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Elucidating the Mechanism of Aripiprazole Action in Treating Circadian Rhythm Sleep Disorders

Aripiprazole enhances the entrainment to external light-dark cycles by weakening the synchronization between neurons in the central circadian clock, thereby improving the symptoms of circadian rhythm sleep disorders.

Tsukuba, Japan—While aripiprazole has long been a standard treatment for psychiatric disorders, such as schizophrenia and bipolar disorder, recent studies indicate that it is effective in treating circadian rhythm sleep disorders, including delayed sleep-phase syndrome. This condition causes patients to sleep and wake extremely late at times. However, the precise mechanism through which aripiprazole addresses these sleep disorder symptoms remains elusive.

Researchers from the University of Tsukuba have discovered that aripiprazole can directly affect the mammalian central circadian clock; specifically, it can modulate the photic entrainment in mice. Located in the hypothalamic suprachiasmatic nucleus (SCN), the central circadian clock comprises clock neurons that synchronize with each other, maintaining a rhythm of approximately 24 h. Simultaneously, SCN is receptive to external inputs like light, aligning itself with the environmental light-dark cycle. The researchers have found that aripiprazole disrupts the synchronization among the clock neurons in the SCN, heightening the responsiveness of these neurons to light stimuli in mice. Additionally, aripiprazole influences intracellular signaling within the SCN by targeting the serotonin 1A receptor, a prominent receptor in the SCN.

These findings suggest that the efficacy of aripiprazole in alleviating circadian rhythm sleep disorder symptoms in psychiatric patients might be attributed to the modulation of the circadian clock by the drug. This study expands the potential clinical usage of aripiprazole as a treatment for circadian rhythm sleep disorders.

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