Is neuroscience facing up to statistical power?

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Abstract

It has been demonstrated that the statistical power of many neuroscience studies is very low, so that the results are unlikely to be robustly reproducible. How are neuroscientists and the journals in which they publish responding to this problem? Here I review the sample size justifications provided for all 15 papers published in one recent issue of the leading journal Nature Neuroscience. Of these, only one claimed it was adequately powered. The others mostly appealed to the sample sizes used in earlier studies, despite a lack of evidence that these earlier studies were adequately powered. Thus, concerns regarding statistical power in neuroscience have mostly not yet been addressed.

Introduction

It is well-documented that the biomedical sciences are beset by bad statistical practices, and that this is one of the reasons for the current ‘reproducibility crisis’ [1][2]. Prominent amongst these problems are n values that provide only low statistical power. Genuine effects that do actually exist are missed, and many effects that are found to be significant are likely to be just random chance. Neuroscience is no exception to this rule [3]. Indeed, due to the particular challenges of this field, studies which can be completed within traditional parameters of time, cost and ethical approval are often restricted to low n values. Furthermore this data is then analysed post-hoc from many different perspectives in the hope of finding significant results, further increasing the probability of false positives.

The purpose of the present article is not to review again these problems, which are well documented. Rather, I consider how the community of authors, reviewers and journal editors in neuroscience is responding to this clearly visible challenge. The leading neuroscience journal Nature Neuroscience provides a good opportunity to do this, since (unlike most neuroscience journals) it requires authors to provide answers to some basic statistical questions about the design of their experiments. It is therefore of interest to see what answers have been forthcoming in recently published papers. Presumably, because the papers were published, the authors, reviewers and editors all thought these answers were acceptable.

Here I reproduce the statements regarding sample size from all 15 papers published in the August 2016 issue, and find that all of them except one essentially confess they are probably statistically underpowered. I do not explicitly identify which papers these came from, because my goal is not to cast doubt on any specific work: this is simply a (somewhat) random subset to illustrate a very broad issue. Furthermore, there is no reason to think these problems are any different in other journals (though a recent study has argued that statistical power is negatively correlated with journal impact factor [4]). What makes Nature Neuroscience attractive for analysis in this regard, besides its current ranking as the highest-impact primary research journal in the field, is that it takes the trouble to require authors to make explicit comments about certain statistical matters.
Statements of powerlessness

These are ordered thematically, and do not reflect the ordering within the issue.

1. The sample size for each experiment was determined based on published studies using similar experimental designs together with pilot experiments from our laboratory. This allowed us to determine the sample size required for each experiment to ensure a statistical power of 0.8 and an alpha level of 0.05.

Here the authors clearly address the issue of statistical power. Although potentially one might want to see the evidence for the claim, this statement provides reassurance that these results are likely to be reproducible.

2. Sample size was predetermined on the basis of published studies, experimental pilots and in-house expertise.

It is encouraging that pilot studies were undertaken, but it is unclear how these pilots or the in-house expertise were used to determine statistical power.

I now group several statements together, since they are all very similar.

3. Sample sizes for each condition of this study are similar to those generally employed in the field... and were not predetermined by a sample size calculation.

4. No statistical methods were used to predetermine sample sizes, but our sample sizes are similar to those generally employed in the field.

5. Sample size choice was based on previous studies, not predetermined by a statistical method.

6. No statistical tests were used to predetermine sample sizes, but our sample sizes are similar to those in previous studies.

7. No statistical methods were used to predetermine sample sizes, but our sample sizes are similar to those generally employed in the field.

8. Group sample sizes were chosen on the basis of previous studies.

9. No statistical methods were used to predetermine sample sizes, but our sample sizes are similar to those previously reported.

10. No statistical methods were used to pre-determine sample sizes but our sample sizes are larger to those reported in previous publications.

The obvious problem with all these statements is that they do not address whether any of these previous studies demonstrated they were adequately powered (that previous work produced significant results says nothing about statistical power, a basic point that appears not to be widely appreciated). In addition, unless exactly the same experiments were performed, the variability and effects sizes are likely to be different, meaning that the sample size required to achieve adequate power will also be different.

11. No statistical methods were used to predetermine sample sizes, but the tissues were randomly chosen in each age group... and uniformly processed. Also, our samples sizes are similar to those of the discovery set of a similar experimental design in a previous publication.

Besides the problems mentioned above, this statement conflates statistical power with other issues of experimental design.

12. No statistical methods were used to predetermine sample sizes. Sample size was decided on the basis of our previous experience in the field and was not pre-determined by a sample size calculation. The sample size are similar to those generally employed in the field and is justified by the high rate of exclusion due to the difficulty of the combined methodological approaches.

Here the authors appeal to practical limitations on sample sizes. These limitations are real and worthy of acknowledgement. However this does not provide information pertinent to the statistical power, and thus reproducibility, of the results.
13. No estimates of statistical power were performed before experiments; animal numbers were
minimized to conform to ethical guidelines while accurately measuring parameters of animal physiology.
Here the authors appeal to ethical limitations on sample sizes. Again, while real and worthy of
acknowledgement, the same arguments apply as mentioned above.
Finally, we come to perhaps the two most worrying statements.
14. No statistical tests were used to predetermine sample sizes, but our sample sizes are similar
to those generally employed in the field. Normal distribution of data was assumed, but not formally
tested.
15. Normality of the data distributions was assumed, but not formally tested.
The last makes no statement about sample sizes at all, despite this supposedly being a requirement
of the journal. More importantly, both statements explicitly state that the authors do not know whether
the statistical tests they applied were actually appropriate.
For comparison the statements in the July 2016 issue were very similar. One article justified sample
sizes in terms of a power calculation, while the remainder bar one (which simply stated that ‘no
statistical methods were used to predetermine our sample sizes’) appealed to similarity with sample
sizes used in previous studies, in one case in a different species.

Discussion

All of the statements reviewed above were approved by the authors, reviewers, and journal editors,
and one must therefore conclude that they reflect currently accepted practice in the field. It is widely
known and understood that statistical power is a key issue affecting reproducibility, yet 14/15 of these
statements (93%) do not address statistical power. Most of them appeal to precedent for sample
sizes, despite the facts that most neuroscience studies are underpowered [3], and that new exper-
iments will most likely have different variances and effect sizes from previous work. It is clearly a
step forward that Nature Neuroscience requires authors to explicitly answer some key questions re-
garding statistical analysis. However, that the journal is willing to accept answers which are clearly
inadequate, and even sometimes admissions that the statistical analysis performed was quite possibly
wrong, suggests that the journal is still contributing to the problem rather than the solution. For
comparison the relatively new journal eNeuro requires authors to provide the statistical power of each
experiment reported. However this is merely the observed power, which provides little or no addi-
tional information beyond the observed p value [5], and thus this policy does not help matters much
either.
I am not attempting to single out these 14 papers as being of any more concern than any other work in
the field, rather they simply provide a revealing window on community standards at the highest level.
Neuroscientists seem willing to accept that work in the field generally uses low n values. Sometimes
this might be reasonable: for instance the effect size of the difference in phenotype between a wild-
type and knockout may be very large (though even in cases such as these power calculations are
rarely provided). Certainly many important findings have been robustly reproduced, even though
the statistical power of the original (or indeed subsequent) results was not established (e.g. [6]).
However, in many experiments the effects are subtle, and low n values and thus power mean that, on
average, reproducibility will be low.
This is a very difficult problem (which I hasten to add I am also struggling with in my own research).
Neuroscience experiments are often intrinsically long-term and low-throughput. For instance uncov-
ering the function of a disease-related gene in a mouse model, or studying the neural correlates of
consciousness in an awake behaving primate model, can require large resources and many years of
work to obtain a single main result. Many of the latest techniques are extremely technically challeng-
ing, and therefore (as alluded to in one of the statements above) a large proportion of experiments
fail. This can lead to a big mismatch between the n values at the start and end of the experiment. Funding is tight, and increasing n by even one animal for a particular experiment can have costly implications in time and money. Increasing ethical pressures on the use of animals in research (as alluded to above) add additional constraints on the n values that are practically achievable. However there is clearly also a cultural component to sample sizes in neuroscience: for instance work in organisms such as *C. elegans* and *Drosophila*, to which some of the above constraints are less applicable, also do not usually consider statistical power.

What can be done? Clearly better education for neuroscientists (at all levels) regarding statistical issues is important to address the lack of statistical scepticism that apparently plagues the field, and books such as [7] should be more widely read and understood (for instance many neuroscientists still appear to think that obtaining $p < 0.05$ means it is 95% likely they have discovered something true, no matter how small the n value [8]). From the perspective of a field such as statistical genetics, one solution seems obvious: neuroscientists should collaborate in larger teams and share data, so that many small and weakly powered results can be replaced with a few strongly powered results. However, while data sharing in general should and is being broadly encouraged, there are problems with this general model for the community of neuroscientists at large (for an interesting discussion see [9]). How would everyone agree what were the right experiments to do? How would cutting-edge and often highly non-trivial methodologies be standardized between labs? How would this model not be detrimental to the entreprenurial spirit that has fuelled so many important discoveries in neuroscience? The risk is that progress in neuroscience, where publication rates are already low compared to some other fields of biomedical science (for the reasons mentioned above), could be reduced to an unviable level.

Another approach is to replace the ubiquitous current statistical paradigm, of null hypothesis significance testing, with estimation [10]. This can be done by confidence intervals and/or Bayesian approaches. Now, instead of there being a ‘bright line of truth’ at an arbitrarily chosen probability threshold relating to the null hypothesis (which, after all, is not what one is actually interested in), the focus is on determining degrees of confidence in quantities such as the effect size and the difference between means. Binary statements about ‘significance’ versus ‘nonsignificance’ are replaced with graded confidence variations which are easier to interpret intuitively. However, this has yet to catch on in neuroscience.

Staying within the confines of null hypothesis significance testing, I have argued that neuroscientists seem willing so far to accept the current situation regarding (lack of) statistical power. Perhaps that is indeed the best that can presently be achieved, given the current statistical paradigm and practical constraints in the field. Perhaps we should just accept that most studies will be likely underpowered and reproducibility will likely be a recurring issue, at least until some more mature stage of development is reached. However if this is the case, it would be helpful if authors, reviewers and journal editors more clearly acknowledged that underpowered studies lead to weak and potentially irreproducible results.
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