COGNITIVE EFFECTS OF ESCALATING DOSES OF ORAL LISDEXAMFETAMINE IN METHAMPHETAMINE DEPENDENT ADULTS

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Introduction and Aims:
Maintenance agonist therapies are effective treatments for a number of substance use disorders. Lisdexamfetamine is a prodrug for dexamphetamine, and its pharmacokinetics suggests potential as an agonist treatment for methamphetamine dependence. As part of a phase 2 safety study examining doses greater than those currently approved for the drug (70mg), the impact of a range of doses on cognitive function were examined.

Design and Methods:
Sixteen methamphetamine dependent individuals underwent an ascending dose regime of lisdexamfetamine, increasing doses from 100mg per day by 50mg each week over 5 weeks (spending 2 weeks at maximal 250mg/day dose). Participants were blinded to timing of dose increase. Assessments were completed at 12 week follow up. Assessments of processing speed, attention, inhibition, learning, and flexibility were conducted at trough (pre-dose) and peak (post-dose) each week.

Results:
Dose dependent improvements in reaction time and errors were apparent in multiple domains: processing speed (digit symbol), attention (rapid visual information processing) and inhibition (flankers/no-go). Performance was maximal at 200 and 250mg doses; was well maintained over time; and there was no evidence for differences between trough and peak.

Discussions and Conclusions:
This range of doses appeared safe and facilitated cognitive performance on a range of fundamental cognitive domains. Enhancement to these cognitive domains has the potential to support treatment engagement (e.g. through improved attention) and reduce relapse risk (through enhanced inhibitory processes). While the absence of a control arm to the protocol renders these results preliminary they suggest promising effects for lisdexamfetamine maintenance treatment enhancing outcomes for methamphetamine dependent individuals.