

EFFECTS OF ETHANOL AND KETAMINE ON FEAR MEMORIES IN RODENT PTSD MODEL

Srestha Mazumder
Email: sara.mazumder@hotmail.com



Introduction

Ketamine has shown efficiency in reducing PTSD symptoms and is currently being used to treat various psychological disorders, mainly those related to anxiety and depression. PTSD patients often have a co-morbid alcohol abuse disorder, which is potentially problematic for PTSD patients that take ketamine medication to help reduce their symptoms. Various studies have illustrated ethanol's enhancing effects in reactivated contextual fear memory. Further, continued abuse of alcohol impairs fear extinction by remodelling the dendritic arbores of the medial prefrontal cortex which could potentially explain the lack of fear extinction. Due to the independent effects of ketamine and alcohol on fear/PTSD memories, it is of clinical interest to view the interaction of these two chemicals.

- > The major aim of this research is to understand potential effects of ketamine and ethanol interactions on fear memories.

Methods

Day one: Rats will be induced with PTSD like symptoms through the use of a stress paradigm adopted from Cohen et al, 2006. Rats will be placed on top of cat litter, used by a cat for two days and sifted for stools, for 10 minutes. All rats will be measured for time spent freezing during this procedure. Following this, PTSD like symptoms will be tested by placing the rat on an elevated plus maze for five minutes.

Day two: Rats that previously displayed PTSD symptoms will have saline (1.5mg/kg), ketamine only (2.5mg/kg), ethanol only (1.5mg/kg) and ketamine and ethanol (2.5mg/kg of ketamine & 1.5mg/kg of ethanol) administered intravenously, depending on the condition they are allocated to

Day three: All rats with the PTSD like symptoms will be tested for contextual freezing. Fear memories will be measured through the time spent freezing when the rat is placed on top of clean cat litter for 10 minutes.



Results

Adopting the stress paradigm from Cohen et al. (2006), intravenously administering ketamine only should facilitate lower rates in freezing than found in the control condition as ketamine is an NMDA antagonist which promotes new learning (Ravindran and Stein, 2009).

It is expected that rats in the ethanol only condition will show significantly higher freezing from baseline in line with Quinones-Laracuente et al. (2015)'s demonstration of significantly increased freezing rates after the administration of ethanol.

The effect of ethanol, increasing fear memory persisted the day after in this study. The rats injected with saline are expected to freeze at baseline, roughly 50% (Cohen et al, 2006).

Based on the studies above, ethanol causes a significant increase in fear memories and ketamine illustrates substantial decreases in fear memories, it is thus expected that the interaction of both these chemicals will lead to an increase in fear memory that is more exacerbated than ethanol alone.

Discussion

It is expected that PTSD memories may be exacerbated as a product of auditory and visual distortions that result from interactions between ketamine and alcohol (Duncan et al, 2001; Krystal et al, 1994).

As PTSD patients experience flashbacks and intrusive memories often, experiencing such distortions may in turn aggravate their PTSD memory (Falls, Miserendino & Davis, 1992; Duncan et al, 2001; Krystal et al, 1994; Victor & Justin, 1958).

Although the amount of ketamine sufficient to reduce PTSD fear memories and symptoms is known, it is possible combining alcohol with ketamine may result in greater expression of ketamine's dissociative symptoms to express more profoundly, leading to hallucinations and flashbacks of the trauma memory (Duncan et al, 2001; Krystal et al, 1994).

As PTSD patients often have a co-morbid alcohol abuse disorder (Holmes et al, 2012), it is of clinical importance to understand potential interactions between the two.



Conclusion

This area is of particular interest as many PTSD patients suffer from comorbid alcohol abuse disorder (Holmes et al, 2012) and as such it is of interest to understand potential detrimental effects of taking medication with ketamine and consuming alcohol, rather than beneficial ones. This may be due to alcohol usage impairing fear extinction by remodelling the dendritic arbores of the medial prefrontal cortex (Holmes et al 2012). Although these results are expected to translate to human populations, further research needs to be conducted on adults suffering from a comorbid PTSD and alcohol abuse disorder. If the results map onto human participants these findings will be clinically significant for PTSD patients as well as patients suffering from Major Depressive Disorder (MDD). MDD patients tend to have a comorbid alcohol abuse disorder (Swendsen, 1998) and many clinicians are considering treating MDD with ketamine as it has shown efficiency in experiments (Berman et al, 2000).

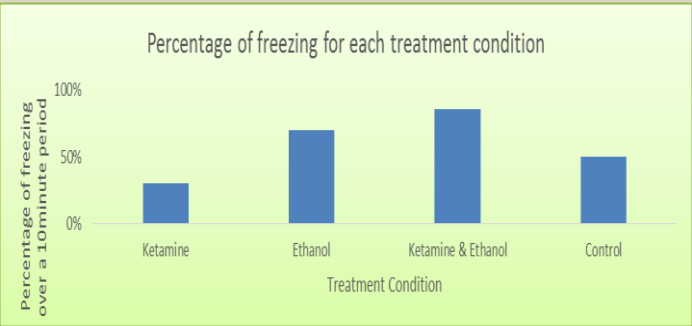


Figure 1. Percentage of freezing for each intravenous administration

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