

Antidepressant effects of ketamine in animal model of depression

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Summer 2008



Depression



- ⌘ General symptoms of depression include: sadness, helplessness, feeling of guilt or worthlessness, etc.
- ⌘ 17.5 million american adults suffer from it
- ⌘ Women experience it twice as often as men
- ⌘ Economic costs is estimated to be 30.4 billion dollars a year
- ⌘ Cost of human suffering cannot be estimated

(<http://medlineplus.gov/>)

Challenges with current treatments:



- ☞ **Delay in onset:** 2 or more weeks for present antidepressants to work
- ☞ **Lack of response:** only helps about 80% of patients, and for most, the first drug they try doesn't work
- ☞ **Side effects:** nausea, nervousness, sexual problems, urinary problems, constipation, blood pressure, etc.

Our animal model of depression:



- ⌘ Need an animal model that can emulate characteristics found in symptoms-presenting depressive patients
- ⌘ Wistar Kyoto (WKY) rats are a suitable model because of their passive activity in Forced Swim Test (FST)
- ⌘ WKY rats show low swim activity and high immobility in FST as compared to other strains

Ketamine



- ☞ A drug used as an anesthetic in both humans and animals
- ☞ Higher doses have dissociative effect (some people feel detached from reality)
- ☞ Human studies reported that ketamine helped patients relieve depression symptoms quickly

John Krystal, (2000)

Methods: drug administration



- ☞ 16 WKY rats
- ☞ 8 WKY rats were treated ketamine and 8 were treated saline as our control
- ☞ Ketamine was dissolved (two doses: 5.0 and 2.5mg) in saline and was administered by intraperitoneal injection (IP) (1ml/kg)

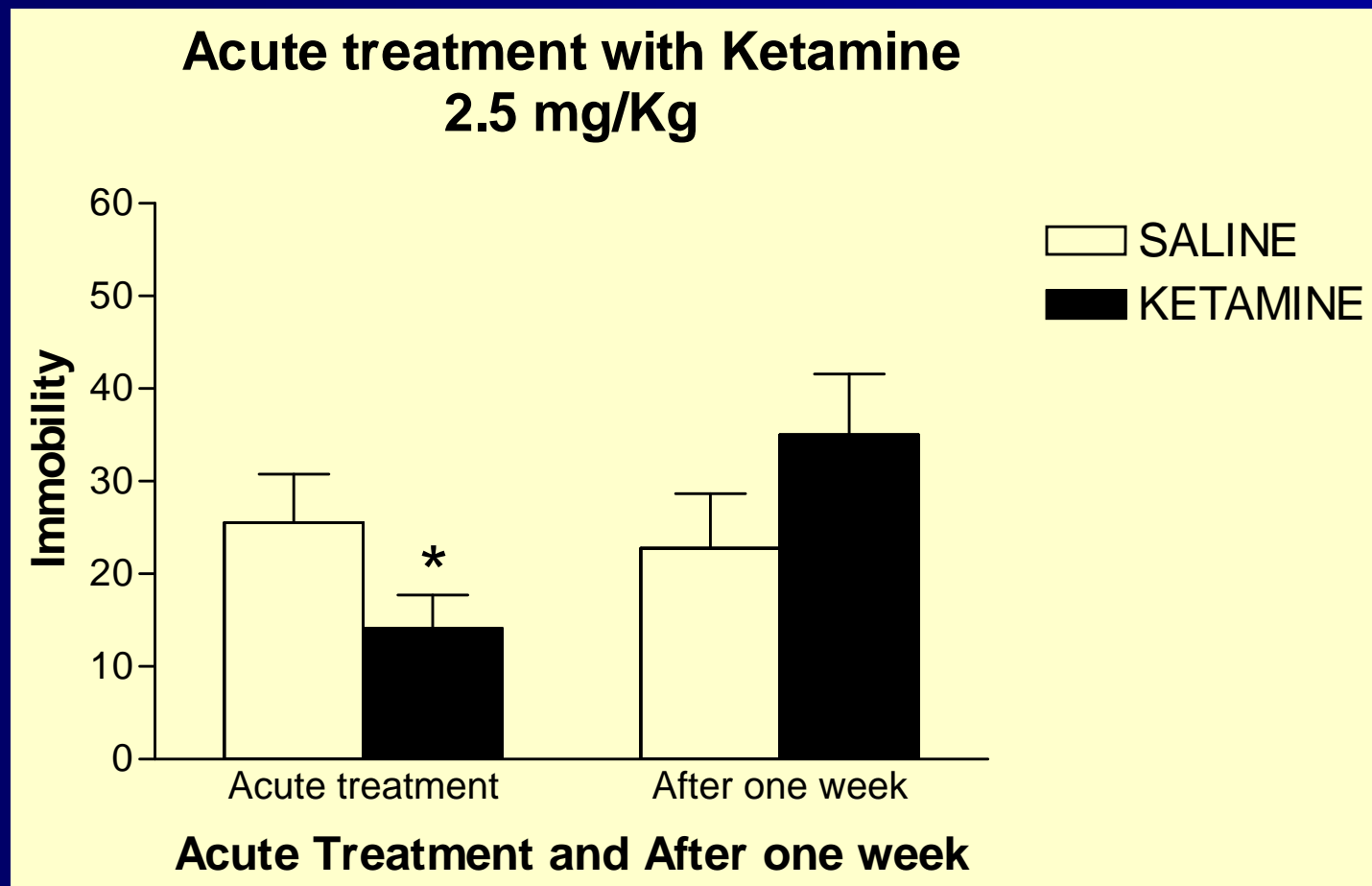
Methods: Forced Swim Test (FST)



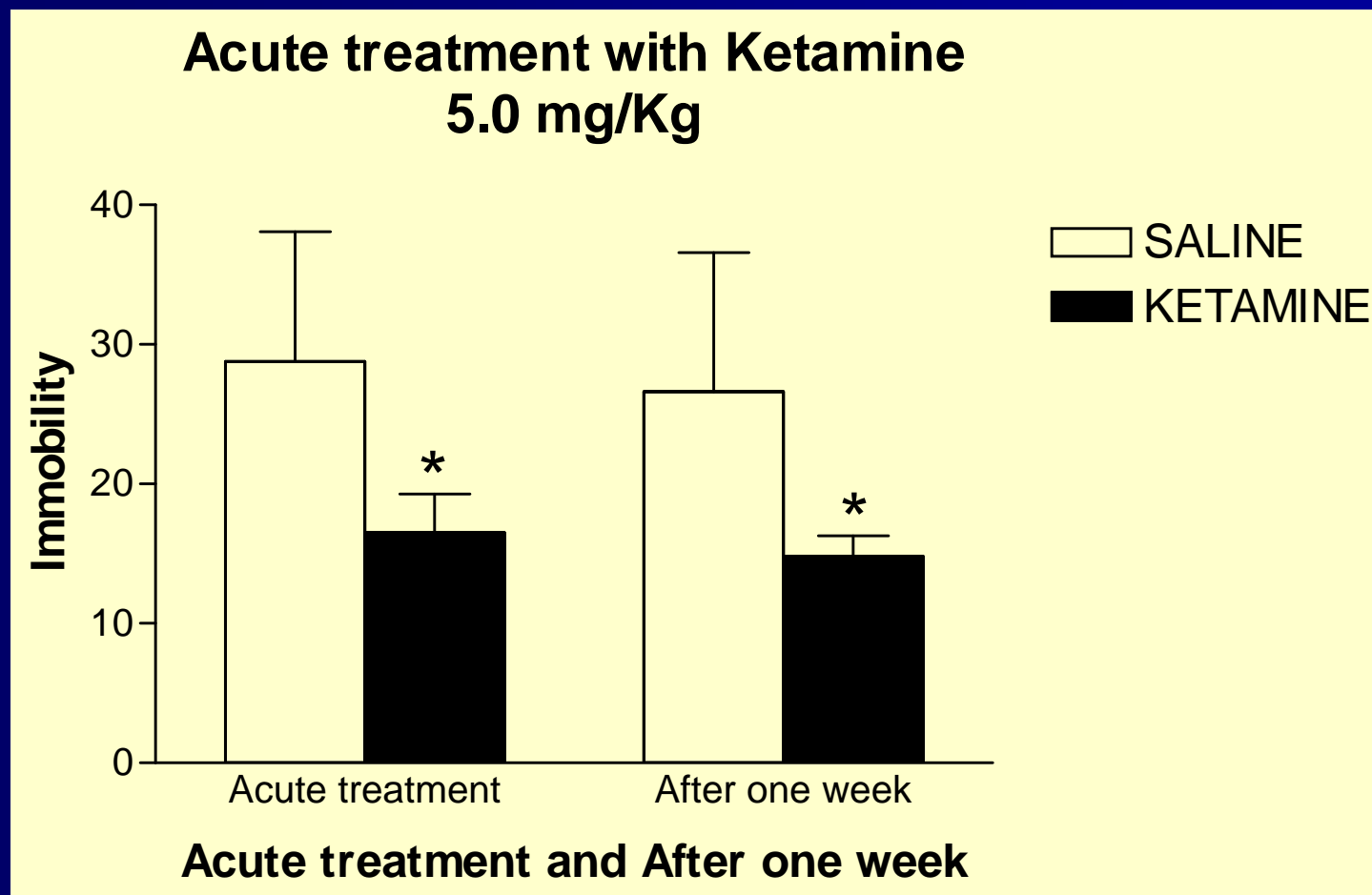
- ⌘ FST is a widely used measurement of helplessness in animal model of depression
- ⌘ Animals were placed in tank containing enough water
- ⌘ Time of immobility (I) and swimming (S) were recorded every 5 seconds

(Krahl et al. 2004)

Results: acute treatment with Ketamine 2.5 mg/Kg



Results: acute treatment with Ketamine 5.0 mg/Kg



Summary of Results

- Acute IP administration of ketamine at doses of 2.5 and 5.0 mg/Kg resulted in reduction of immobility in FST in WKY rats
- The antidepressant like effects of 5.0 mg/Kg but not of 2.5 mg/Kg ketamine was still evident after one week

Conclusion

- Results of this study suggest a rapid and lasting effect of relatively low dose of ketamine in WKY rat
- Ketamine or drugs with similar mechanism of action may have beneficial effects in treatment of depression

References

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Acknowledgments

- AMGEN Scholars Program
- Howard University
- Dr. Yousef Tizabi (Mentor)
- Dr. Lemuel Russell
- Dr. Babur Bhatti
- Kayla Thomas
- Bizu Irving