AMPHETAMINE WITHDRAWAL: NATURE, TIME COURSE AND TREATMENT

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Abstract

Increased demands on amphetamine dependence treatment services point to a need for effective pharmacotherapies for withdrawal symptom suppression. However, empirical data on which to base effective treatments are scarce. To address the need for an evidence base, four studies were conducted in two countries – Australia and Thailand. Firstly, the time course and severity of amphetamine withdrawal symptoms were characterised in two inpatient samples of amphetamine users. Results identified the first week of abstinence as an acute withdrawal phase characterised by increased sleeping, eating and a cluster of mood and anxiety-related symptoms. Following the acute phase, most withdrawal symptoms remained stable and at low levels for the remaining two weeks of abstinence (the sub-acute phase). Data from these two studies formed the basis for a new instrument, the Amphetamine Cessation Symptom Assessment scale (ACSA). On psychometric testing, the ACSA showed satisfactory reliability and a clear psychometric structure, delineating symptom clusters and their correlates with a three factor solution providing the best fit to the data. Using the ACSA to measure outcome, the safety and efficacy of the serotonin and noradrenaline reuptake inhibitor antidepressant mirtazapine (15–60 mg per day, \(n = 13\)), and the wake-promoting drug, modafinil (400mg per day, \(n = 14\)) were assessed in successive, open-label, inpatient pilot trials. Study medication was administered for up to ten days. An historical comparison group (\(n = 22\)) who received treatment as usual consisting of pericyazine 2.5–10mg per day for control of agitation served as a comparison. Results showed that modafinil and mirtazapine were well tolerated, producing minimal positive subjective effects. There were significant group differences in withdrawal severity (\(F = 18.6, \text{df} 2,219 \ p< 0.001\)). Post-hoc analysis showed that modafinil was more effective than mirtazapine (\(p = 0.041\)), and both were more effective than treatment as usual (both \(p< 0.001\)) in ameliorating withdrawal severity. Overall, these studies identified a peak in withdrawal severity during the first week of abstinence; demonstrated the reliability and validity of the ACSA and identified modafinil as a safe and potentially effective pharmacotherapy for the treatment of amphetamine withdrawal symptoms.
Declaration

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis, when deposited in the University Library, being available for loan and photocopying.

Catherine McGregor

Date
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Lastly, I would like to thank the many patients both in Australia and in Thailand who contributed freely of their time and experiential knowledge in the hope that it may help others in the future.
Publications in support of this thesis


## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ACQ</td>
<td>Amphetamine Craving Questionnaire</td>
</tr>
<tr>
<td>ACSA</td>
<td>Amphetamine Cessation Symptom Assessment</td>
</tr>
<tr>
<td>ASSA</td>
<td>Amphetamine Selective Severity Assessment</td>
</tr>
<tr>
<td>AWQ</td>
<td>Amphetamine Withdrawal Questionnaire</td>
</tr>
<tr>
<td>BDI</td>
<td>Beck Depression Inventory</td>
</tr>
<tr>
<td>CCQ</td>
<td>Cocaine Craving Questionnaire</td>
</tr>
<tr>
<td>CGI</td>
<td>Clinical Global Impressions Scale</td>
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<tr>
<td>CSSA</td>
<td>Cocaine Selective Severity Assessment</td>
</tr>
<tr>
<td>DV</td>
<td>Dependent variable</td>
</tr>
<tr>
<td>IV</td>
<td>Independent variable</td>
</tr>
<tr>
<td>MAOI</td>
<td>Monoamine oxidase inhibitor</td>
</tr>
<tr>
<td>PCA</td>
<td>Principal Components Analysis</td>
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<tr>
<td>SDS</td>
<td>Severity of Dependence Scale</td>
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<tr>
<td>SMHSQ</td>
<td>St Mary’s Hospital Sleep Questionnaire</td>
</tr>
<tr>
<td>SSRI</td>
<td>Selective serotonin reuptake inhibitor</td>
</tr>
<tr>
<td>Sr²</td>
<td>Squared semipartial correlation</td>
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</tbody>
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