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Bridging the gap: Lessons we have learnt from the merging of psychology and psychiatry for the optimisation of treatments for emotional disorders

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ABSTRACT

In recent years the gap between psychological and psychiatric research and practice has lessened. In turn, greater attention has been paid toward how psychological and pharmacological treatments interact. Unfortunately, the majority of research has indicated no additive effect of anxiolytics and antidepressants when combined with psychological treatments, and in many cases pharmacological treatments attenuate the effectiveness of psychological treatments. However, as psychology and psychiatry have come closer together, research has started to investigate the neural and molecular mechanisms underlying psychological treatments. Such research has utilised preclinical models of psychological treatments, such as fear extinction, in both rodents and humans to determine multiple neural and molecular changes that may be responsible for the long-term cognitive and behavioural changes that psychological treatments induce. Currently, researchers are attempting to identify pharmacological agents that directly augment these neural/molecular changes, and which may be more effective adjuncts to psychological treatments than traditional anxiolytics and antidepressants. In this review we describe the research that has led to this new wave of thinking about combined psychological/pharmacological treatments. We also argue that an increased emphasis on identifying individual difference factors that predict the effectiveness of pharmacological adjuncts is critical in facilitating the translation of this preclinical research into clinical practice.

Psychology and Psychiatry have traditionally operated in parallel, with too little communication between the disciplines. In particular, the two disciplines have vastly different approaches to the treatment of mental illness, with Psychiatrists mainly utilising pharmacological/physiological interventions and Psychologists mainly utilising skills-based interventions that directly alter cognitions and behaviours. In addition, researchers within these disciplines have taken a "silo" approach, which has led to the development of very different theoretical viewpoints on the critical mechanisms underlying mental illness, with little attempt to reconcile the two. Specifically, Psychiatrists have typically emphasised the importance of neurotransmitter and neural circuitry dysfunction whereas Psychologists have focused on the role of maladaptive cognitive biases and behavioural patterns. In more recent years, however, the gap between Psychology and Psychiatry, both in terms of research and clinical practice, has started to be bridged. This has in part been brought about by a much more refined understanding of the neural and molecular basis of mental illness that has allowed specific cognitive and behavioural deficits to be mapped onto specific aberrations in neural functioning. This has also been fostered by an increased recognition that psychological treatments may directly or indirectly attenuate the molecular/neural abnormalities thought to underlie mental illness.

One consequence of the increased communication between the disciplines is that greater attention has been paid to how psychological and pharmacological treatments interact. From this, we have gained two broad insights. The first is that pharmacotherapy does not always complement psychological treatment (i.e., many studies show no additive effects) and in the worst of cases, pharmacotherapy may attenuate the efficacy of psychological treatment. The second insight is that if we can increase our understanding of how psychological treatments work at the neural and molecular levels, then this may pave the way for the development of novel pharmacological adjuncts that directly augment these neural/molecular processes, thus creating a more potent treatment for mental illness.

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In this review we first outline the transdiagnostic components of the most widely used and empirically validated psychological treatment for emotional (i.e., mood and anxiety) disorders, cognitive behavioural therapy (CBT). We then describe research from animal models and human neuroimaging studies that has identified several molecular and neural targets that likely underpin the success of CBT. Next, we describe the outcomes of research examining the efficacy of combining current pharmacotherapies with CBT, and we account for these outcomes by considering how the neural/molecular targets of pharmacotherapy complement/interfere with the putative neural/molecular underpinnings of CBT. Finally, we describe a burgeoning field of research that is attempting to bridge the gap between pharmacological and psychological approaches to treatment. This field is capitalising on our increased understanding of the neural/molecular substrates of psychological treatments, and attempting to identify potential pharmacological adjuncts that may enhance these substrates. Moreover, beyond merely developing adjuncts to enhance CBT, emerging research in this field is also attempting to identify various individual difference factors that may increase or decrease the effectiveness of such adjuncts. This type of research has the potential to increase our ability to predict treatment responsiveness, which would allow health professionals to tailor treatments at the outset to match the idiosyncrasies of the individual, thus increasing the number of people who benefit from treatment.

Cognitive behavioural therapy for emotional disorders

CBT rests on the assumption that most symptoms in emotional disorders are experienced by most people from time to time, but that, due to maladaptive response tendencies, some people become "stuck" in a cycle in which they experience these symptoms with a greater severity, intensity, and/or frequency than people in the general population (Beck, 1976). Consistent with this assumption, CBT does not attempt to address the cause of distressing symptoms; or indeed, the symptoms themselves. Rather, CBT purports to target the hypothesised cognitive and behavioural factors that maintain distressing symptoms (i.e., those factors that prevent symptoms from spontaneously remitting, as occurs in the general population; Clark, 2004). These factors include maladaptive cognitive appraisals (e.g., overestimation of the probability and cost of catastrophic outcomes in anxiety disorders, Otto, Smits, & Reese, 2004; or negative views about the self, the world, and the future in depression, Beck, 1976), unhelpful behavioural responses to strong emotions (e.g., withdrawal in depression, Jacobson, Martell, & Dimidjian, 2001), and emotional/experiential avoidance (e.g., avoidance of feared stimuli/situations in anxiety, Otto et al., 2004). CBT stands in contrast to the psychiatric approach to treatment of psychopathology with latter placing much more emphasis on direct modulation of the symptoms themselves, usually via pharmacological intervention.

CBT is predominantly skills focused; patients are taught new ways of thinking, responding, and problem solving. Initially patients rely heavily on guidance from the therapist, but as cognitive flexibility improves, patients become more independent, ultimately becoming their own "therapist". As such, CBT depends on patients being able to integrate and consolidate new information-in other words, to learn and retain new memories (Otto et al., 2004). This may account for CBT's long-lasting effects, as well as the finding that recipients of CBT often exhibit continued improvement even once treatment has officially terminated (e.g., Haug et al., 2003; Marks et al., 1993).

The initial development of CBT protocols was directed toward discrete disorders. This resulted in a plethora of manualised treatments, each purporting to target the individual features of a specific diagnosis. In the last decade, however, there has been a shift toward a transdiagnostic approach to CBT, spurred by epidemiological data highlighting strong comorbidity between different diagnoses, the finding that CBT aimed at one diagnosis often leads to symptom reduction associated with comorbid diagnoses, and the growing contention that there may be common mechanisms of dysfunction across different diagnoses (Barlow, Allen, & Choate, 2004). Currently, many researchers are attempting to extract the underlying principles of CBT that may be effective when applied transdiagnostically. Indeed, such principles may represent the critical components underlying the efficacy of earlier CBT protocols aimed at specific disorders. The most influential transdiagnostic CBT protocol has been Barlow's "Unified Protocol" (UP) for emotional disorders (Ellard, Fairholme, Boisseau, Farchione, & Barlow, 2010). UP contains a number of core modules designed to target the main factors thought to underlie and maintain emotional disorders, described above. For example, maladaptive cognitive appraisals are targeted by cognitive reappraisal training (i.e., learning to re-evaluate a situation in a more positive, or at least neutral, manner so that the emotional consequence is altered). Maladaptive emotion-driven behaviours are targeted by modules designed to train more adaptive behavioural responses to strong emotions (e.g., engagement in activities when feeling depressed), and emotional/experiential avoidance is targeted by exposure therapy modules that encourage gradual engagement with previously avoided emotions, situations, and physical sensations.

A thorough critique of the advantages versus disadvantages of transdiagnostic CBT is beyond the scope of this review; we describe UP here merely because it highlights the common components of CBT that have been empirically demonstrated to be effective in the treatment of emotional disorders. More pertinent to the purposes of this review is that transdiagnostic approaches to CBT may aid research at the preclinical level. This is because treatments that are composed of distilled common principles (and that are designed to target common underlying mechanisms of dysfunction, rather than specific symptoms characteristic of discrete disorders) are more amenable to being modelled in laboratory settings. Preclinical research in both non-human animals and healthy humans has the capacity to increase our understanding of the neural and molecular substrates of mental illness, the neural and molecular substrates underlying effective treatment, and the individual difference factors that predict treatment response (Graham, Langton, & Richardson, 2011; Holmes & Singewald, 2013). Such understanding will allow us to further refine our treatment of emotional disorders by developing pharmacological adjuncts to augment the neural/molecular processes underlying CBT, and to make more informed decisions about which treatments and adjuncts will work best for particular individuals. The methods by which emotional disorders and their treatment have been modelled preclinically, and the utility of this approach, are reviewed next.

Preclinical models of emotional disorders and their treatment

Animal models of fear learning and fear inhibition, as well as more recent neuroimaging studies examining the same processes in humans, have been instrumental in our understanding of the neural and molecular basis of CBT's long-term effectiveness. In both rodent and human studies, fear learning occurs when a subject is given multiple pairings of an initially neutral stimulus such as a light (i.e., the conditioned stimulus; CS) followed by an aversive outcome such as a loud noise or shock (i.e., the unconditioned stimulus; US). Following such pairings the subject eventually learns that the CS predicts the US and begins to show a variety of conditioned fear behaviours to that CS (e.g., increased skin conductance response (SCR) in humans and freezing in rodents). After fear

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