Fear avoidance and neuroimaging: Falsification or just failure to confirm?

I am visiting Chicago for the first time and see three blue taxis. Based on these observations I hypothesise that all Chicago cabs are blue. Karl Popper [5] argued that this type of inductive inference (in which a general rule is derived from a set of observations) cannot be the basis for building a rigorous scientific theory. No number of confirmatory blue taxi sightings would prove my hypothesis true. Popper instead argued for a deductive approach where a prediction is derived from the theory and investigators seek data to falsify the prediction. Thus, the most rigorous way to test my hypothesis would be to look for Chicago cabs that are not blue, rather than simply counting blue taxis.

While this framework for testing theories has been widely accepted, inductive approaches remain an important tool for generating hypotheses (after all, I wouldn’t have a hypothesis if I hadn’t first observed blue cabs). Inductive approaches are particularly common in neuroimaging research where theories of complex brain processes are largely based on accumulation of confirmatory evidence. However, strengthening these theories through falsification is challenging. Predictions about the expected locations of activation in brain imaging studies are often too vague to be realistically falsifiable. (e.g. “we predicted activation in pain modulation regions”). Alternately, hypotheses are so close to the ultimate findings that one suspects they were formed post-hoc. It is difficult to publish negative findings so there is an understandable tendency to weaken theoretical frameworks to make studies appear confirmatory. This harms efforts to build theories that are specific and readily falsifiable. It is therefore encouraging to see neuroimaging studies make specific predictions and present results that do not confirm those predictions, as is the case in the paper by Barke et al. in this issue of PAIN [1].

Barke et al. examined a key tenet of the fear-avoidance model of pain [3], namely that exaggerated fear of pain drives maladaptive avoidance behaviours. Although measures of “fear of pain” predict disability, reduced physical performance and increased attention to pain, there has been debate about the precise contribution of fear in the model [2,7]. Thus, Barke and colleagues’ investigation is timely and topical.

At first glance, their findings suggest that fear is not the motivating force underlying avoidant behaviour. The authors tested 2 groups of low back pain patients (high and low avoidance), as well as healthy controls and individuals with spider phobia. Functional MRI data were collected while subjects viewed images depicting potentially painful movements. High avoidance pain patients did not show increased activation (compared to neutral slides) in presumptive “fear regions” (amygdala, insula, anterior cingulate etc.). Importantly, high avoidance patients’ neural responses (aversive > neutral movements) did not differ from low avoidance patients or healthy controls. These findings were in stark contrast with the robust activations observed in “fear regions” when avoidant patients viewed general fear-related slides or when spider phobics viewed pictures of spiders. Based on their findings the authors suggest “the concept of fear of movement as postulated in the model is not really a fearful emotional state”.

Evaluating the implications of this study for the fear avoidance model requires a differentiation between “failure to confirm” and falsification. To demonstrate this distinction, we return to our taxi-cab analogy: a yellow cab would fail to confirm my hypothesis, but would only falsify it if I were still in Chicago. Barke and colleagues hypothesise that fear-avoidant patients would show increased activation in fear regions. The study fails to confirm this hypothesis. But do the methods employed allow for inferences about whether the fear component of the model is false?

An initial question is whether neuroimaging is an appropriate tool for inferring the presence (or absence) of fear. As noted by Poldrack [4] and others, inferring a particular psychological state from imaging data relies on reverse inference (e.g. “pain elicits response in the insula, task X elicits activation in the insula, therefore task X is painful”). As reverse inference relies on a logical fallacy (“affirming the consequent”) it cannot be used as the basis of strong deductive conclusions. Nevertheless, reverse inference is widely used to generate new hypotheses and research questions (e.g. “Is task X painful? What components does it share with pain?”). The limitations of reverse inference-based arguments need to be recognised, however. The probability of a reverse inference being true is a function of the degree to which the region of interest is exclusively activated by the proposed psychological state (i.e. “insula only activated by pain?”) [4]. In the context of the Barke paper, we might ask how specific the regions (e.g. insula, anterior cingulate and amygdala) are to the construct being tested (fear). In fact, these regions are not specific to fear but rather are associated with numerous cognitive and affective states [6,8]. Thus, while lack of activation in these regions might suggest that fear was not elicited, such findings could be used as evidence against any number of other motivationally relevant states. This, in turn, leads to questions about the salience of the task and its validity as a test of the fear avoidance model.

The fear avoidance model suggests that fear of experiencing pain motivates avoidant behaviour. To examine neural mechanisms consistent with this hypothesis, the task would have to evoke fear of experiencing pain. Would viewing slides of other individuals performing movements do this? In fact, fear of movement may have been mitigated by the restricted range of movement available to patients while lying in the scanner.

Alternately, to demonstrate that the motivation for avoidant behaviour is a psychological state other than fear, it would be necessary to generate a state capable of motivating avoidant
behaviour. While highly avoidant patients rated the slides as more negative and more arousing than healthy controls did (but notably, not higher than low avoidant pain patients did), this finding doesn’t validate the task as a test of the model. Was this unspecified affective state the same as the motivational state underlying avoidant behaviours? Was it elicited powerfully enough to motivate such behaviours? Without answers to these questions, drawing inferences from these data about the relationship between fear and avoidant behaviour does not seem warranted. Such inferences might be stronger if self-reported affective responses to this slide set predicted the same abnormal cognitive and behavioural responses as do fear of pain measures [2,7].

The study fails to confirm the authors’ initial hypothesis (that high-avoidance subjects would show increased activation in fear regions), but does it represent falsification of the fear component of the fear avoidance model? To their credit, Barke and colleagues thoroughly discuss alternative explanations of their data. Nevertheless, they conclude by suggesting that their findings call the fear component of the model into question. Before accepting such a conclusion, we urge readers to consider the validity of this experimental task as a test of the fear avoidance model, as well as the deductive limitations of reverse inference.

**Conflict of interest statement**

The authors declare no conflict of interest.

**References**


