

Building and testing coherent models of treatment: commentary on Garland

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Garland's topical review, presenting a mindfulness intervention to address chronic pain and opioid misuse [8], is an unusually detailed and well-integrated account of mechanisms and treatment components to address them, supported by neuroimaging and other evidence that those components act on intended targets. Too many treatment packages have serious disjunctions between motivations for treatment, methods used, and outcomes by which methods are evaluated. Mechanisms of change of treatment components are often described in broad terms, and additivity or synergy with other components assumed. Here the focus is on improving motivation for reward and responsiveness to reward, blunted by both chronic pain and opioid use.

Despite the terminology of mechanisms, intended targets and methods are expressed in human terms, with discussion of 'cultivating' positive emotions and experiences. Positive experience, or enjoyment of life, was the highest rated outcome in a large sample of people with chronic pain [21] but is generally rarely assessed. Patients often describe refraining from

activities of which they are physically capable because pleasure and satisfaction in those activities has been eroded by pain or by the sense of imminent threat of worse pain.

So how do psychologically-informed therapies “modulate reward system function”? Garland outlines three main processes in the package he designed and promotes: focusing on pleasant experiences, including somatic ones (“savoring”); limiting pain by promoting pleasant internal states; and cultivating meaning and self-transcendence by disrupting cognitive biases. He draws on familiar mechanisms in pain, such as operant learning [13], attention-grabbing [6], and interoceptive attention [7]. Other connections could be made with: cognitive exposure [16]; self-compassion [18]; solution-focused therapy [5]; and various elements of CBT and ACT [10,12].

In particular, cultivating meaning and self-transcendence could be framed in other terms. Although they may be intended *outcomes* of Buddhism-inspired mindfulness practice [3], Garland recognizes that many mindfulness practitioners encourage a *non-judgmental* approach to noticing (and in ACT, defusing from) their thoughts. This is held to be incompatible with reappraisal of thoughts, however positively [2,4]. By contrast, reappraisal is central in CBT, challenging assumptions and biases in thinking and thereby reducing threat [11].

The focus on positive aspects (rarely addressed in opioid users, given the hedonistic myths still associated with use) may be particularly welcome to patients, who often find problem-focused discussion depressing, providing little motivation to make it a habit. Garland identifies ways to strike the balance between avoiding tackling difficult aspects of life and

recognizing strengths and resources; and between seeking pleasant experiences and presenting trivial or culturally unfamiliar ‘natural rewards’.

Garland’s meta-analysis of ‘mind-body therapies’ [9] shows that several psychological therapies reduce pain and opioid use. As with many other psychological therapies, some mechanisms are well established and demonstrable in other mammals, such as attention and learning mechanisms; others are more abstract processes that require a homunculus controlling the brain to make decisions. “One of the most challenging problems facing cognitive psychology and cognitive neuroscience is to explain how mental processes are voluntarily controlled, allowing the computational resources of the brain to be selected flexibly and deployed to achieve changing goals” [14]. For a state of mindfulness to occur, the homunculus may need to direct attention away from anxious rumination, purposefully, to the present moment. Unfortunately, many people with pain find this hard to voluntarily sustain. Further, many such processes are assessed by asking people to report cognitive contents and processes, some of which are inaccessible to subjective experience. Figure 1 [8] is therefore speculative, and for reasons of complexity and of incapacity to report mental processes, hard to test.

Garland rightly points out that we do not know how other effective therapies work. Additive studies or dismantling studies that attempt to address the challenges above are rarely sufficiently powered to detect small differences. Meta-analysis of psychological treatments consistently shows that putative critical therapeutic ingredients are not responsible for therapeutic benefits [1]. Not only are separate elements of interventions interrelated, conceptually or pragmatically [17], but different participants interact differently with

particular treatment elements, or similarly with different elements, confounding the linkage of conditions to outcomes [15,20].

Rather than seek the perfect combination of elements, we should provide effective, coherent, evidence-based methods that can promote change (see also [9]), that make sense to the person with pain, and apply to her or his problems. We also need to widen the focus from presumed deficits in the individual to changes in her or his social systems, and to socioeconomic and cultural changes. The quest for the perfect program or treatment package is seductive, assuming that more (treatment) is always better (more effective), and/or that the patient (or her or his homunculus) will somehow choose from the mixture the elements that best suit. It has generated many – too many – treatment packages that differ little, are tested as randomized controlled trials, with all the effort they demand from all participants, and become the material for systematic reviews or meta-analyses that identify disappointingly small effect sizes [15].

A novel extension of meta-analysis, Qualitative Comparative Analysis [19], tries to identify necessary and sufficient components of treatment for each outcome of interest. Boolean algebra is applied to all examples of every possible combination of treatment elements, with their outcomes, to derive logical implications that describe the causal relationships between variables and outcomes. Our experiments with this method applied to chronic pain treatment components has identified some essential components, but also some counterproductive combinations, highlighting the risks of assuming additivity.

We certainly need new ways to understand existing and novel treatments. Garland provides in Table 1 some essential leads to follow: a focus on the dynamics and processes of change,

with better control for nonspecific therapeutic aspects of treatment; investigating trajectories of change short and long term; wider use of direct measures of behavior; and exploring pleasure as a mediator of treatment effectiveness. Rather than continuing the hunt for the perfect treatment package, following these suggestions (and others), and using novel approaches to meta-analysis, could help researchers better model the effects of and interactions between treatment components.

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