

AMPHETAMINE WITHDRAWAL: NATURE, TIME COURSE AND TREATMENT

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July, 2005

A thesis submitted for the degree of Doctor of Philosophy

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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 ($F = 18.6$, $df 2,219$ $p < 0.001$). 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

Acknowledgements

Many people supported the work involved in creating this thesis. My gratitude goes firstly to Jason White for his calm, reasoned and expert guidance over the past four years. I would also like to thank sincerely Manit Srisurapanont for his enthusiastic and energetic support of this work, particularly in negotiating with the Thai authorities and for his indispensable work in document translation and training of staff.

Sincere thanks to Drug and Alcohol Services South Australia, in particular the staff of Warinilla Clinic for their enthusiastic support of this work. Thanks to Amanda Mitchell and Wendy Wickes for their valuable contribution to the design and conduct of the questionnaire and pharmacotherapies studies. Sincere thanks to the staff of the Northern Drug Dependence Treatment Centre, Chiang Mai, Thailand for their support and in particular the staff of Ward 2 for their generous assistance in subject recruitment and data collection – and for all the wonderful food. Thanks to Jaroon Jittiwutikarn, Suchart Laobhripatr, Thirawat Wongtan and Sunee Keeratipongsathorn for their valuable support.

My thanks go to my fellow 'green room' residents for their encouragement and beer. Many thanks to Rachel Humeniuk, Paul Callahan, Elizabeth Elliot and David Newcombe for their explanations of various pharmacological mysteries – particularly in the first year. To Rod Irvine and Abdullah Salem for sitting through more practice presentations than any man should have to endure.

My love and gratitude go to my husband, Frank Radke for his inexhaustible patience and support, both emotional and practical.

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.

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Abbreviations

ACQ	Amphetamine Craving Questionnaire
ACSA	Amphetamine Cessation Symptom Assessment
ASSA	Amphetamine Selective Severity Assessment
AWQ	Amphetamine Withdrawal Questionnaire
BDI	Beck Depression Inventory
CCQ	Cocaine Craving Questionnaire
CGI	Clinical Global Impressions Scale
CSSA	Cocaine Selective Severity Assessment
DV	Dependent variable
IV	Independent variable
MAOI	Monoamine oxidase inhibitor
PCA	Principal Components Analysis
SDS	Severity of Dependence Scale
SMHSQ	St Mary's Hospital Sleep Questionnaire
SSRI	Selective serotonin reuptake inhibitor
Sr^2	Squared semipartial correlation