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“Well, I wouldn’t start from here”

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Some 30 years ago Barron and Kenny [1] published an article on mediation in psychological studies, illustrating how to test for mediation using a sequence of multiple regression routines. This statistical tool is useful for exploring two big themes in pain: (1) what are the mechanisms involved in the development of chronic pain, and (2) what are the mechanisms of change in treatment [5]. Although the concept of mediation was already established, Barron and Kenny's article made it particularly accessible. The appeal of the article [1] lies perhaps in the apparent simplicity of a logic that could be captured in simple diagrams and a set of analytic skills apparently well within the reach of non-statisticians.

In this issue of PAIN, Lee and colleagues [6] review the available data on possible psychosocial mediators between pain and disability. The novelty of their study is that they explicitly identified only studies that had used Barron and Kenny's methods, combining the observed regression coefficients in a series of meta-analyses. If we had firm evidence of mediation – the identification of specific causal mechanisms through robust repeated observations – it would indicate potential targets for interventions to prevent the development of chronicity and thereby alleviate considerable suffering.

Lee et al. retrieved data from 12 studies that reported a total of 36 mediator analyses. 3 tested a superseded version of the fear-avoidance hypothesis (catastrophizing → fear → disability) [3; 8], anomalous in relation to the main purpose of the study and not further discussed here. The 33 remaining analyses tested some variant of the pain → mediator → disability relationship. The identified mediators were fear (mainly measured as fear of movement), catastrophizing, distress and self-efficacy. Pain was mainly measured with single item unidimensional scales of intensity, and disability with multi-item checklists or the general perception of disability. (Readers should consult Table 1 of [6] for details of measures.) Marked heterogeneity of measures in this field is common. This can either be viewed as problematic

or, when repeated analyses of the same construct via different indicators confirm the relationship, as a testimony to the robustness of the constructs being assessed.

Of the 36 analyses included in the meta-analysis, 22 of them used cross-sectional data where the observations of pain, mediator and disability, were obtained at a single time point. Under these conditions a mediation analysis can tell us nothing about a likely causal relationship between the mediator and disability. At best it can confirm that the addition of the proposed mediator adds to the statistical prediction of disability.

What of the remaining 14 studies reporting longitudinal data? As a minimum criterion for the detection of a causal relationship measurement of the mediator should occur after the measurement of pain and precede the measurement of disability: three observation time points are needed. Furthermore, each link – pain → mediator and mediator → disability – should have a plausible explanation of how the mechanism operates, and should distinguish between this causal hypothesis and plausible rival hypotheses including third variable confounds, method variance and regression artefacts [2]. What is apparent from Table 1 in Lee et al. is just how few source studies appear to have met these criteria.

One key issue is the measurement of change in the mediator. Knowing that the levels of predictor, mediator and outcome correlate is not sufficient. For causal mediation, change in the mediator should statistically predict change in the outcome. Lee et al. captured these conditions in their quality assessment, and Table 3 clearly shows that none of the studies met these change criteria, and only 3 actively examined confounding variables.

So what have we learned from this meta-analysis? First, although we have some reasonable conjectures about what psychosocial factors might be invoked as mediators of disability, strong evidence for them is not available. This may not be unusual; a similar conclusion can be drawn about mediators

of change in psychological treatments as a whole [5]. Second, critical appraisal of the available studies indicates where we need to focus future research efforts. Current theoretical modelling of mediation has developed beyond Barron and Kenny's original conception [4; 7] and the statistical modeling of mediation is considerably more sophisticated. Building plausible conceptual models of mediation to be tested by observation is a non-trivial effort, and more attention to recent reformulation of the fear and avoidance model [3] would have strengthened the conceptual basis of the paper. Neither is collecting repeated data from cohorts of sufficient size an easy task. Particular challenges are the identification and explication of the relevant construct and the development of measures that are free from criterion contamination. For example, the measure of self-efficacy (surely a plausible mediator) used in the current set of studies is probably contaminated, as the items refer to behavior also sampled by the disability construct.

We are reminded of the apocryphal tale of the city dweller lost in the country who asks a local countryman for directions. The countryman pauses, strokes his beard, narrows his eyes and replies 'Well, if I were you, I wouldn't start from here.' Like the city dweller we do not have that option but Lee et al have at least shown us what needs doing.

Conflict of interest

The authors declare no conflicts of interest.

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