The validity of laboratory-based treatment research: Bridging the gap between fear extinction and exposure treatment

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ABSTRACT

A major objective of experimental psychopathology research is to improve clinical practice via the experimental study of treatment mechanisms. The success of this endeavor depends on the external validity of the procedures used to model the treatment component in the laboratory. We propose a general framework and a set of specific criteria that will allow evaluating whether a certain laboratory procedure is a valid model for a certain clinical treatment. We illustrate this framework by evaluating the validity of extinction as a laboratory model for clinical exposure therapy. Although we acknowledge the merits of the extinction model, we argue that its validity might not be as firmly established as the research community assumes. We also use extinction as an example to demonstrate how considerations of the proposed criteria can stimulate further improvements to existing models of treatment. We conclude that the systematic assessment of external validity of treatment models is an important step towards bridging the gap between science and practice in the field of experimental psychopathology.

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Experimental psychopathologists study the causal factors of pathological behavior under highly controlled conditions. According to Kimmel (1971), experimental psychopathology (EP) can be approached as both "the experimental study of pathological behavior" and "the study of experimental pathological behavior" (p. 7, see also Forsyth & Zvolensky, 2002; Zvolensky, Forsyth, & Johnson, 2013). The former approach concerns the experimental study of (factors that influence) pre-existing pathological behavior in clinical or subclinical subjects. In the latter approach of EP, 'pathological behavior' is experimentally induced in healthy (animal or human) subjects. A prerequisite for research in healthy subjects is a laboratory model of the pathological behavior: a set of behavioral, pharmacological, genetic or surgical manipulations that result in behavior that is similar to the pathological behavior. Pavlov (1927), to give an early behavioral example, produced behavior similar to neurosis by presenting his dogs with ambiguous stimuli. In a first phase of a relatively easy discrimination task, a circle but not an ellipse was presented together with food. Subsequent presentation with a stimulus somewhere in between a circle and an ellipse resulted in symptoms characteristic of neurosis. An example of a genetic manipulation is the cannabinoid receptor gene knockout mouse that exhibits behavioral changes that are similar to symptoms of schizophrenia (Fritzsche, 2001). Once the prerequisite of having a laboratory model of the pathological behavior is met, a plethora of research questions can be investigated (e.g., about individual differences or about the environmental factors that exacerbate such behavior; Vervliet & Raes, 2013), and hence a better understanding of this behavior can be attained.

However, the ultimate aim of experimental psychopathologists is not to merely understand, but also to reduce pathological behavior. Despite a great amount of EP research, there are still opportunities for the further enhancement of clinical treatments. Only about half of the patients experience a full remission or respond to psychological treatment in a clinically meaningful way (Holmes, Craske, & Graybiel, 2014). Moreover, an important subgroup of patients fails to maintain the effects of treatment in the long term and experiences relapse (e.g., Lipsitz, Mannuzza, Klein, Ross, & Fyer, 1999; Steinert, Hofmann, Kruse, & Leichsenring, 2014).

A straightforward factor that might add to the continued development of clinical treatment is more interaction between scientists and clinicians (e.g., Barlow, 1981; Berke, Rozell, Hogan,

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Norcross, & Karpiak, 2011). In line with this, evidence-based strategies to disseminate and implement evidence-based interventions have recently started to develop (McHugh & Barlow, 2010). In addition to enhancing communication, investing in the external validity of treatment models provides an opportunity to further improve clinical treatment. In laboratory research, complex psychological treatments are reduced to the putative core mechanisms (e.g., Van den Hout, 1999). Such reduction contributes to the internal validity of the model: by providing control over confounding variables, reliable causal inferences can be made (Van den Hout, Engelhard, & McNally, 2016). This is indeed considered one of the major strengths of EP research. Also, from a pragmatic point of view, it is more cost-effective and less time consuming to first test hypotheses in healthy volunteers using a basic treatment model before testing them in clinical trials. The question is, however, whether findings obtained with these simplified treatment models are still informative for clinical practice. In the present paper, we propose a general framework to answer this question. In particular, we discuss three criteria that have long been outlined in pharmacological research and have recently been used to evaluate the external validity of experimental models for psychopathology: face validity, construct validity and predictive validity (e.g., Abramson & Seligman, 1977; Boddez et al., 2013; Luyten, Vansteenwegen, van Kuyck, Gabriels, & Nuttin, 2011; Vervliet & Raes, 2013). To the best of our knowledge, this is the first time that these validity criteria are applied to a psychological treatment model. We illustrate this framework by evaluating the validity of extinction as a treatment model for clinical exposure therapy.

Fear extinction is seen as one of the most successful treatment models in the history of EP (Vervliet, Craske, & Hermans, 2013). Its laboratory procedure entails unreinforced presentations of the conditioned stimulus (CS; e.g., geometrical shape), resulting in a decrease in the fear responses that were previously established by pairing the CS with an aversive (unconditioned) stimulus (US; e.g., electrical shock). This procedure is used to model clinical exposure therapy (e.g., Craske, Hermans, & Vansteenwegen, 2006). In exposure-based treatments, the anxious client is repeatedly and systematically confronted with the fear-provoking situation (e.g., McNally, 2007). Despite being an efficacious treatment for a range of anxiety disorders, relapse is not uncommon after exposure-based treatments (e.g., Simpson et al., 2004). Limited generalization of extinction is generally considered to be the preeminent laboratory model for relapse following exposure therapy (e.g., Bouton, 2002). But how can we know whether continued research into fear extinction will teach us more about exposure treatment and ways to improve it? This question is fundamental to the issue of external validity and speaks directly to the challenge of bridging the gap between science and treatment.

Below, we discuss each of the three validity criteria (face validity, construct validity and predictive validity) in separate sections. We start each section with a definition of the criterion as applied to treatment models. Subsequently, we evaluate the extinction model using this criterion. We end each section by using extinction as an example to demonstrate how the validity approach can guide future developments in laboratory-based treatment research.

1. Face validity

1.1. Definition

In the present context, face validity refers to the surface similarity between the treatment model and the treatment itself. Surface similarity (face validity) is generally seen as a good starting point for the development of experimental models, but it is deemed as not very informative for the external validity of a model (e.g.,

Vervliet & Raes, 2013). That is because mere similarities in procedure or result, however compelling, do not imply that similar mechanisms are involved (i.e., construct validity) or that treatment enhancing strategies that prove to be successful in the laboratory will also be successful in clinical practice (i.e., predictive validity). Nevertheless, surface similarity with clinical treatment does remain important, because it can serve as a continuing source of inspiration for creating new laboratory models or updating existing ones.

1.2. Extinction and return of fear

We now turn to the assessment of the extinction model using this criterion. Many researchers do refer to surface similarity when justifying their choice for fear extinction as a model of exposure treatment, as evidenced by the introduction sections of many published studies on extinction (e.g., Culver, Vervliet, & Craske, 2015; Kindt & Soeter, 2013; Leer & Engelhard, 2015). In both extinction training and exposure-based treatment, the repeated confrontation with a fear-evoking situation or stimulus results in a decrease in outcome variables that are indicative of fear and anxiety (e.g., US-expectancy, subjective units of distress ratings). The same holds for laboratory models of relapse. Return of fear is a well-documented phenomenon after fear extinction in the laboratory (Vervliet, Baeyens et al., 2013; Vervliet, Craske et al., 2013). Two paradigms frequently used for this purpose are renewal and reinstatement (Vervliet et al., 2013). In renewal, a context switch between the extinction phase and the test phase causes a return of fear responses similar to a clinical relapse after successful treatment when the feared object or situation is encountered outside the therapy context (Effting & Kindt, 2007). Reinstatement refers to the return of fear after unsignaled US-presentations between extinction and test, and can be seen as the equivalent of relapse after unsignaled panic attacks or if the previously feared stimulus is encountered after a stressful event or in a distressing situation (Dirikx, Hermans, Vansteenwegen, Baeyens, & Eelen, 2007; Haaker, Golkar, Hermans, & Lonsdorf, 2014). In conclusion, at face value fear extinction seems to be a sufficiently good treatment model of exposure therapy.

1.3. Future research

Researchers can continue to invest in increasing the surface similarity between the extinction procedure and exposure treatment. For example, it has been argued that basic stimulus sets such as geometrical shapes lack the complexity of real-world experiences (e.g., Barry, Griffith, De Rossi, & Hermans, 2014). Some researchers therefore turn to the use of 3-D virtual reality technology that allows administering extinction training under conditions that are closer to real-life situations (e.g., Dunsmoor, Ahs, Zielinski, & LaBar, 2014). Using more complex, multi-sensory stimuli (e.g., auditory, tactile, olfactory, visual) can be a conceivable step in increasing the procedural overlap between extinction and exposure therapy (for a similar argument, see Waters, LeBeau, & Craske, 2016). In addition, extensions of the extinction model aimed at improving its face validity can target similarities in outcome measures. Behavioral avoidance is an important source of impairment in daily functioning in pathological anxiety (Barlow, 2002) and is frequently used as an outcome measure in clinical exposure studies, by using a behavioral approach task (e.g., Niles, Craske, Lieberman, & Hur, 2015). The external validity of extinction research might therefore benefit from including behavioral avoidance as an outcome measure in addition to expectancy or fear ratings and psychophysiological indices of fear (e.g., Van Meurs, Wiggert, Wicker, & Lissek, 2014; Vervliet & Indekeu, 2015).