**ABSTRACT**

Major depressive disorder (MDD) is among the most prevalent and costly mental health conditions, affecting more than 268 million people worldwide in 2017. Long-term deficits in executive function, attention, and memory are associated with MDD, alongside daily occupational and social impairment. Currently, suicide attempts (SA) are prevalent amongst one-third of MDD patients, with higher rates for patients currently undergoing an episode opposed to MDD patients fully readmitted to hospitals. Chronic social defeat stress is a relevant psychosocial paradigm that can cause depression-like behavior, alongside long-lasting effects on episodic memory and hippocampal gene expression when left untreated. MDD is commonly treated with antidepressants, however currently approved antidepressants targeting neurotransmitters have delayed response times and are ineffective in approximately a third of MDD patients. Fast-acting ketamine, a NMDA receptor antagonist, has been found effective against MDD symptoms in the recent literature. Ketamine reverses stress-induced cognitive deficits, coupled with long-lasting effects on episodic memory and hippocampal gene expression when left untreated. MDD is associated with impaired pattern separation and cognitive flexibility in mice, and can fast-acting ketamine antidepressant reverse stress-induced cognitive deficits.

**MARKER TERMS**

- **Pattern Separation**
- **Cognitive Flexibility**
- **Psychosocial stress**
- **Ketamine**
- **MDD**
- **Suicide attempts**
- **Antidepressants**
- **Narrative memory**
- **Hippocampus**

**METHODS**

The ability to distinguish similar stimuli (i.e., pattern, place or time changes) to different inputs is a hallmark of pattern separation. This mechanism allows for the effective encoding and storage of different memories, by partitioning and preventing the interference of similar stimuli. Cognitive Flexibility: The ability to appropriately adapt to changes in the environment.

**RESULTS**

The operant touch screen (TS) allows for the investigation of pattern separation and cognitive flexibility. The analysis of the behavior using the TS operant chamber revealed that mice trained on large separation paradigms took longer to reach reversal compared to small separation paradigms. This finding is consistent with previous research demonstrating the hippocampus-dependent nature of cognitive flexibility.

**DISCUSSION**

1. Ketamine reverses stress-induced cognitive deficits in mice.
2. Our study adds to limited TS literature on both psychosocial stress and fast-acting ketamine.