N-Acetylcysteine changes glutamate levels in cocaine dependent subjects: an open label $^1$H MRS pilot study

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Introduction

Disturbances in glutamate homeostasis play an important role in addiction, especially in relapse. Treatment with N-acetylcysteine has proven to restore glutamate homeostasis and prevent relapse into drug seeking behavior in preclinical studies.

Proton magnetic resonance spectroscopy ($^1$H MRS) provides a noninvasive means of examining metabolites such as glutamate in the human brain.

Until date, the effects of NAC on brain glutamate concentrations in humans have not yet been examined.

Aim

- To investigate glutamate changes in the anterior cingulate after administration of NAC in cocaine dependent subjects compared to healthy controls.
- To delineate the relationship between glutamate concentrations, impulsivity and cocaine use.

Methods

Subjects

- Cocaine dependent (CD) subjects with comorbid alcohol problems
- Age and education matched healthy controls (HC)

<table>
<thead>
<tr>
<th>Cocaine dependent</th>
<th>Controls</th>
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<tbody>
<tr>
<td>N</td>
<td>9</td>
</tr>
<tr>
<td>Age (years)</td>
<td>35.6 ± 6.5</td>
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<tr>
<td>IQ</td>
<td>91.4 ± 6.7</td>
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N-acetylcysteine administration

- Single dose 2400 mg one hour before scanning

$^1$H MRS protocol

- Open label design
- 2 scan sessions: Baseline-NAC (counterbalanced)
- PRESS sequence, TR/TE = 38/2000
- Voxel (5.0 x 1.6 x 1.0 cm) placed in left dorsal anterior cingulate cortex (BA24/32), see Fig. 1

Questionnaire

- Barratt Impulsiveness Scale, Version 11 (BIS-11)

Conclusions

NAC restored the disturbed glutamate concentration within the ACC in cocaine dependent subjects found at baseline. This could be an important implication for treatment, because disturbed glutamate concentrations have been related to relapse and treatment with NAC to prevention of relapse.

Higher impulsivity was associated with elevated glutamate levels within the dorsal ACC, a brain area involved in cognitive control. Impulsive subjects benefit most from NAC in terms of glutamate reduction.

Subjects with the lowest amount of cocaine use in the last six months had lower glutamate levels at baseline. These subjects were also more impulsive at baseline and longer abstinent from cocaine.

No potential conflicts of interest

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