

NIH R Grant Applications:

thoughts about what works and what does not
(a distinctly personal view)

Gordon S. Mitchell, PhD

Preeminence Professor of Neuroscience

Director of Center for Respiratory Research and Rehabilitation

Department of Physical Therapy and McKnight Brain Institute

University of Florida

Getting started with your R application:

- Think about your scientific plan for months to years
- Collect strategic preliminary data to guide the proposal
- Go on the NIH web site and read the directions!
- Follow the requirements (fonts, margins, page limits, required sections, etc.)
- Note: If you cannot find and follow the directions, you have no business submitting a grant at this time!
- **Although these steps are necessary, they are not sufficient to assure funding.**

To appreciate the essential elements of a fundable grant, you need to know what the instructions do not tell you!

- Lessons from Joe (*circa* 1994)
- Chair of the first study section I served on (RAP)
- He expressed the opinion that you can usually tell which grants will be funded—even those outside your area—even those you did not review.
- He estimated this could be done with ~85% success.
- What??? How?????

Successful grants **tell a story!**

- If you cannot tell a story, the logic behind your proposal is probably not sound.
- **logic** must be explicit, conveying the idea that your proposal does have merit.
- **teach** reviewers about scientific issues that are less familiar:
 - Reviewers are educated (not in your sub-specialty)
 - Reviewers want to do a good job, but are tired.
 - Make it easy for them to write their critique and present their evaluation to the study section.

Story telling:

- The story begins with the abstract (first impressions)
- The specific aims page is the most important page of the grant, and should frame the **entire** story of this grant.
- The aims should be written to inspire confidence that this is a mechanistic, hypothesis testing grant. Or....be explicit that it is discovery or applied science.
- Support your story with adequate preliminary data.
- Follow through in all grant sections of the research plan. Each section should directly address your story.

Scoring criteria and other factors

- Of 5 scoring criteria, significance and (especially) approach dominate the final score
- But you most often win or lose with the specific aims.
- Practice word economy in all sections. If you can say the same thing with fewer words----do it! **Reviewer fatigue is a thing.**
- Significance does not mean the clinical significance of the disease *per se* (we all know cancer is a bad thing). It is about:
 - How your proposed aims will advance our understanding or treatment of a disorder (**clinical relevance**) **OR** change the way we think about a fundamental problem (**basic science**).
 - Carefully explain the scientific premise in significance section

Remember that you are in a competition

- Many strong grants are not funded (at least not the first time) because others were simply better.
- The competition is with all other grants submitted in the same time frame (which you cannot control).
- The difference between a 10%ile versus 30%ile grant (ie funding versus no funding) is small, and reviewers are not reliable about getting it right. **It is up to you to sway them!**
 - Small differences in impact score can make a big difference in final percentile rank. If grants are clustered at an impact score of 3, then a 2.9 becomes 10%ile and a 3.1 becomes 30%ile (it is just math).
 - You can make the difference between that 2.9 versus 3.1 by: 1) telling a story, 2) writing clearly with word economy, and 3) providing appropriate preliminary data to support your hypotheses.

Scoring criteria and other factors

- **Innovation:** Only a few proposals are truly innovative (state of the art is not innovation unless you created it) and reviewers are not adept at identifying true innovation. Do not over-sell innovation where none exists, but do identify conceptual and technical innovation (if present) in clear statements.
- **Investigators:** Reviewers usually find investigators “above average” --unless they forgot to publish (rarely discriminates)
- **Environment:** the environment always seems to be excellent (very rarely discriminates).
- **These scoring criteria contribute relatively little to the overall impact score of the grant, except:**
 - When true and obvious innovation is present (a plus)
 - There are clear deficiencies in the PI’s publication record (a minus)

Relevant Biologic Variables

- ***Explain how relevant biological variables, such as sex, are factored into research designs and analyses for studies in vertebrate animals and humans. For example, strong justification from the scientific literature, preliminary data, or other relevant considerations, must be provided for applications proposing to study only one sex.***

Examples of Relevant Biological Variables for vertebrate animals:

- Sex (versus gender)
- Age
- Genetic Backgrounds
- Vendors
- Housing conditions

Examples of Relevant Biological Variables for humans:

- Body mass index
- Socioeconomic status
- Underlying health conditions
- Lifestyle

Early Stage Investigators

- **Fantastic mechanism!** It gives those with less than 10 years post-degree an advantage (often 10%ile higher pay line).
- Do not let this advantage slip by!
- Although reviewers are not supposed to go easy on these proposals, they often do.
- **However**, reviewers are not supposed to be as demanding about preliminary data (don't wait forever!)
- What is most common error made by less experienced applicants?
 - **“Too Ambitious!”**

The reviewers

- Write for hard working and accomplished **people** that want to do a good job, but are tired and distracted. Be clear. Make their life easy!
- Reviewers are normal people: they do not want to sound stupid. If you write a good story, it helps them present your proposal in a way that makes them sound smart and feel good about it.
- **It is not a reviewers job to understand your grant--it is your job to make it understandable.** Be clear, be concise, use word economy.
- There are some "bad reviewers" that are not competent or have an agenda. **MOST** reviewers just want to do a good job and get home!
- There is no "they." Study section composition turns over each year and sometimes from one panel to the next. The panel does not function with one mind, and some reviewers argue vehemently. They are individuals with wide ranging opinions. So write in a way that captures most reviewers most of the time. That is all you can do.

Study sections **rank** grants

- Three reviewers are assigned to write a critique and orally present your proposal. They are generally in your area of research.
 - **Primary**—describe the proposal to the entire study section with focus on strengths/weaknesses. They are asked not to read their critique.
 - **Secondary**—is asked to listen carefully and: 1) bring up new points and 2) agree/disagree with comments of the primary reviewer.
 - **Reader**—adds comments as they see fit.
- The grant opens to general discussion--more prominent today vs decades ago.
- Committee members seldom read unassigned grants; however, they commonly ask questions, and sometimes add new critique based on what they heard.
- Reviewers are then asked to “revisit their scores”
- All study section members then “vote their conscience”
- Panel members must vote within the range of reviewer scores or must say why.
- Things I think I see:
 - Panel members most often “average” individual reviewer scores, however:
 - The longer reviewers drone on, the worse other panel members score the grant
 - Scoring disagreement arises from assessment of clinical significance, score calibration, lack of reviewer clarity

Preliminary data

- A common reviewer default: “insufficient preliminary data.”
- Preliminary data should:
 - demonstrate that you can do the experiments proposed
 - convince reviewers that your ideas are good.
- What to do?
 - Simplify figures; you do not want this reaction: “Huh?”
 - Provide enough data to convince, and then no more.
 - Reinforce data with schematics to explain/simplify concepts
- What not to do?
 - Don’t make reviewers dig through your papers to find key methods or data. It all belongs in the 12 pages allowed.
 - Don’t show data just because you have it
 - All data should clearly relate to the specific aims as stated.

Revising a grant

- Answer big criticisms, but go beyond and do everything possible to improve the grant.
- The next study section does not owe you a better score.
- Being unscored is not banishment, especially if the main concern was lack of preliminary data.
- Consider what the critiques mean versus what they say:
 - Comments are made because they have to justify their score somehow.
 - Many comments are pro-forma: “incremental,” “descriptive” or “insufficient preliminary data.”
 - A claim of insufficient preliminary data is easy to fix in revision!
 - Consider criticisms your fault for not being clear enough (tell a story?).

A good grant proposal should

- **TELL A STORY!**
- Explicitly describe the scientific premise (help reviewers write their critique).
- Explicitly consider strengths and weakness of published research.
- Explicitly identify gaps in our understanding and why it matters that we fill that gap.
- Explicitly describe how the proposed research will address those gaps/weaknesses.
- Provide sufficient preliminary data to demonstrate you can do it—but not more.