

# **Why should we be *Skeptical* *Neuroscientists*?**

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# Challenges for neuroscience research

- Heterogeneity of response in populations
  - Biological variability
  - Interactions between biology and the experimental design
- Methodological sources of variation
  - Confounds to “quality control”
  - Inherent tension between control of factors contributing to variance and the “cutting edge”
- Fundamental limits to inferential confidence
  - If you don’t know what a needle looks like, it is tempting to call discovery too early when struggling with a haystack
  - The Winner’s Curse

# Heterogeneity of response in populations

- Appropriate constraint of the experimental paradigm is difficult to assess *a priori* in discovery science
- Human experiments address an “outbred” population, typically self-selected
- “Disease” populations usually are defined on clinical expression, while the assumption is that the neurobiological/imaging phenotype is distinct
- Human studies often are small, exacerbating confounds of the above
- Conceptual confounds to interpretation of individual brain activity in a common framework

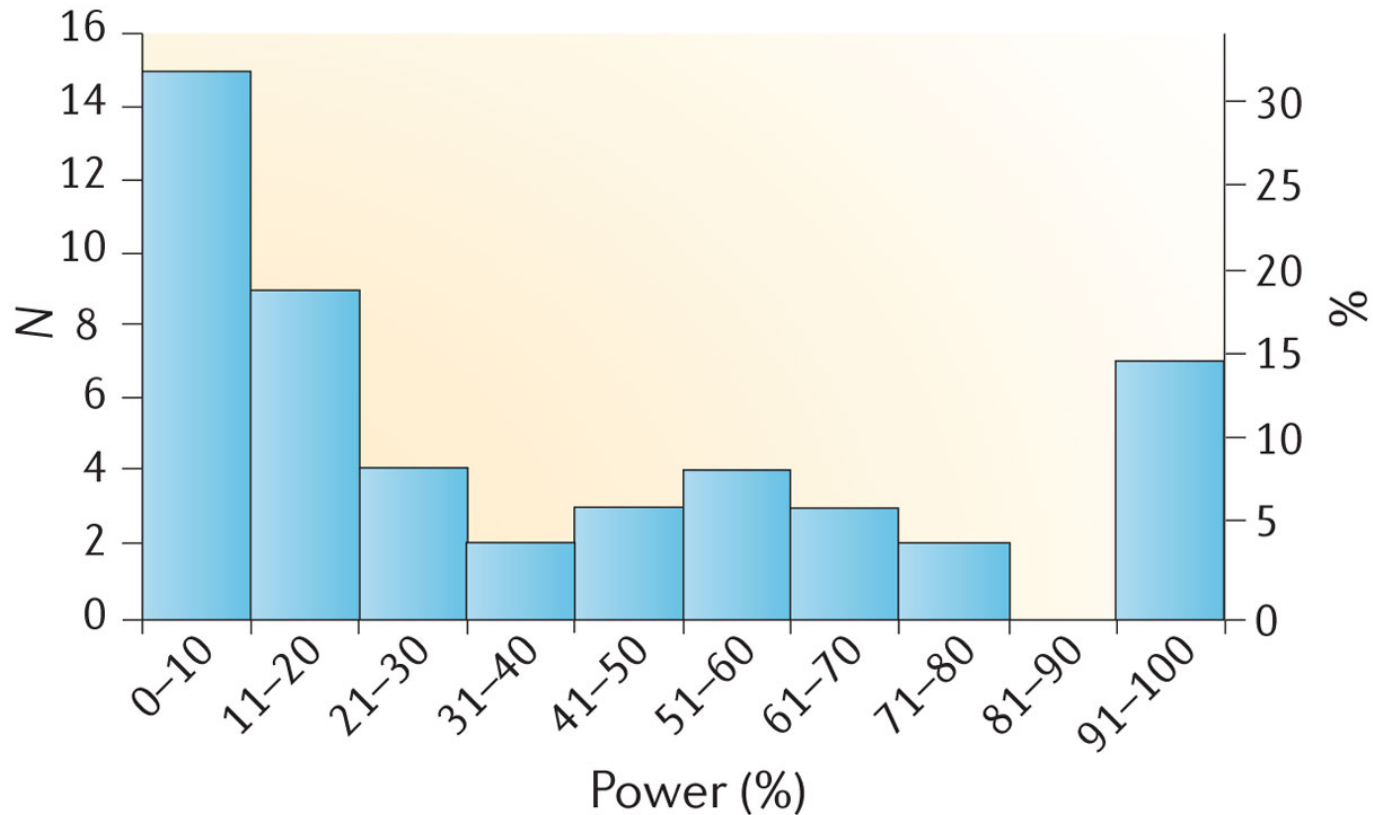
# Methodological sources of variation abound- *especially in imaging*

- Small effects are sought- most typically, interactions of small effects with small effects
- Multiple sources of structured “noise” that can show population specific effects (e.g., movement artifacts in contrasts between healthy and disease populations)
- Interactions between pre-processing, individual data and outcome measures
- Common low precision of definition of outcomes

# Fundamental limits to inferential confidence

- The low prior probability of an effect in discovery science
- Low prior probabilities not only lower positive predictive value of a study, but also lower the likelihood that a statistically significant effect is a true effect
- When an underpowered study discovers a true effect, its magnitude is likely exaggerated (the “winner’s curse”)

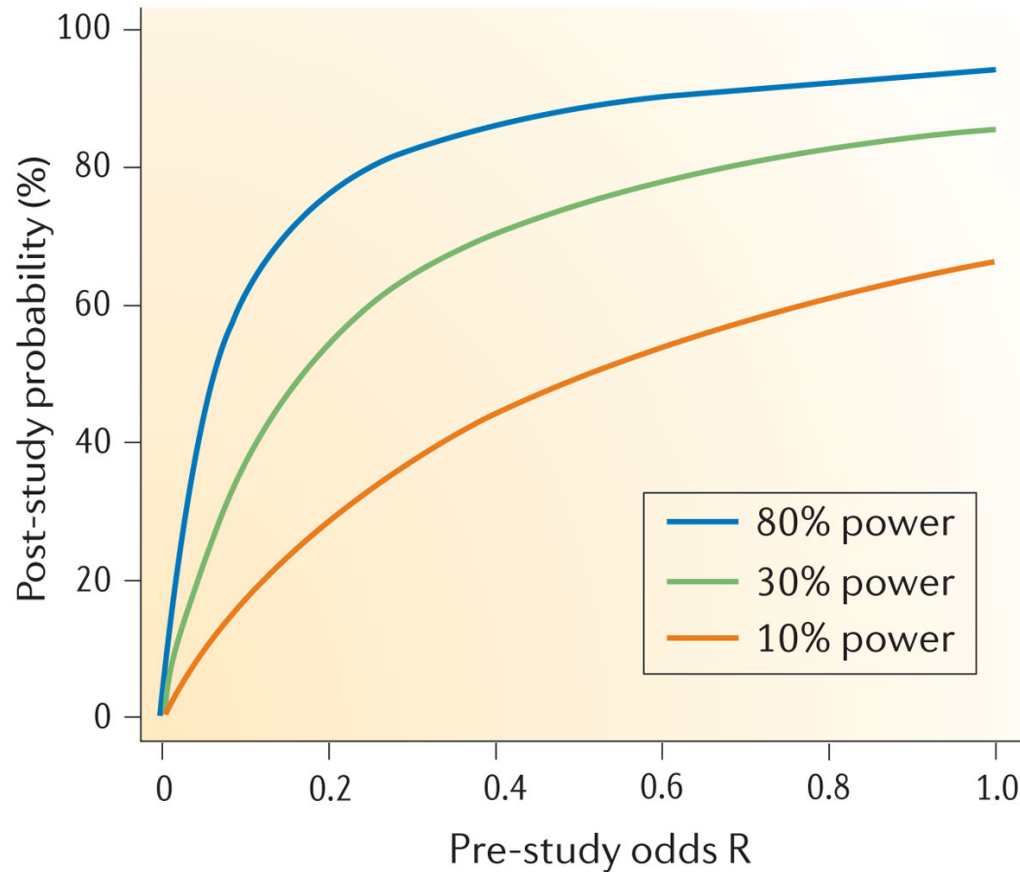
# Median power of studies included in 49 meta-analyses of neuroscience articles published in 2011



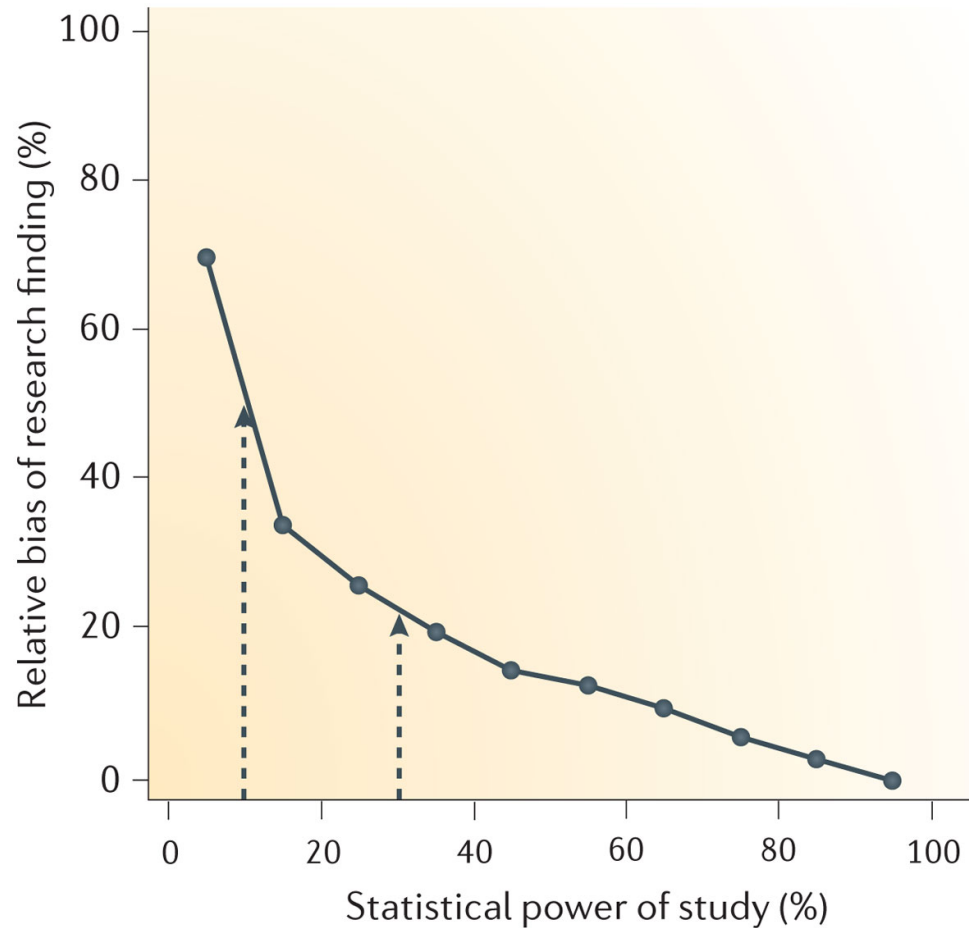
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# Positive predictive value as a function of pre-study odds of association



# Effect size inflation as a function of statistical power: the “winner’s curse”



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