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The importance of task design and behavioral control for understanding the neural basis of cognitive functions

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The success of systems neuroscience depends on the ability to forge quantitative links between neural activity and behavior. Traditionally, this process has benefited from the rigorous development and testing of hypotheses using tools derived from classical psychophysics and computational motor control. As our capacity for measuring neural activity improves, accompanied by powerful new analysis strategies, it seems prudent to remember what these traditional approaches have to offer. Here I present a perspective on the merits of principled task design and tight behavioral control, along with some words of caution about interpretation in unguided, large-scale neural recording studies. I argue that a judicious combination of new and old approaches is the best way to advance our understanding of higher brain function in health and disease.

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Introduction

It is an exciting time for systems and cognitive neuroscience. Methods for collecting and analyzing data are improving at a remarkable pace [1,2], and questions once limited to human and nonhuman primate studies are now being addressed in smaller animal models for which large-scale data collection and powerful circuit dissection techniques are more tractable [3••,4]. However, the pursuit of advanced technology and 'big data' should not come at the expense of well-defined hypotheses and rigorous behavioral control. For although we wish to understand the inner workings of the mind, we only have access to a coarse distillation thereof, namely behavior. The degree of insight attainable in an experiment is therefore limited not by how many neurons we record, but by the quality of the mapping we can create between internal states and behavioral reports.

The first part of this review describes some principles of task design that originate in the quantitative study of perception or movement, yet should prove useful for probing processes that lie squarely in between. The second part consists of a brief commentary on recent approaches in the literature that might benefit from such 'old fashioned' behavioral tools. My goal is not to suppress enthusiasm for new methods or to criticize any particular approach, but to encourage renewed emphasis on smart task design and careful quantification of behavior to help make the most of these advances.

What is meant by behavioral control, and why is it important?

If we want to understand how neural activity gives rise to our sensations, thoughts, memories, and decisions, we must come to grips with the fact that everything we know about such internal processes can only be inferred by observing external behavior. This is obviously true for animal models, but also applies in human subjects for whom introspection can be misleading and whose verbal reports are just another form of behavioral assay. Making things worse, this inference problem is ill posed: many internal states could lead to the same behavioral outcome.

So how do we make progress? The key is to constrain the space of possibilities as much as possible. Psychophysics does this by (a) carefully controlling sensory input, (b) measuring behavioral responses in a principled, quantitative fashion, and (c) accounting for response variability with an underlying statistical process, which then informs the search for neural mechanism. Similarly, research in computational motor control relies on monitoring the output of the system (i.e. eye or limb movements) with high resolution, and constructing normative models that explain the variability of behavior in terms of what is being optimized, and how [5–7]. In both cases, this kind of groundwork has been highly successful in advancing our understanding of sensory and motor processes. My contention is that the same degree of rigor will be needed to support inferences about the neural basis of cognitive functions.

Lessons from psychophysics

When vision scientists gained access to the physiology of visual neurons in the mid-20th century, there was great initial excitement but also caution [8,9]. Brindley [10] and Teller [11] developed the concept of a 'linking hypothesis' as way to formalize what one can and cannot conclude about how perception works based on properties of sensory neurons. This idea, together with the insights of Barlow

[12], Marr [9], and others, began to codify the brain–mind relationship in a way that emphasized testable predictions and an understanding of the computations the system must perform. The resulting synthesis included a recognition that strong interpretive statements about neurophysiology should be predicated on a robust characterization of behavior (e.g. psychophysics) and a mathematical framework that connects this behavior to a postulated internal state.

Several authors have recently articulated the basic principles of psychophysics as they pertain to neuroscience [3••,13••,14,15]. Here are a few considerations to keep in mind when designing a behavioral task, and especially when training animal subjects to perform it.

Account for errors

One of the most critical benchmarks is to ensure that subjects are working 'at threshold' or nearly so — that is, trained to asymptotic performance and fully engaged in the task. To illustrate this point, imagine we want to understand the stochastic process that leads to errors in a perceptual judgment. To do this we have to convince ourselves that the observed errors are not generated by a separate process, distinct from the one we wish to study. This is why, whenever possible, it is important to include multiple levels of difficulty that span the range from (near) perfect to chance performance, and to vary them randomly from trial to trial. If your subjects can perform near 100% correct on the easiest trials, even when they cannot predict trial difficulty in advance, you can rule out a large class of so-called 'lapses' — also termed guesses or random choices — for explaining behavior on more difficult trials.

It might seem like a maximum of 85–90% correct is sufficient, but consider that a lapse rate of 10–15% on a binary choice task — not uncommon in animal studies, particularly with rodents — implies that the subject is guessing on 20–30% of the trials (because half the guesses will be correct). Crucially, these trials are random from the experimenter's point of view and cannot simply be detected and removed. No scientist would tolerate a software glitch that covertly replaced a substantial fraction of their data with random numbers, yet this is essentially what a high lapse rate permits, at least in principle. Although sophisticated behavioral modeling [16] can isolate the contribution of lapses from other sources of variability, this only applies to probabilities over ensembles of trials. It does not prevent lapses from corrupting attempts to relate single-trial neural activity to behavior. It is worth noting here that rodents are capable of achieving very low lapse rates, at least in certain tasks [17•]. However, if high performance cannot be demonstrated, this may be a sign that the chosen species is not a good model for the task or process being studied.

In summary, experimenters should make every attempt to design tasks and training procedures such that subjects are capable of near-perfect performance on the easiest conditions, even though most analyses ought to focus on the difficult ones.[1] Along with selecting an appropriate task structure (e.g. 2-alternative forced choice) [3••,18] and normative modeling framework, this strategy will facilitate an accounting of how different types of errors arise. This issue seems particularly important for interpreting large-scale, exploratory studies, which may be more likely to zero in on features of neural activity that end up being red herrings due to uncontrolled behavioral variables.

Care about time

Time is fundamental to cognition, not only in the explicit way in which it supports abilities like learning and prediction, but more generally for structuring and regulating internal processes. The real world is not partitioned into discrete trials [13••], so the brain has evolved to implement rules for terminating or switching between processes in the absence of external cues. In many cases, simply measuring the time it takes subjects to respond can be a powerful constraint for models of the internal process governing behavior [19–21]. Most importantly for the present topic, response-time (RT) tasks [22,23] are often the best way to identify the relevant time window(s) for analysis of neural data.

For example, many types of decisions involve the accumulation of evidence up to a threshold, or bound [24]. To study this process and its neural correlates it is essential to demonstrate behaviorally that the subject is indeed accumulating evidence. With well-trained subjects and an appropriate balance between reward and punishment (e.g. to discourage fast guessing), a choice-RT design allows the experimenter to analyze neural data restricted to the epoch of decision formation, barring sensory and motor delays.

In cases where RT measurements are not attainable or inappropriate for the task, other temporal constraints can be quite useful. One approach is to 'compel' subjects to initiate the motor response at a specific time [25], even — remarkably — before the sensory information for the decision becomes available [26]. These designs help to isolate the decision process from motor preparation and other variables such as the speed-accuracy trade-off. Alternatively, one can embrace this trade-off and simply vary the stimulus duration, using accuracy as a function of time to infer the presence of a bound and to estimate the time window of accumulation [27,28]. To promote engagement and discourage procrastination, it is often advisable to draw durations from a distribution with an early peak and a long

[1] Indeed concentrating the bulk of trials on difficult conditions (e.g., varying discriminability on a logarithmic scale) can be an effective way to ensure sufficient behavioral variability for testing models of the underlying process. This strategy also maximizes one's sensitivity for detecting differences between conditions — or effects of causal manipulations — that may be subtle but nonetheless provide key insights.