Trends in Neurosciences

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Forum

The tricky business of defining brain functions

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Neuroscience has a long history of investigating the neural correlates of brain functions. One example is fear, which has been studied intensely in a variety of species. In parallel, unease about definitions of brain functions has existed for over 100 years. Because the translational impact of basic research hinges on how we define these functions, these definitions should be carefully considered.

Basic brain research has a multitude of goals, including establishing the foundational knowledge required to develop new treatments for brain dysfunction. Many neuroscience researchers apply the reasonable strategy of investigating how the healthy brain supports functions that have presumed clinical relevance, such as perception, attention, memory, pain, reward, and emotion. But given that what we understand about the brain hinges on what we look for, how should these functions be defined?

In the late 1950s, George Mandler and William Kessen noted that scientific concepts are often rooted in common sense and that this is especially problematic in psychology [1]. These common-sense (folk psychological) accounts of mind and behavior were central to Darwin's folk psychological theory of emotional inheritance in the 19th century. He viewed emotions as states of mind passed on to humans from mammalian ancestors. According to this account, fleeing or freezing in the face of danger, for example, was caused by the mental state of fear.

Unease about folk psychological definitions of psychological concepts was on the rise in the early 20th century. This contributed to the introduction of behaviorism, which imposed a strict ban on all talk of mental states, opting instead to emphasize the functional relationship between stimuli and responses, absent all reference to internal factors. But although behaviorists got rid of mental states, they retained mental state terms. For example, fear was used to describe the relationship between threatening stimuli and defensive responses. By the 1960s, behaviorism was largely falling out of favor. In part, this was because cognitive psychology was offering a viable approach to understanding how humans think as well as behave. But with the 'mental' element back, folk psychological concepts re-emerged, often labeled as 'brain functions', and they remain popular today in both psychology and neuroscience, despite continuing to be problematic.

What is the problem, exactly? After all, physicists, chemists, and cell biologists sometimes label their phenomena with common terms, often without concern. For example, biologists call a family of genes 'hedgehog' because mutations in those genes can lead to fly embryos that vaguely resemble microscopic versions of adult hedgehogs, but no one in biology believes the gene has anything to do with the animal called 'hedgehog'. The problem lies in the fact that when psychologists use a mental state word from vernacular language, the assumption is that the subject matter is the everyday experiences of the mental state; for example, that 'fear' refers to the feeling that occurs in a situation where one is in harm's way. In turn, when neuroscientists label brain circuits with mental state terms such as 'fear', those circuits are implicitly assumed to be responsible for causing that mental state, regardless of the strength of the evidence supporting a causal relationship.

Considerable evidence suggests that circuits involving the amygdala control behavioral and physiological responses to threats [2]. In animal research labs, threats are often recapitulated by pairing a tone with an aversive stimulus such as a weak shock to elicit 'fear-related behaviors' such as freezing upon hearing the tone again. The neural circuits that learn the association between the tone and shock and produce freezing behavior are among the best understood in the brain [3]. The problem lies in labeling these circuits with the term 'fear', because it presumes that the threat elicits a mental state, a subjective experience, of fear that is caused by activity in the amygdala. However, mounting evidence suggests that the amygdala is not required for the mental state of fear [4,5]. Instead, the mental state of fear crucially depends, at least in part, on cortical circuits that interpret or conceptualize what is occurring in the social and physical environment and in one's body [2,5,6]. In this framework, amygdala circuits control nonconscious defense behaviors (such as freezing) as opposed to conscious experience. Should this framework be correct, the extensive ongoing efforts devoted to targeting amygdala circuits and rodent behaviors such as freezing and avoidance are unlikely to provide a direct route to treatments for human fear and anxiety disorders. These lines of research can help, but not without recognizing the centrality of subjective experience.

Broadly, neuroscientists often have a sense of the brain function that they want to measure (e.g., 'attention' or 'self-regulation' or 'mood') coupled with a multitude of ideas about how to go about it. How should they go about defining and measuring that function? Here we offer three suggestions.

First and foremost, for the reasons described above, neuroscientists should

avoid conflating circuits that control behavior with mental states, especially in the absence of evidence that the two map onto one another. These equivalencies need to be very carefully investigated rather than presumed.

Second, it has to be acknowledged that defining brain functions in an impactful way is not trivial and that it amounts to figuring out how to measure something that we often do not yet fully understand. One implication of this is that we are unlikely to get it right from the outset and that we must allow for the continuous evolution of our definitions of brain functions, as well as our measurements of them. In this, some researchers are drawing inspiration from historical accounts of the development of thermometry and measuring temperature in the 17th century via 'epistemic iteration' [7]. When applied to the brain, definitions of function and dysfunction (such as mood and depression) and measurements of these functions are tied to theories about how they work, and both measurements and theories are continuously refined as new information is acquired. This approach can be contrasted with the desire to lock in and preserve definitions of brain function and dysfunction for historical comparability (e.g., in the case of depression, the most widely used measurements today were developed in the 1960s, despite being problematic [7]).

Third, more work needs to be done in neuroscience regarding the issue of 'ontology' and the principles that are used to define brain functions [8]. One seemingly obvious approach is to define brain functions based on behaviors that group together empirically. However, a multitude of ways to do this have been proposed, including grouping via analyses of a large number of behavioral measures (e.g., [9]), or their neural correlates (e.g., [10]), or via comparisons across species (e.g., [11]). In addition, some have argued that grouping similar but diverse behaviors into a unitary concept can be misleading and unproductive, at least in some cases, such as with 'attention' [12]. Neuroscientists needs to work toward more consensus regarding how to define brain functions.

Some have argued that as neuroscience becomes more sophisticated, folk psychology will simply disappear. For others, however, concepts from folk psychology are the basis of understanding our own minds and the minds of others. The challenge being faced, we would argue, is not necessarily how to get rid of folk psychology concepts and terminology, but to set ground rules for when folk psychological explanations are useful and when they are not. For starters, in humans, behaviors that are correlated with a certain mental state, such as fear, should not be assumed to be caused by that mental state in the absence of evidence that this is the case. Accordingly, when the evidence is lacking in humans, analogy with human behavior should not be called upon to explain similar behaviors in non-human organisms. Even if the evidence is present in humans, one should be cautious in claiming that the human-like mental state underlies the behavior in non-human animals.

So much depends on how scientists conceptualize the problems they work on. Observations lead to interpretations. Interpretations become concepts. And concepts may become dogmas that feel so intuitive, so natural, that they are accepted without question. We should, from time to time, re-evaluate the core beliefs of our fields of study.

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