# Mirtazapine Induced Musical Hallucinations: Does Glutamate Play a Role?

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## Abstract

Mirtazapine is a commonly prescribed antidepressant with a unique receptor profile and whose primary mechanism of action is thought to be mediated by presynaptic alpha 2 antagonism in addition to postsynaptic serotonin receptor antagonism. Review of literature has also found that mirtazapine has had several reported cases of hallucinations or perceptual disturbances, with a significant proportion of these cases reporting musical hallucinations. We present today a case of mirtazapine associated musical hallucinations and demonstrate in this particular case an association between dose and level of psychotic symptoms reported. Additionally we propose that glutamate modulation may be the primary mechanism, which has implications for the targeted use of not only mirtazapine but other glutamate modulators for targeted treatment of psychosis and mood

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## Introduction

- Mirtazapine is a tetracyclic antidepressant with a unique receptor profile and whose primary effects are believed to be modulated by presynaptic a-2 antagonism as well as postsynaptic 5HT2 and 5HT3 antagonism

- Mirtazapine has also more rarely been associated with psychotic symptoms such as visual and auditory hallucinations. Previous case reports have suggested the likely mechanism of this phenomenon to be an increase in prefrontal dopamine levels

## Case

- A 75-year-old man with a history of Bipolar I disorder presented to clinic for worsening depression and was taking 15mg of mirtazapine as well as 5mg of aripiprazole and 300mg of lamotrigine. He also reported “years” of musical hallucinations (MH) that he associated with mirtazapine and that had not improved with aripiprazole.

- Over the next 18 months the patient had several medication adjustments with consistent report of MH that corresponded with mirtazapine dose and that was unresponsive to aripiprazole and quetiapine.

- At 20 months from initial evaluation, mirtazapine was discontinued. Frequency of MH improved over the next 3 months with no mention of MH at 24 months from initial presentation. He has now remained free from MH over the past 6 months.

## Review of Literature

- Reports were identified by keyword, MeSH-based, and Emtree-based electronic searches of PubMed, Embase, and the Cochrane Library
- The search process used a combination of terms including, “mirtazapine + hallucination,“ “mirtazapine + perceptual”, “mirtazapine + auditory,” “mirtazapine + musical”.

**Figure 1. The relative concentration of brain metabolites of female rats from the 1H MR spectra**

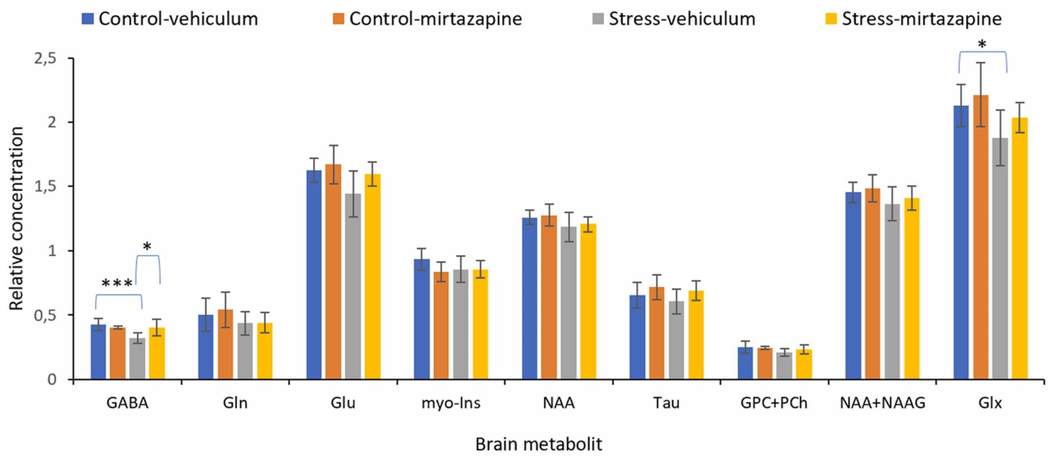
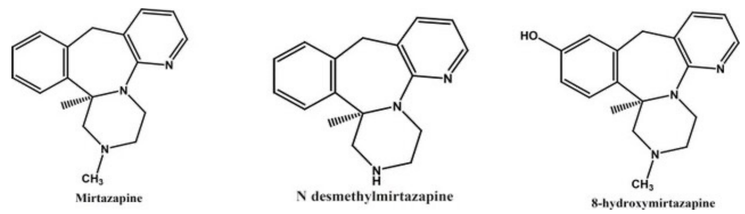



**Figure 2.** Mirtazapine and its metabolites




## Conclusion

- Mirtazapine has in past case reports been associated with hallucinations, however our presented case shows a consistent association between dose and level of psychosis over several years.

- Additionally we propose that glutamate modulation may be the primary mechanism, which has implications for the targeted use of not only mirtazapine but other glutamate modulators for targeted treatment of psychosis and mood

## References

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