国際交流基金助成事業報告書

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1. Starting by the JSNP meeting

At first, we attended at the 46th Annual Meeting of the Japanese Society of Neuropsychopharmacology (JSNP) at COEX convention center (Fig. 1 and 2) in Seoul, South Korea, from July 2nd through 3rd. This meeting was made mostly by Japanese speakers and presentations.

Figure 1: COEX convention center in Seoul, South Korea

In the first day I attended at symposiums with the theme “addiction and electro convulsive therapy”, where pathophysiological mechanism and responses to treatments in human and animal models were presented.

Figure 2: Meeting room used for JSNP symposium

Discussions on abuse of cocaine, alcohol and methamphetamine were addressed. Exceptionally, at this time one presenter showed some evidences against and pro the existence of a caffeine addiction and even further, for a cocoa addiction. It was showed that caffeine, theobromine and theophylline (present in tea and cocoa) could elicit some withdraw symptoms, but it was not enough to receive the DSM-5 (6 or more symptoms) classification of abuse drugs.

Gambling as an addictive behavior was also highlighted, gambling was defined within 4 different categories going from entertainment to social problem and, in the worst, psychopathy. They also explained the different circuit involved in each case, including social and environmental effects.

Some effects of addiction were also addressed: in the cognition, when the compulsion suppresses the logical reasoning. Exemplified by a research on the IOWA gambling test (earn and loss, safety and risk test) showing that methamphetamine and cocaine impair learning and avoidance behavior, also affecting GABA, GLU, D2R and histamine levels; in the depression and bipolar disorders, after some definitions on the classification of the two basic forms of bipolar disorders (I-severe form varying for mania to depression and II-milder form varying for hypomania with severe episodes of depression) they presented evidences on treatment with lithium and/or anti-depressives; and finally, in the aggressive behavior, showing data on zebrafish and mice aggressive behavior experiment using gene manipulation (gene silencing and optogenic approaches) on different nuclei of habenula. Activation of the dorsal habenula medial nucleus increased victory and aggressive attack rate, while activation of ventral habenula caused active avoidance.

They also showed a retrospective study presenting many different models of depression created until now (mutation-, stress- and drug-induced), using different tests to evaluate depression episodes (locomotor test, DSM-5, corticosterone levels).Then, evidences on brain activity, the changes from ventral to dorsal striatum as the main reward pathway during compulsion. In addition, they showed that brain activity in compulsive patients is altered from cortex to basal ganglia.

Addiction-related symptoms treatment was also addressed a common topic was the ketamine. Ketamine administration could ease the effect of acute increase in dopamine caused by cocaine-like drugs that is used followed by a downfall on dopamine on the amygdala-thalamus pathway (electrical stimulation validation) showing a possible use in drug addicted rehabilitation treatment.

The second theme in this day, electro convulsive therapy (ECT) was presented for treating many conditions: internal bleeding; neuropathic pain; and if in combination with aripripazole in long-action injection, also could be used in schizophrenia and bipolar disease treatment to reduce aripripazole dose and its side-effects (extrapyramidal symptoms). At last, evidences on ECS in NAc-VTA pathway to reduce nociception in short- and long-term pain models were presented.

Finishing, an interesting subject was presented showing the use of aromatherapy as an alternative or supplement in the addiction treatment, evidences showed that aromatherapy can affect the dopaminergic and GABAergic system to ameliorate locomotor and aggressive changes, usually found in drug addicted patients.

At the second day many effects of nicotine and nicotinic receptors on: anxiety and depression in cancer treatment with cyclophosphamide (CPA) and doxorubicin (DOX); on motor excitement leading to tremor and seizures; on microglial glutamate-aspartate transporter (GLAST) to recover the balance between astrocyte and microglial GLAST in neuroinflammation; finally, on nicotine intake in pregnancy and early childhood resulting in aggravation of cognition impairment were the main subject in the first session.

Another session showed statistical strategies to psychopharmacological research, showing different choices for descriptive and inference tests, when to use correlation and regressions for predict symptom(s). Also showing new trend techniques like optogenics, and how to deal with big data samples by grouping and analyzing them in different batches.

A new assay data was also presented using aptamers, chemical equivalent to antibodies, in this case DNA/RNA fragments with tertiary structures that bind to specific molecules, in major depressive disorder, bipolar disorder and schizophrenia patients. These data showed a relation of fibrinogen increment and white matter decrement in those patients. Finishing by displaying new forms to use old assay, for example, use of brain activity to predict the psychosis in schizophrenia, bipolar disease and teenagers at risk of metal state (ARMS).

Another two hot topics in the JSNP were clozapine, showing effect on induction of autophagy (ULK1), and ECS that induced, increased (with clozapine) and recovered (MK-801 model of schizophrenia) the expression of ULK1.

Final presentations showed how rare mutations and animals models can be put together to study complex diseases, the most interesting point in this presentation was that the presenter made a quite elaborated study on different forms of vocalization of perinatal mice and their mothers, showing the effect of psychiatric conditions that impair the social behavior. By knock-in the T-box transcription factor (Tbx1) gene, they found a defective formation in the striatal and hippocampal area, that was found to be due reduction in BrdU in granulate cell cultures and made mothers ignore their offspring cries.

2. Followed by the CINP meeting

Figure 3: Main auditorium used for CNIP symposiums

The 30th The International College of Neuropsychopharmacology (CINP) World Congress of Neuropsychopharmacology was made fully on English speaker's presentation (Fig. 3 and 4). Apart of some difficulties of some non-native English speakers, a lighter atmosphere made it more prompt to discussion and question than the JSNP meeting, even I made some questions and participate in a discussion about differences on psychiatric patients' versus criminals' attempt/success rate on suicidal, also, in neurotransmitters and hormones difference in whose who failed or succeeded to suicide.

Similar to the JSNP meeting, ketamine in psychopathies treatment were discussed, however, at this time side-effects were presented (e.g., abuse due hallucinogenic effects) and that blocking the muscarinic acetylcholine receptor 2 and 3 could improve ketamine-effects on depression. Also, data on benzoate chronic administration for Alzheimer disease, Scopolamine effects in the affective illness, showing different biomarkers in patients responding and non-responding to the treatment, stressing that tailored medicine still a very promising area.

Figure 4: CINP certificate of attendance

At the final day, the main role of serotonin in the waiting for delayed reward process by dorsal striatum-Raphe nuclei pathway. Use of galanin showed to improve depressing related effects. Then, I finish by attending in a presentation about suicide, where they stressed difference in eastern high suicidal rate and westerns high schizophrenia and bipolar disorders showing that environmental effects should not be forgot when studying this subject. Following, the relation of suicide and violent people, evidences were presented showing that violent people have a 3 fold higher attempt/success rate. The last presenter finished by showing evidences that not only men are responsible to have 4 time

fold higher suicidal (success) than women due their impulsivity, but other factors like socio-cultural stress, not being priority on government health programs, and not being so well-treated by psychiatrics as women as causation of this great difference.

3. Poster presentations

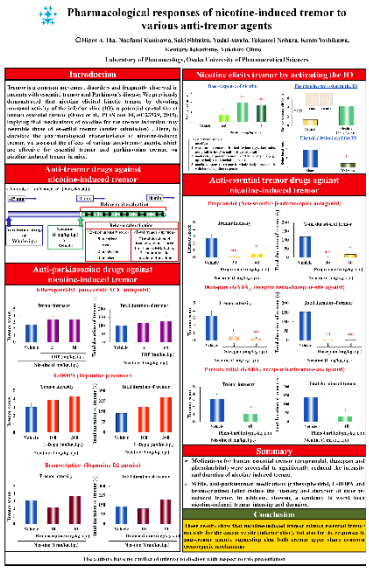

Figure 5*:* JSNP presented poster

In the JSNP meeting, I presented a poster regarding the evaluation of anti-tremor drugs against nicotine-induced tremor (Fig.5), the presentation was organized by poster number with a considerable audience, questions on anti-tremor drugs dose and behavioral evaluation were made and easily answered, since they are essential part of our work methodology.

Next, in the CINP meeting, I presented a poster regarding the investigation of nicotine-induced seizures, from evoking convulsive seizures until finding the causative site of the later (Fig. 6). At that time, presentation was made on free-discussion style, most questions were about the procedure of guide cannula placement in the amygdala region. Since microinjection experiment is hard and delicate process, it is a common question, however, unexpectedly at this time I was asked which part of work I was directly and indirectly involved and how those experiments were carried out, since our laboratory work in groups of 6-8 students with responsibilities gave due how long they are used to perform experiments it was ease to explain which part I was involved and how it was possible to produce that amount of data.

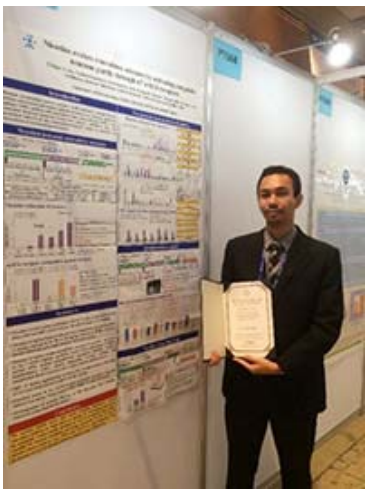

Figure 6: Photo with the presented poster in CINP and holding the received award

Finally in the JSNP-CINP meeting I attended in the open ceremony dinner, where I received an award for excellent presentation (Fig.6 and 7).

Figure 7: Received JSNP-CINP Excellent Presentation Award

4. Final impressions

The opportunity to present our work to experts of different parts of the world was a priceless opportunity to divulge and have our work evaluated by different people with different line of thoughts. International scientific meetings lead wide broad of new ideas and research network that are essential to new projects and collaborations. Of course, any scientific meeting gave the opportunity to learn the new trends on scientific affairs and helps to direct the focus on research subjects, showing which scientific fields requires more attention and investigation, and those who does not need priority.

5. Acknowledgments

I wish to thank the Japan Foundation Grant Program that made possible for me to attend in an international meeting of that importance. I also thank Professor Ohno, Instructor Shimizu and all students whom participated actively in the both confection and execution of the presented works. Finally, I thank all organizers and staffs of CINP and JSNP who made an excellent work in creating and organizing that large-scale meeting.