Relationships between intracellular Na levels and circadian rhythms in SCN2.2 cell

Seockhoon Chung[1], Seung-Yong Yoon[2], Jangho Park[1], Yu Jung Park[1]

[1]Department of Psychiatry, [2]Department of Anatomy and Cell Biology, Asan Medical Center, University of Ulsan College of Medicine

Research question and background

Bipolar disorders are characterized by elevations of intracellular sodium concentrations, and this observation has been considered to be related with the pathophysiology of abnormal moods in bipolar disorders. We assumed that treatment with Ouabain, a potent inhibitor of Na,K-ATPase, in Suprachiasmatic nucleus(SCN) cells can increase intracellular sodium levels similar to bipolar disorder. It has been observed that Ouabain increased Na pump mRNA and protein levels, and pretreatment with Li normalized these effects in human glioblastoma cells. However, those findings were not observed in SCN cells.

Methods and tissues used

Immortalized SCN2.2 cells (NBB, derived from Suprachiasmatic nucleus) were seeded on laminin-coated culture. To facilitate cell cycle and circadian clock synchronization across cultures, cells were subjected to medium replacement and exposed to neurobasal medium. Ouabains were treated in the half of the plates. Proteins for immunoblots were also extracted at 2-h intervals for 36 h after the treatment. Bmal 1 protein levels (by immunoblot) were measured.

Results and conclusion

We verified expected differences between normal control and the group with Ouabain treatment. Although we could not replicate our findings, treatment of SCN2.2 cells with Ouabain resulted in phase advances 10hr in immunoblots. The maximal expressions of Bmal-1 in Ouabain groups were at 12hr after the treatment and controls at 22hr. This finding suggests that phase advancing in SCN 2.2cells with Ouabain treatment may represent the circadian oscillations of BPD patients. It also corresponds with other study that the acrophase (time of peak daily activity) in BPD patients remained phase advanced compared to that of controls. Therefore, we may regard SCN2.2 cells with Ouabain treatment as a cellular model for BPD.