**Introduction: What is Bipolar Disorder?**

Bipolar disorder is a mental illness that affects 2.6% of Americans over the age of 18 (1). Bipolar disorder affects an individual’s mood, causing those with the illness to experience bouts of mania and depression. The American Psychiatric Association classifies a manic episode as “a distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 week” and a depressive episode as five or more symptoms of a depressed mood present at the same time for at least two weeks (2).

**Introduction: SGG and Bipolar Disorder**

The clock protein SGG is influenced by neurotransmitters like dopamine and serotonin and, by extension, the psychotropic medications, which act on these neurotransmitters (14). SGG is involved in many different pathways and processes, meaning it is constitutively active in cells (15). There is evidence that bipolar disorder could be at least partially caused by over activation of SGG (15). A logical treatment option, therefore, may be the inhibition of SGG (16).

**Discussion: Bipolar Disorder Treatment and the Circadian Clock**

The mechanism of action for lithium, risperidone, and fluoxetine each lead to a number of implications for treatment. First, bipolar disorder is a two-sided disease with a depressive side and a manic side. This introduces the problem of understanding how each treatment mechanism reacts with the clock and how each affects the depressive or manic side of bipolar disorder. Multiple hypotheses have been developed to describe the manic side of bipolar disorder. Once a comprehensive Drosophila clock has been created, there is potential for these hypotheses to be incorporated. However, a hypothesis describing the mechanism for the depressive side of bipolar disorder has yet to be established.

**Discussion: What’s next?**

An understanding of howmania and depression specifically affect the Drosophila clock would be an excellent addition to the goal of a comprehensive Drosophila model. Once established this information can be used to create a simple mammalian model based on mice or rats. Following this, information can be converted to form a model of the more complex human clock. Availability of a working human clock model would allow for more complete research about the interactions of bipolar disorder with the circadian clock.

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**Methods**

In order to determine the effects of lithium, risperidone, and fluoxetine on SGG, the online databases were searched with keywords “lithium”, “risperidone”, “fluoxetine”, “GGG-3’p”, “bipolar disorder” “SGG”, and “Drosophila melanogaster”. Studies were selected based on inclusion of the test subject (Drosophila), and information about SGG or GSG-3p in relation to the treatments.

**Results: Bipolar Disorder Treatment Mechanisms**

Lithium, Risperidone and Fluoxetine are all common treatments for bipolar disorder. The figure above describes the mechanism by which each treatment inhibits SGG, hypothetically leading to a decrease in symptoms of bipolar disorder.

- **Fluoxetine** is an antidepressant categorized as a selective serotonin reuptake inhibitor (SSRI) (5). Inhibition of SGG is thought to occur initially by the inability of the 5-HT_1A receptor to be regenerated at the synapse. This activates PI3-K, which activates AKT. This increases phosphorylation of SGG and results in inhibition (5).

- **Side effects** of fluoxetine include:
  - Overdose (6)
  - Birth defects: pulmonary hypertension. Transmission of medication through breast milk to child (7).

- **Risperidone** is an atypical antipsychotic used as a mood stabilizer when treating bipolar disorder (10). Inhibition of SGG is thought to occur by the blockade of the 5-HT_2A serotonin receptor. This increases phosphorylation of SGG, resulting in inhibition (10).

- **Side effects** of risperidone include:
  - Overdose: minor central nervous system, and heart problems lasting no longer than 72 hours (6).
  - Transfusion of medication through breast milk to child (8).

- **Lithium** is a mood stabilizer primarily used to treat manic episodes of bipolar disorder (11). Inhibition of SGG via lithium is hypothesized to occur in the cell. Lithium directly increases phosphorylation at Ser9 resulting in inhibition of SGG (12).

**Side effects** of lithium include:
- Overdose: due to small therapeutic range and relatively high toxicity (13)
- Birth defects: Ebstein’s anomaly, a heart valve defect. Transmission of medication through breast milk to child (9).

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**References**