Antidepressant effects of ketamine in animal model of depression

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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

Methods: drug administration

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

(Krah et al. 2004)
Results: acute treatment with Ketamine 2.5 mg/Kg

Acute treatment with Ketamine 2.5 mg/Kg

<table>
<thead>
<tr>
<th>Immobility</th>
<th>Acute treatment</th>
<th>After one week</th>
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</thead>
<tbody>
<tr>
<td>SALINE</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>KETAMINE</td>
<td>30</td>
<td>50</td>
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</tbody>
</table>

* Significant difference

Acute Treatment and After one week
Results: acute treatment with Ketamine 5.0 mg/Kg

Acute treatment with Ketamine 5.0 mg/Kg

Immobility

Acute treatment and After one week

Acute treatment and After one week
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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