



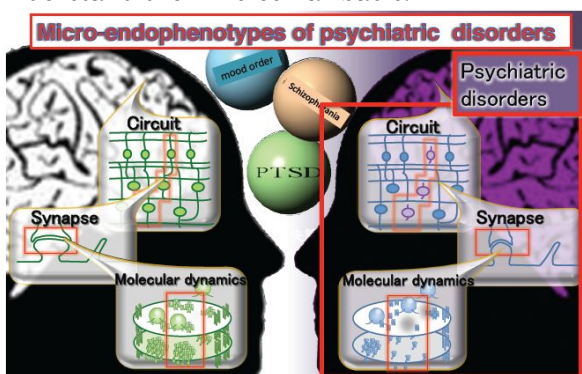
Title of Project : Unraveling the micro-endophenotypes of psychiatric disorders at the molecular, cellular and circuit levels.

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【Purpose of the Research Project】

Psychiatric disorders are now one of the five major diseases in Japan; therefore, it is important to understand the mechanisms of these disorders and to develop therapeutic strategies. Importantly, the development of psychiatric disorders is not only due to genetic factors; rather they are strongly influenced by interactions between environmental and genetic factors. Furthermore, the mechanisms by which brain functions are controlled at the molecular, cellular, and circuit levels are still unknown. Therefore, unraveling the mechanisms of psychiatric disorders requires a variety of approaches including both basic and clinical studies. However, current collaborations between basic and clinical scientists are poorly organized as the endophenotypes of psychiatric disorders, which are their phenotypes at the psychological, physiological and behavioral levels, have not been studied sufficiently in basic research. Additionally, there are much less basic researchers studying psychiatric disorders in Japan compared to those in other fields of research such as cancer and metabolic syndromes. On the basis of this background, we will develop a new and innovative area studying psychiatric disorders, in which basic researchers using state-of-the-art techniques will collaborate with clinical researchers to use basic and clinical studies to understand psychiatric disorders. Especially, to develop basic research on psychiatric disorders, we propose to develop “micro-endophenotypes” that are the visualized phenotypes of psychiatric disorders at the molecular, cellular and circuit levels, as an interface between basic and clinical studies. We will identify micro-endophenotypes and understand their molecular basis.



【Content of the Research Project】

We will identify micro-endophenotypes using animal models and human materials such as iPS cells derived from patients and postmortem brains and then elucidate the molecular basis of micro-endophenotypes using state-of-the-art technologies. Our research team consists of three groups; A01, A02 and A03. Groups A01 and A02 focus on micro-endophenotypes at the molecular - cellular and circuit - behavioral levels, respectively, whereas group A03 focuses on micro-endophenotypes induced by environmental factors. In addition, we will develop new mouse models of psychiatric disorders that receive micro-infusions of iPS and iN cells derived from patients into the brain and analyze these mice. We will also develop state-of-the-art technologies to identify and analyze micro-endophenotypes.

【Expected Research Achievements and Scientific Significance】

Little progress has been made in unraveling phenotypes of psychiatric disorders at the molecular, cellular and circuit levels. Furthermore, the in vivo functions and dynamics of candidate molecules identified through genome-wide analyses of psychiatric disorders have not been well examined. The “micro-endophenotypes” proposed by our research group would be useful subjects for basic research and play crucial roles as an interface between basic and clinical studies of psychiatric disorders. Most importantly, the study of micro-endophenotypes in basic research would enable to the recruitment of Japanese basic researchers such as neuroscientists, molecular biologists, structural biologists and so on into the field of psychiatric disorders, and generate a new and strong research area to understand the molecular basis of psychiatric disorders in Japan.

【Key Words】

Micro-endophenotypes; the visualized phenotypes of psychiatric disorders at the molecular, cellular and circuit levels.

【Term of Project】 FY2012-2016

【Budget Allocation】 1, 135, 000 Thousand Yen

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