Antidepressant-like Effects of Kynurenic Acid Analougues

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Abstract

• Kynurenic acid (KYNA) - a metabolite of the L-tryptophan (TRP)-kynurenine (KYN) metabolic pathway
• KYNA triggered antidepressant-like effects intracerebroventricularly (i.c.v.) in modified forced swimming test (FST) of mouse
• KYNA is impermeable to the blood-brain-barrier (BBB)
• New KYNA analogues permeable to the BBB in vitro - SZR72, SZR81, SZR104
• KYNA analogues (i.c.v.)
  - SZR72: no effect
  - SZR81: antidepressant-like effect
  - SZR104: no effect
• KYNA analogues intraperitoneally (i.p.)
  - SZR72: no effect
  - SZR81: no effect
  - SZR104: no effect
• KYNA analogues
  - Changed biological properties?
  - Impermeable to the BBB in vivo?
  - Peripherally metabolized?

Conclusion

• i.c.v. administration of SZR81 significantly decreased immobility time and significantly increased swimming time
• The antidepressant-like effects were triggered at least in part through the serotonin 5-HT nervous system
• SZR72 and SZR104 may have lost original biological activities upon i.p. administration
• SZR72 and SZR104 may not cross the BBB in vivo
• Findings in this study may be limited to the dose tested

Introduction

• TRP-KYN metabolic pathway
  - > 95% TRP metabolized in the pathway
  - Synthesizes various bioactive molecules
  - Oxidants, antioxidants
  - Neurotoxins, neuroprotective
  - Immunomodulators
• KYNA
  - Antioxidant
  - Neuroprotective
  - Antidepressant-like
  - KYNA impermeable to the BBB

Materials and Methods

• Ethics: The Committee of Animal Research at the University of Szeged (I.74-24/2018) and the Scientific Ethics Committee for Animal Research of the Protection of Animals Advisory Board (M.240/2019)
• Charles Dawley (CD) 1 male mouse
• 15 mins pretest 24 hours before
• i.c.v.: administration 30 mins before behavior sampling
• i.p.: administration 30 mins before behavior sampling
• Open field (OF) test
• one-way ANOVA

Results

<table>
<thead>
<tr>
<th>Antidepressant-like effects</th>
<th>i.c.v.</th>
<th>i.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td>KYNA</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>SZR72</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>SZR81</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>SZR104</td>
<td>-</td>
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</tbody>
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References


Funding

The Economic Development and Innovation Operational Programme (GINOP)
GINOP 2.3.2-15-2016-00034
GINOP 2.3.2-15-2016-00048
TUDFO/4738/1-2019-ITM

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