Amphetamines for Improving Stroke Recovery
A Systematic Cochrane Review

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The search for pharmacological therapies, which may facilitate the recovery process after a permanent brain injury, has been intensified during the past decade. One of the most extensively studied pharmacological approaches to stimulate recovery after experimental stroke is treatment with amphetamines. Experimental animal studies suggest that treatment with amphetamines improve recovery after focal cerebral ischemia. If the effect were similar in humans, amphetamine treatment could have a major impact on recovery from stroke. This systematic review aims to assess the effects of amphetamine treatment, as compared with placebo, in patients with stroke.

Methods
We searched the Cochrane Stroke Group Trials Register (last searched November 2002). In addition, we searched the Cochrane Controlled Trials Register (Cochrane Library, Issue 4 2002), MEDLINE (1966–September 2002), EMBASE (1980–November 2002), and Science Citation Index (1992–December 2002). The reference lists of all relevant articles and reviews were checked, and we contacted researchers in the field to identify further published and unpublished studies.

We considered randomized unconfounded trials comparing amphetamine with placebo.

Two reviewers independently selected trials for inclusion, assessed trial quality, and extracted the data.

Results
Seven studies involving 172 patients were included. Based on 2 trials (85 patients), there was no evidence that amphetamine treatment reduced death or dependence (Peto’s odds ratio [Peto OR] 1.54; 95% confidence interval [CI] 0.64 to 3.73). In these 2 trials, there were imbalances at baseline, with more severe strokes allocated to amphetamine. This imbalance may account for the trend for more deaths at the end of follow-up among amphetamine-allocated patients (Peto OR 3.33; 95% CI 0.99 to 11.24). Based on 4 studies (95 patients), there was evidence of a better relative change in motor function according to the Fugl-Meyer motor scale (weighted mean difference [WMD] −8.17; 95% CI −13.58 to −2.76), and based on 1 study (21 patients), there was evidence of a better change in language function as assessed by the Porch Index of Communicative Ability score (WMD −7.51; 95% CI −14.42 to −0.60) in amphetamine-allocated patients. There was no evidence of a better relative change in amphetamine-treated patients regarding activities of daily living (WMD −1.14; 95% CI −12.32 to 10.04), assessed by the Barthel Index, neurological function (WMD 3.65; 95% CI −11.61 to 4.31), assessed by the Scandinavian stroke scale or depression (WMD −2.00; 95% CI −10.32 to 6.32), assessed by the Zung Self-rating depression scale.

Discussion and Implications for Clinical Practice and Future Research
At present, too few patients have been studied to draw any definite conclusions about the effects of amphetamine treatment on recovery from stroke. The suggested benefits on motor and language function, and the nonsignificant trend toward increased risk of death, could be related to imbalances in prognostic variables or other bias in studies. Based on the present evidence, there is no indication for the routine use of amphetamines to improve recovery after stroke, but further research in this area is justified. Further trials should be balanced for important prognostic factors, evaluating the long-term effects of amphetamine on substantive outcomes and a broad range of outcome variables, especially motor and language functions.

In this brief summary, it is not possible to give the full detail of analyses on the 27 outcomes studied. Full details and all the graphical plots are available in the version of this review published in the Cochrane Library.1

Reference
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