# Background:

Catatonia, a neuropsychiatric syndrome characterized by a range of motor, behavioral, and cognitive symptoms, remains a mysterious condition with unclear underlying mechanisms (Kline et al., 2022). Patients with catatonia may exhibit symptoms such as mutism, immobility, echolalia (repeating others' speech), echopraxia (imitating others' actions), and waxy flexibility, where they maintain unusual body positions for extended periods (Rasmussen et al., 2016). The syndrome can be subdivided into different categories, with some forms being characterized by excessive movement or agitation, and others having decreased movement and responsiveness (Burrow et al., 2023). This diversity in the symptoms suggests that multiple underlying neurobiological pathways may be involved in the development of Catatonia.

Neurotransmitter systems associated with catatonia, particularly the GABAergic system play a significant role in regulating brain activity by inhibiting neural signals and maintaining a balance between excitation and inhibition in the brain, which is needed for normal cognitive and motor function. Dysregulation in the GABAergic system, which involves the neurotransmitter gamma-aminobutyric acid (GABA), has been observed in patients with catatonia and is believed to contribute to their motor and behavioral symptoms (Ariza-Salamanca et al., 2022). GABA is known to exert a calming effect on the brain by reducing excessive excitatory signals. Medications that enhance GABAergic activity, such as benzodiazepines, have been shown to reduce catatonic symptoms in many cases, further resulting in GABA dysfunction in this condition (Edinoff et al., 2021). However, benzodiazepines come with dependency risks, which increases interest in alternative treatments and animal models to study GABAergic pathways (Tan et al., 2011).

**Previous Studies**

Neurotransmitter dysregulation in catatonia have been studied using rodent models, where pharmacological alterations of the GABAergic and dopaminergic systems were shown to induce catatonia-like behaviors. For instance, a prior study examined the role of GABAA receptors in neurodevelopment, particularly focusing on how deficiencies in the gabrb3 gene in mice impacted social behaviors (Delorey et al., 2007). The researchers found that these gabrb3-deficient mice had abnormal social behaviors, an important deficit associated with autism spectrum disorder (ASD), suggesting that disruptions in GABAergic signaling can lead to behavioral abnormalities related to social interaction (Delorey et al., 2007). This link between GABAergic dysregulation and social deficits shows the potential for similar mechanisms to underlie catatonia-like symptoms, including social withdrawal and behavioral rigidity.

**Knowledge Gaps**

Despite these findings, many gaps remain in understanding catatonia's neurochemical and genetic bases. Current models have only been able to replicate certain aspects of the syndrome. Moreover, no studies have fully explored how interactions between the GABAergic and dopaminergic systems contribute to catatonia.

**Relevance**

Catatonia is a neuropsychiatric disorder with an unclear cause and limited treatment options. Additionally, current animal models used to research this specific disorder are vertebrates which are not accessible to use all the time. Therefore, A scalable and reasonably priced model for examining the part GABA deficiency plays in catatonia is needed and is provided for by Drosophila Melanogaster. This research is significant as it will result in new findings regarding GABAergic signaling and its connection to catatonia-like symptoms. With catatonia becoming increasingly recognized in patients across various neuropsychiatric conditions, understanding its mechanisms could pave the way for more effective treatments, ultimately benefiting a growing population affected by this debilitating disorder.