contact between devices is one of the most important reasons behind the decline of the brain machine's performance.

This scientific research is an ambitious challenging, aiming to elucidate how dysfunction of neuron connects to that of synapses and vulnerability of the circuit in 5 years. We will clarify some prototypes that reflect the core of the synapse pathology. It will be a basis of the truly effective treatment that stops progress of symptoms of brain diseases in early stage and promotes recovery.

【Content of the Research Project】

This research area includes three projects : the project to analyze the molecular pathway from causative gene products to synapse dysfunction via various cellular functional abnormalities (A01), the project to clarify the molecular mechanisms underlying selective vulnerability of specific circuits (A02), the development of new techniques to directly approach the abovementioned projects (A03).



【Expected Research Achievements】

A01: We will elucidate a molecular process from gene mutation to synapse abnormality after going through various dysfunctions of neuron in different degenerative diseases, developmental disorders and mental disorders. Also, by integrating knowledge provided from different brain diseases researches, we will try to clarify the similarity beyond difference of progression of pathology and of lesion distribution. Based on the above, we also intend to establish new classification of brain diseases based on synapse pathology. A02: From research aiming to elucidate a basic mechanism of the selectivity, it is expected to identify certain factors which promote neurocircuit-specific dysfunction of neurons as well as those which keep neuronal viability of specific neurocircuit.
A03: We will develop new molecular imaging techniques and stem cell biotechnologies in order to stimulate collaboration and raise the academic level of this whole project.

【Key Words】

synapse, circuit, neurodegenerative diseases, developmental disorders, stem cells, molecular imaging

【Homepage Address】

http://www.tmd.ac.jp/mri/shingakujutu/