Japan-U.S. Brain Research Cooperation Program
Researchers Dispatched to the U.S. Program FY2021: Report

Field: Cellular/ Molecular

1. Researcher

Name: Takafumi Kawai
Title: Assistant Professor, Dept of Medicine, Osaka university
Affiliation: Yamada-oka 2-2, Suita, Osaka, Japan

2. Research Title: Function of calcium-activated ion channels in medial habenula neurons

Please give the name, title and affiliation.

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Host Researcher: Huanghe Yang
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4. Research Period, from/to (yyyy/mm/dd):
2021/6/1-2021/10/1

5. Abstract, Results, and Research Significance (300 Words):
Medial habenula (MHb) neurons highly expresses diverse types of nicotinic acetylcholine receptors (nAChRs) and plays substantial roles in nicotine addiction, withdrawal and nicotine aversion. Previous studies suggest that MHb neurons also show the high expression level of two different types of Ca2+ activated ion channels; K+ channels (BK) and Cl- channels (CaCCs). In the present study, we investigated the effect of strong nicotine stimulation on MHb neurons by electrophysiological technique. We found that strong nicotinic stimulation of MHb largely changes the pattern of neural firings. Interestingly, inhibiting or manipulating CaCC activities alter the appearance of firing patterns in response to nicotinic stimulation. Therefore, our results indicated that CaCC seems to be involved in the regulation of firing pattern in MHb. Pharmacological inhibition or genetic activation of BK channels experiments suggested that BK channels also play important role in regulating firing activities in MHb. Furthermore, different types of high threshold voltage-gated Ca2+ channels (VGCCs) also appear to be functionally coupled with the CaCC activities and may play important role in maintaining the above-mentioned CaCC function. We also found that milder nicotinic stimulation of MHb neurons could be somewhat regulated by CaCC activities. The present study proposes the novel model about the nicotinic regulation of firing activities in MHb neurons that could potentially involve the nicotine aversive behavior.

6. Other (Research-related concerns, particular points to note):
First I visited Huanghe Yang lab to study the functional significance of the potential TMEM16B regulation by PI(4,5)P2. However, I found that there seems to be little or no regulation of TMEM16B by PI(4,5)P2. So, we changed the research topic to another Ca2+-activated Cl- channel, TMEM16A.

*Please attach any reference materials as necessary.