

Outcome heterogeneity and bias in acute experimental spinal cord injury

A meta-analysis

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Study objective and summary result

The influence of methodologic and reporting biases on intervention effect sizes in preclinical studies of experimental treatments for spinal cord injury (SCI) was examined. The results showed prevalent methodologic and reporting biases that may inflate effect sizes of neurologic recovery.

What is known and what this paper adds

Systematic reviews and meta-analyses have found evidence of inflated effect sizes in preclinical studies of treatments for ischemic brain injury. This shows that similar problems exist for preclinical studies of treatments for SCI.

Design, size, and duration

PubMed, Embase, and Web of Science databases were searched for studies published by October 2014 that tested decompression, hypothermia, pharmaceutical inhibitors of the Rho/Rock pathway, cellular treatments, and physical exercise as ways of promoting locomotor recovery in animal models of SCI. The selected studies' data were obtained from the CAMARADES database, which collects data from animal studies of various diseases. Then, meta-regression analyses were used to evaluate reported effect sizes and various potential sources of bias.

Participants and setting

In total, 303 published studies were selected for inclusion in the meta-analysis. These studies were published between 1967 and 2014 and collectively described 549 experiments involving 9,535 animals.

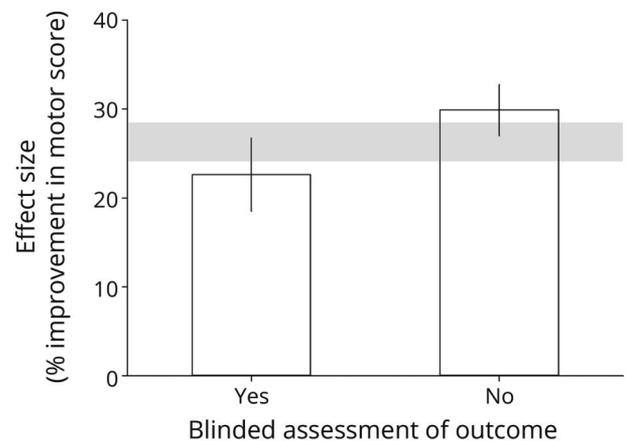
Primary outcome measures

The primary outcomes were the reported effect sizes of neurologic recovery and the examinations of potential sources of bias.

Main results and the role of chance

The overall reported improvement in neurobehavioral outcomes was 26.3% (95% confidence interval, 24.3%–28.4%). Only 48.8% of the studies used blinded assessments, and the lack of blinding could have inflated effect sizes by 7.2% ($p < 0.001$). An estimated 2%–41% of relevant experiments

Figure Inflated effect sizes for studies that did not use blinded outcome assessments



The gray zone represents the 95% confidence interval for the overall effect size.

were unpublished, and including these experiments could have reduced effect sizes for various interventions by 0.9%–14.3%.

Bias, confounding, and other reasons for caution

Key study design characteristics were sometimes not reported in the original publications. The meta-regression analyses were univariate rather than multivariate.

Generalizability to other populations

Data were analyzed from experiments conducted with various animals in diverse countries. This favors the generalizability of the results.

Study funding/potential competing interests

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A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.

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