Statistical Issues in the Analysis of Data from Neuroprotective Trials

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  - Hypothesis testing, with its tight control of type I error, is not unique among methods of scientific induction, and p-values are not the best way to weigh evidence in favor of one hypothesis versus others.

Statistical Issues

- Screening problem
  - We know that population screens or diagnostic tests with even excellent sensitivity and specificity have poor positive predictive value in low prevalence settings.

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  - Translation: if there is only a small a priori likelihood that a given neuroprotective agent will actually work (low prevalence of success), then phase III trials with 5% significance levels and 80% power will have a low positive predictive value.

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  - That’s also why skeptics may not be persuaded by the same evidence that persuades partisans.

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    - Dose levels
    - Combination therapies
    - Classes of compounds

Statistical Resolutions

- You want provocative?

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- Here's provocative...

Statistical Resolutions

- Change the paradigm / Change the goal

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- The goal of early phase testing should be to increase the odds of future success through better marshalling of resources and better assessment of evidence.

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  - Non-superiority ("futility") testing for phase II studies.
  - Selection procedures to pick potential winners for further phase II or III testing.
  - Minimize loss functions other than the zero-one of hypothesis testing, e.g., minimize an ethical cost function.
  - Use a risk-based allocation design (non-randomized)