Form 3-3-2

Japan-US Brain Research Cooperation Program
The Report of Information Exchange Seminar in 2004 fiscal year
[f i e l d :]

1. The Seminar Title: Stress-induced hippocampal neuroplasticity and cognitive impairment

2. The T e r m : **F r o m** 2003. 11. 9 **T o** 2003. 11. 15

3. The Location: Department of Psychiatry and Behavioral Science, Johns Hopkins University

4. The Representative 's Name, Title and Affiliation:
Japanese Coordinator: Nobumasa Kato, Professor, Department of Neuropsychiatry, Graduate School of Medicine, the University of Tokyo

US Coordinator: Akira Sawa, Associate Professor, Department of Psychiatry and Behavioral Science, Johns Hopkins University

5. The Participants:
Japan: The Invited participants _9_ people The others _0_ people
Name, Title and Affiliation of the Invited participants
Nobumasa Kato, professor, the University of Tokyo
Hideshi Sakamoto, assistant, the University of Tokyo
Seiichiro Jinde, graduate student, the University of Tokyo
Hidenori Yamasue, graduate student, the University of Tokyo
Hirohiko Kanai, assistant, Shiga University of medical science
Atsushi Yoshimura, graduate student, Shiga University of medical science
Toshihumi Kishimoto, professor, Nara medical university
Yoshinari Takahashi, assistant, Nara medical university
Hiroki Yoshino, assistant, Nara medical university

US : The Invited participants _9_ people The others _10_ people
Name, Title and Affiliation of the Invited participants
Raymond DePaulo,Jr., professor, Johns Hopkins University
Timothy Moran, professor, Johns Hopkins University
Michael Kaminsky, associate professor, Johns Hopkins University
Akira Sawa, associate professor, Johns Hopkins University
Adam Kaplin, researcher, Johns Hopkins University

Russel Margolis, researcher, Johns Hopkins University
Sheng Bi, researcher, Johns Hopkins University
Ellen Ladenheim, researcher, Johns Hopkins University
Constantine Lyketsos, researcher, Johns Hopkins University

6. The Abstract and the Significance of this seminar (300 words):
The understanding of the molecular events underlying the neuroendocrine and behavioral sequelae of the response to stress has advanced rapidly over recent years. A large body of evidence has established a link between stressful life events and development or exacerbation of psychiatric disorders. At cellular level, evidence has emerged indicating neuronal atrophy and cell loss in response to stress. At the molecular level, it has been suggested that these cellular deficiencies, mostly detected in the hippocampus, result from a change in the intracellular signaling pathways associated with elevation of glucocorticoid. Stress is also known to be a biologically significant factor that can disturb cognitive processes such as learning and memory.
We have investigated the stress-induced neuroplasticity and cognitive impairment, and have reported that stress influences various neuroendocrinological, morphological and functional changes in the rodent and human brain. However, the precise mechanism of these effects has not been clarified yet. Dr. Sawa, who is a chief of U.S. side, and his group at Johns Hopkins University have revealed several molecular basis on the psychiatric diseases. Especially, their recent study suggests that Disrupted-in-Schizophrenia-1 (DISC-1), a gene whose mutant truncation is associated with major psychiatric illness, interacts with a cytoskeletal protein which is associated with cortical development. To advance the understanding of stress vulnerability including the influence of stress-induced hippocampal neuroplasticity on the cognitive function, we planed to discuss with them how to optimally combine our knowledge. In this seminar, total 12 subjects (basic research: 6, clinical research: 6) were presented. In addition, the clinical program for treating eating disorder and geriatric psychiatry were lectured, and the chairman 's round was held by Prof. Raymond DePaulo (refer to attached sheets).

7. The Result of this seminar and the results expected(300 words):
In this seminar, the psychiatric researchers of both basic and clinical fields from Japan and the Johns Hopkins University widely discussed current studies of neuroendocrinology, immunology, physiology, neuroimaging and genetics in relation to stress and cognitive function. It was very stimulative for us to talk over various themes noted above with the members of the Johns Hopkins University, known to make great progress in CNS researches for decades. And all findings from this meeting developed our understanding of stress vulnerability and stress-induced cognitive impairment mediated the hippocampus.
With regard to longer-term scientific directions, we should have a comprehensive strategy for understanding the biological mechanism of stress vulnerability including neural plasticity

and cognitive impairment. Since one of the keys to our success will be an effort to collaborate among basic neuroscientists, clinical scientists and geneticists, we proposed each other to collaborate in several researches after the seminar for successful advance of our research. This is an attempt, even if initially in the rodent but ultimately in the human, to discover underlying mechanisms for developing and maintaining stress vulnerability. If the collaboration will be succeeded, it will lead to further biological studies in developing novel screening tools and epidemiologic methods that will help us to elucidate what will be functionally important in stress-induced psychiatric disorders, and it will also lead to develop novel biological therapies.

8. The Others (Practical Issues, Special Mention Matters):