[Grant-in-Aid for Specially Promoted Research]

Biological Sciences



Title of Project :Elucidating the primate basis of neurobiologicalmechanisms underlying developmental disorders

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Research Project Number : 19H05467 Researcher Number : 00236233

Keyword : Developmental disorders, Social behavior, Neural networks, Cognitive genome, Primates

[Purpose and Background of the Research] Social mind is crucial to live our social life adaptively and create our society itself. Nurturing the social mind is indispensable to keep good relationships between the self and others for our comfortable daily life through social/collective behaviors. Therefore, it is a critical issue for us to consider how a group or individuals within the group should behave. However, individuals suffering from developmental disorders, such as autism spectrum disorder and schizophrenia, cannot take social/collective behaviors in a proper fashion. Exploration of the neural mechanisms underlying the social mind and developmental disorders caused by its disruption is of high necessity and emergency not only for understanding ourselves and our society, but also for proposing effective intervention/therapy programs against the issue that the contemporary society faces, based on the scientific evidence. The present research project aims at elucidating the primate basis of neurobiological mechanisms underlying the social mind and developmental disorders caused by its disruption, by employing monkeys (macaques, marmosets) as primate models and attempting a paradigm shift from previous "individual-level life science" to novel "society/group-level life science". The major objective of this project is to clarify the fundamental mechanisms underlying the linkage of a biological triangle that comprises social behavior (collective behavior, inter-individual interaction) executed by a group or individuals within the group, neural network activity regulating the social behavior, and cognitive gene expression governing the network activity, through identifications and functional analyses of genes and neural networks involved in generation and control of the social mind.



Figure 1 Social mind and developmental disorders **[Research Methods]**

In the present research project, we employ a wide variety

of innovative technologies as well as the excellent research environment at the PRI (collective cages, open enclosures): comprehensive search and functional analysis of risk genes for developmental disorders, neuronal activity manipulation by intracranial gene transfer with viral vector systems, multi-individual behavior simultaneous tracing, and dual neuronal activity measuring on two monkeys. Six research plans are conducted comprehensively to establish pathway-selective optogenetic/chemogenetic manipulation and whole-brain level gene transfer, product primate disorder models by these techniques, and analyze collective behaviors with multi-individual behavior simultaneous tracing.

[Expected Research Achievements and Scientific Significance]

The outcome issued by the present research project will lead to understanding not only the behavioral properties of developmental disorders from a collective viewpoint, but also the behavioral features of developmental disorder patients within a group or in the society, and may also expand into early detection of serious social problems in adolescence (i.e., bullying and suicide) and development of novel approaches to intervention/therapy against them.

(Publications Relevant to the Project)

- Nagai Y, Inoue K, Takada M, Minamimoto T et al. (2016) PET imaging-guided chemogenetic silencing reveals a critical role of primate rostromedial caudate in reward evaluation. Nature Communications 7:13605.
- Inoue K, Takada M, Matsumoto M (2015) Neuronal and behavioral modulations by pathway-selective optogenetic stimulation of the primate oculomotor system. Nature Communications 6:8378.

Term of Project FY2019-2023

(Budget Allocation) 391,400 Thousand Yen

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