EFFECTS OF INTRACEREBRAL INFUSION OF RIMONABANT ON LOCOMOTOR ACTIVITY

<table>
<thead>
<tr>
<th>Regions</th>
<th>Vehicle</th>
<th>Rimonabant 30 ng</th>
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</thead>
<tbody>
<tr>
<td>Shell Nucleus accumbens</td>
<td>377 ± 52</td>
<td>373 ± 61</td>
</tr>
<tr>
<td>Basolateral amygdala</td>
<td>364 ± 26</td>
<td>344 ± 34</td>
</tr>
<tr>
<td>Prelimbic cortex</td>
<td>412 ± 56</td>
<td>402 ± 57</td>
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</tbody>
</table>

Rimonabant did not alter locomotor activity when infused into tested regions.

Conclusion

The shell of the Nacc, the BLA and the PLCx are targets of rimonabant for its anti-motivational effects towards nicotine seeking.

Together with recent preclinical and clinical findings, these results confirm that rimonabant represents a promising therapeutic treatment for smoking cessation.

Acknowledgments

The authors thank Stephanie Hamon for her excellent technical assistance.

References


The CB1 receptor antagonist, rimonabant, reduced nicotine-seeking behaviour maintained by nicotine-associated cues: brain structures involved.

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THE CB1 RECEPTOR ANTAGONIST, RIMONABANT, REDUCED NICOTINE-SEEKING BEHAVIOUR MAINTAINED BY NICOTINE-ASSOCIATED CUES: BRAIN STRUCTURES INVOLVED

Introduction

Environmental stimuli repeatedly associated with smoking acquire conditioned reinforcing properties. These stimuli become capable by themselves of inducing nicotine-seeking behaviour. The presence of cues during nicotine self-administration has been extensively studied and validated in animals. In order to test the effect of rimonabant on nicotine-seeking behaviour in mice, this study assessed the action of rimonabant administered intracerebrally.

Material and Methods

EFFECTS OF RIMONABANT ON NICOTINE-SEEKING BEHAVIOUR

1. SELECTION OF THE RATS: Male Sprague-Dawley rats (120-200 g) were selected for their locomotor response to a stimulating dose of nicotine (0.45 mg/kg) and for their potential for self-administration of nicotine. Rats with a mean increase of locomotor activity of at least 80% compared to baseline were selected for further analysis.

2. DRUG ADMINISTRATION: Rats were anaesthetized with Zoletil® (60 mg/kg, i.p.) and catheterized with a chronic silastic catheter in the right jugular vein. Rats were then treated with either saline or rimonabant (0.3, 3, or 30 ng/0.5 µl/site) dissolved in saline and 6% dimethylsulfoxide (DMSO) or vehicle.

3. IMPLANTATION OF GUIDE CANNULAE: Guide cannulae were implanted into the Nacc (AP +1.7, ML ± 0.8, DV - 6.7 mm), the BLA (AP -2.87, ML ± 5.0, DV - 7.4 mm), or the PLCx (AP + 2.9, ML ± 1.0, DV = - 2.4 mm, tilt 7° angle), according to the atlas of Paxinos and Watson.

4. CONDITIONS OF THE EXPERIMENT: Each active lever press delivered a dose of nicotine (30 ng) or vehicle. After nicotine removal, no responses on either lever were reinforced.

5. TESTING THE CONDITIONS OF EXTINCTION: After nicotine self-administration acquisition (> 12 presses/h), rats were submitted to extinction (20 sec schedule; session duration: 30 minutes, 15-20 days).

6. RESULTS ANALYSIS: For each comparison, the control value was the mean number of presses performed by the vehicle group. Data obtained in the Nacc were analysed using one-way ANOVA followed by Dunnett’s test. Data obtained in the BLA and the PLCx were compared using Student’s t-test.

RESULTS

EFFECTS OF RIMONABANT ON NICOTINE-SEEKING BEHAVIOUR

Rimonabant did not alter locomotor activity when infused into tested regions.

Conclusion

The shell of the Nacc, the BLA and the PLCx are targets of rimonabant for its anti-motivational effects towards nicotine seeking.

Together with recent preclinical and clinical findings, these results confirm that rimonabant represents a promising therapeutic treatment for smoking cessation.