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Advancing psychotherapy and evidence-based psychological interventions

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Abstract

Psychological models of mental disorders guide research into psychological and environmental factors that elicit and maintain mental disorders as well as interventions to reduce them. This paper addresses four areas. (1) Psychological models of mental disorders have become increasingly transdiagnostic, focusing on core cognitive endophenotypes of psychopathology from an integrative cognitive psychology perspective rather than offering explanations for unitary mental disorders. It is argued that psychological interventions for mental disorders will increasingly target specific cognitive dysfunctions rather than symptom-based mental disorders as a result. (2) Psychotherapy research still lacks a comprehensive conceptual framework that brings together the wide variety of findings, models and perspectives. Analysing the state-of-the-art in psychotherapy treatment research, "component analyses" aiming at an optimal identification of core ingredients and the mechanisms of change is highlighted as the core need towards improved efficacy and effectiveness of psychotherapy, and improved translation to routine care. (3) In order to provide more effective psychological interventions to children and adolescents, there is a need to develop new and/or improved psychotherapeutic interventions on the basis of developmental psychopathology research taking into account knowledge of mediators and moderators. Developmental neuroscience research might be instrumental to uncover associated aberrant brain processes in children and adolescents with mental health problems and to better examine mechanisms of their correction by means of psychotherapy and psychological interventions. (4) Psychotherapy research needs to broaden in terms of adoption of large-scale public health strategies and treatments that can be applied to more patients in a simpler and cost-effective way. Increased research on efficacy and moderators of Internet-based treatments and e-mental health tools (e.g. to support "real time" clinical decision-making to prevent treatment failure or relapse) might be one promising way forward.

Developments and future challenges of psychological models and paradigms of mental disorders from a cognitive perspective

Psychological models of mental disorders help to guide research into the psychological and environmental factors that cause and maintain mental disorders and to identify interventions that can reduce them. In recent years, psychological models of mental disorder have become increasingly transdiagnostic, focusing on core cognitive endophenotypes of psychopathology from an integrative cognitive psychology perspective rather than offering explanations for unitary mental disorders. This evolution is connected to a shift from a categorical and nomothetic to a more dimensional perspective on mental disorders. We anticipate that psychological interventions for mental disorders will increasingly target specific cognitive dysfunctions rather than symptom-based mental disorders as a result. We further argue that a dimensional perspective on mental disorders will necessitate the development of psychological paradigms that instantiate "weak" rather than "strong" situations and will require a multi-faceted assessment of the external validity of psychological paradigms for mental disorders. Further we point to the possibilities conferred by a closer integration of psychopharmacological and psychological research and interventions and discuss gaps and needs in research that follow from our analysis. After a brief introduction on the nature of psychological explanations for mental disorders, we will sketch in the first part of this paper from a focused "cognitive" perspective a few important developments in how mental disorders are conceptualized and studied in psychology over the last decades. We will also point out likely evolutions and important challenges for the years to come. Along the way, we will discuss implications for psychological interventions for mental disorders.

What characterizes psychological models of mental disorders?

Aristotle argued that a full understanding of any phenomenon implies understanding in terms of four kinds of explanation (cited in Killeen, 2001): *Formal*, *efficient*, *final*, and *material* explanations. Applied to psychopathology, a full understanding of mental disorders would thus require according to Killeen *et al.* (2012) insight into their triggers and enabling conditions (*efficient* explanation), knowledge of their substrate and mechanisms (*material* explanation), identification of their function, i.e. the factors that maintain disorders (*final* explanation), and a theoretical model of the various processes that are involved in disordered behaviour (*formal* explanation). Accordingly, psychological accounts of mental disorders can be described as being mainly concerned with the first, third and fourth kind of explanation. Examples are issues like: (i) What kind of personality traits or other psychological vulnerability factors predispose for the development of mental disorders (distal *efficient* causes; e.g. anxiety sensitivity as a vulnerability factor for the development of panic disorder; McNally, 2002)? (ii) What kind of situational factors or stimulus contingencies promote or elicit problem behaviour [proximal *efficient* causes; e.g. boredom as a trigger for attention deficit hyperactivity disorder (ADHD) behaviour; Killeen *et al.*, 2012]? (iii) What psychological processes are involved in various forms of psychopathology (*formal* analysis; e.g. the role of deviant attentional processes in schizophrenia; Luck and Gold, 2008; or impaired executive functioning versus impaired reward sensitivity as two rivalling theoretical accounts for ADHD; Sonuga-Barke, 2003), (iv) Which factors maintain mental disorders (what psychological function does the abnormal behaviour serve, e.g. does it somehow confer reinforcement, serve a communicative function, proximal *final* explanation; e.g. avoidance behaviour that reduces immediate anxiety but prevents fear-reduction through exposure in the long run; Foa and Kozak, 1986)?

In this framework, "final explanations" of a more ultimate nature (selection by consequences at the level of individuals with certain traits rather than at the level of instances of behaviour; e.g. how the evolutionary utility of a certain distribution of impulsiveness in the population may set some individuals up for addiction; Williams and Taylor, 2006) fall beyond a strictly psychological analysis. Similarly material explanations in terms of the biological substrate or neural mechanisms that underlie mental disorders (e.g. the role of grey matter abnormality in autism spectrum disorders; Cauda *et al.*, 2011) or "efficient explanations" in terms of societal or biological triggers of mental disorders (e.g. on the role of standards of beauty in advertising in triggering eating disorders; Derenne and Beresin, 2006; or how corticosteroids induce psychosis or mania; Brown and Suppes, 1998) evidently cross the disciplinary borders.

Psychological accounts of mental disorders can be regarded as "functional" in nature, in at least two different regards. At the formal level, they often aim to understand and model mental disorders in terms of (disturbances in) core psychological functions (attention, learning, memory, decision-making, cognitive control, emotion regulation, etc.; for an excellent example, see Goschke, 2014). For instance, biased attention to threat cues might help to understand why the same physical environment is more stressful to some individuals than to others (Bar-Haim *et al.*, 2007). At the "final" level, they try to understand the origin and maintenance of abnormal behaviour in terms of the objective or subjective benefits that it might confer (see the assumption that a bias towards over general autobiographical memory retrieval in depression, although detrimental for every-day problem solving, may help ward off unpleasant, traumatic or threatening memories; Williams *et al.*, 2007).

State-of-the-art: advances in psychological theories and models of mental disorders in the last decades

From schools of thought to a unified cognitive psychology framework

Historically, psychological theories for mental disorders where for the larger part firmly rooted in encapsulated schools of thought. So, a psychodynamic theory of depression would for instance explain depression as the result of repressed anger converted into self-hatred, due to unresolved conflict between conscious and unconscious motives (Blatt and Homann, 1992); a learning theory perspective on anxiety might explain phobic behaviour as the result of a combination of Pavlovian and instrumental conditioning processes (Mineka and Sutton, 2006); a humanistic theory of addiction could point to temporary barriers that prevent fulfillment of an inherent drive to self-actualization (Maslow, 1968); a systems theory perspective may point to dysfunctional communication patterns in the family ("double-bind") as a cause for schizophrenia (Bateson *et al.*, 1956). These schools of thought all had their own conceptual frameworks and jargon, effectively preventing cross-talk between them and precluding a unified psychological perspective on mental disorders. Apart from the learning theory perspective perhaps, these schools of thought were

also largely disconnected from evolutions in mainstream empirical psychological science.

In recent years, there is considerable convergence towards a common cognitive psychology framework. Indeed, the advent of the cognitive perspective in empirical psychological science has allowed to broaden our understanding by integrating many seemingly disparate theoretical accounts that variously point to the importance of unconscious schemas, motivational processes or learning and reinforcement principles, into an integrative framework and connect those accounts with available findings from mainstream experimental psychology (for examples, see Hofmann, 2008; Hofmann *et al.*, 2013). This integration hinges on the parsing of mental processes into separable but interconnected functions like attention, memory, reasoning and decision-making, learning, motivation, action planning and the like, along with its distinction between fast and automatic, often unconscious processes and slow and effortful, conscious processes. Psychological interventions within the various therapeutic orientations are getting increasingly evidence-based, and psychotherapy as a whole more integrative, as a result.

Indeed, interventions are increasingly based on ideas gleaned from experimental cognitive psychology, not from a particular perspective such as psychodynamic theory, learning theory, humanistic psychology (e.g. memory specificity training for depression, see Raes *et al.*, 2009; Neshat-Doost *et al.*, 2013; executive function training for ADHD, e.g. Van der Oord *et al.*, ; attentional bias modification training for alcohol abuse, e.g. Schoenmakers *et al.*, 2010). Even if they are derived from a specific school, efforts are increasingly made to align them within a common framework and creatively combine effective interventions that target distinct subprocesses or functions, e.g. incorporating motivational interviewing techniques in behaviour therapy interventions (e.g. Geller and Dunn, 2011).

From mental disorders to endophenotypes as units of analysis

In parallel with the shaping of a unified cognitive psychology framework came a shift in focus in the conceptualization and explanation of mental disorders from whole to parts. Historical approaches would indeed try to provide an account for mental disorders as entities – e.g. internal conflict causes depression, and depression is then expressed in a number of symptoms.

The recent focus on separate cognitive functions has been accompanied by a tendency to examine separate symptoms or core deficits associated with certain mental disorders, rather than mental disorders in Globo. This could be exemplified with research on cognitive *endophenotypes*, i.e. specific cognitive traits or deficits that underlie part of the symptoms of a disorder. Endophenotypes or intermediate phenotypes are specific clusters of symptoms that constitute building blocks or intermediate processes for mental disorders and supposedly carry a more specific and consistent genetic load than the overall disorders that they contribute to (Skuse, 2001). Such endophenotypes can often be related to specific functions in a cognitive psychology framework, such as memory, attention, executive functions, or others. In some domains, considerable progress has been made in the identification of meaningful cognitive endophenotypes in the last decades. For instance, impulsivity across a number of tasks and situations has been recognized as a core endophenotype for ADHD, occurring not only in affected individuals but also in first-degree relatives (Robbins *et al.*, 2011). Recognition of such endophenotypes facilitates translational research by focusing on cognitive processes that can be readily investigated in animal models and in human laboratory research with non-clinical groups.

Towards dimensions of mental disorder

The increasing focus on such cognitive endophenotypes as the unit of analysis can also be related to the increasingly dimensional conceptualization of psychopathology. Indeed, the fundamentally gradual or dimensional nature of cognitive endophenotypes such as impulsivity, overgenerality of autobiographical memory, rumination does not always fit well with the categorical nature of existing psychiatric classification systems like the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, American Psychiatric Association (APA), 1994; DSM-IV-TR, American Psychiatric Association (APA), 2000). The exclusive reliance on symptoms and syndromes derived from diagnostic classificatory systems of the past can be an obstacle for further research and therapy (Insel *et al.*, 2010) not only in the realm of mental disorders, but in medicine in general. So, while diagnostic classification systems serve several purposes (i.e. administrative, legal, public health), research on mental disorders might profit from approaches that additionally allow classifying patients based on underlying psychological and biological mechanisms, with the goal of improving treatment outcomes.

Promising first steps in this direction have been taken in psychological science. Research has unveiled that emotion dysregulation is involved in a variety of mood and anxiety disorders (Hofmann *et al.*, 2012b). Autobiographical

memory biases may be involved in obsessive-compulsive disorders, trauma and depression (Williams *et al.*, 2007). Executive function deficits including impaired working memory and inhibition and increased impulsivity are endophenotypic not only of ADHD but also of addiction, obsessive-compulsive disorders and eating disorders (Robbins *et al.*, 2011). Repetitive negative thinking is a cognitive marker of mental disorders as diverse as depression, anxiety disorders, bipolar disorder and psychosis (Ehring and Watkins, 2008). Findings such as those fit much better with a modular cognitive psychology framework and a dimensional endophenotype perspective than with a categorical, nomothetic view of mental disorders.

Implications for psychological treatment and psychotherapy

Specific psychological treatment manuals have been developed for virtually all mental disorders. Because these treatments are relatively complex, dissemination of even one of them to providers is a serious obstacle to delivery of evidence-based treatment. Even more importantly, as noted earlier, the empirical justification to develop such highly specific symptom-based treatments is relatively weak – recent research supports the notion that supposedly distinct mental disorders share many commonalities. It is therefore to be expected that future interventions will increasingly consist of evidence-based treatment programmes targeting specific psychological processes (e.g. memory specificity training for mood disorders and post-traumatic stress disorder (PTSD), executive function training in ADHD, addiction and eating disorders; attentional bias modification training for addiction and anxiety disorders) in replacement of school-of-thought-based or disorder-based interventions.

Challenges and opportunities regarding psychological theories and models of mental disorders from a cognitive perspective

Focus on the dimensional nature

In the common diathesis-stress models of psychopathology and mental disorders, endophenotypes arguably represent vulnerability factors or (bio-)markers for mental disorders rather than being indicators for the full-blown disorder. This is supported by the finding that they can typically be observed not only in affected individuals but also – with higher than chance probability – in first-degree relatives. Many experimental models of psychopathology manage well to discriminate between clinical and non-clinical populations, but they fail often to differentiate meaningfully within non-clinical or sub-clinical populations. As an example, many studies have found differences in basic fear conditioning processes between people with anxiety disorders and appropriate controls (e.g. Lissek *et al.*, 2008, 2009; Michael *et al.*, 2007). Far fewer studies have been able to demonstrate similar differences in susceptibility or sensitivity to fear conditioning between people with higher and lower risk of developing anxiety disorders, such as people with high versus low trait anxiety (Otto *et al.*, 2007; Pineles *et al.*, 2009). It has been argued that such failures may be tied to the nature of the fear conditioning procedures that are typically employed in such research (Beckers *et al.*, 2013), which are typically "strong situations", that is, situations that involve little ambiguity and in which a strong conditioned fear response is highly adaptive, such that also people low in trait anxiety would be expected to exhibit relatively strong fear learning. In research with sub-clinical, at-risk populations, more insight might be gained from focusing on "weak situations", that is situations that involve a considerable degree of ambiguity or for which a dominant response cannot readily be identified (Lissek *et al.*, 2006).

For fear learning, an example of such a weak situation is a blocking procedure. In that procedure, a conditioned cue A is first paired with shock (A + training), after which the combination of that cue A with a second cue X is also paired with shock (AX + training). In animals, such a procedure often results in attenuated fear responding to X, relative to a control group that did not receive A + training. Yet, the status of X is inherently ambiguous: No direct evidence is presented as to whether it would be followed by shock when presented in isolation. In a recent study, Boddez *et al.* (2012) demonstrated that blocking might represent a biomarker for vulnerability to development of anxiety disorders, as trait anxiety correlated positively with the anticipation of a shock upon presentation of X after blocking training. That is, people with high trait anxiety anticipated shock more strongly than people with low trait anxiety specifically in the presence of ambiguous cue X, whereas anticipation in the presence of other cues was not reliably affected.

The idea that weak situations might provide better grounds for unveiling meaningful endophenotypic differences within non-clinical populations can be supported by findings in depression research. Relative to normal controls, individuals with clinical depression were observed to be impaired in retrieving specific autobiographical events from memory when explicitly prompted to do so (Williams *et al.*, 2007). Studies have largely failed to find similar differences in autobiographical memory specificity between dysphoric and non-dysphoric non-depressed

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individuals or between other groups that differ in vulnerability for depression. However, meaningful differences are observed when the assessment of autobiographical memory is modified such that specificity of autobiographical memory retrieval is not explicitly asked for and people are merely given the instruction to come up with any autobiographical memory in response to a set of cue words (the so-called minimal instructions autobiographical memory test; Debeer *et al.*, 2009). Clearly, the explicit instructions in the original version of the test leave little room for sub-clinical response tendencies to manifest; it is only in the context of a more ambiguous testing situation that does not imply one dominant or appropriate response, that individual differences on sub-clinical dimensions are revealed. Another example might be executive function deficits in ADHD. Clinical ADHD is associated with deficits on a range of executive function tasks (Willcutt *et al.*, 2005). Remarkably, strong incentives can greatly reduce (although not completely abolish) differences in performance between adolescents with ADHD and normal controls (Dovis *et al.*, 2012). This suggests that when investigating ADHD and other impulse control disorders (addiction, eating disorders) from a dimensional perspective, it might be wise not to give too much incentive but to rather keep motivation at an intermediate level, so as to create a "weak situation" in which chances for finding dimensional differences are maximized. We believe that increased efforts to devise and evaluate weak situation paradigms in experimental psychopathology research are warranted.

Linking psychological and psychopharmacological research for intervention

So far, medical/biological and psychological interventions are developed largely side-by-side, evaluated as competitors or at best hoped to reinforce one another non-selectively. Examples include: methylphenidate versus behaviour therapy in ADHD (Van der Oord *et al.*, 2008, 2012); psychotherapy as a means to prevent relapse after continued use or discontinuation of antidepressant medication (Guidi *et al.*, 2011); benzodiazepines as an adjuvans during exposure therapy for panic disorder (Watanabe *et al.*, 2007).

Increased understanding of how pharmacological processes can affect specific psychological functions, e.g. memory processes, will likely allow for much more targeted, interactive interventions, in which pharmacological agents are specifically used to impact a psychological process that is causally implicated in mental disorder. Currently, the most prominent example concerns trauma memory in PTSD and other anxiety disorders. Whereas present pharmacological treatment for anxiety disorders is by and large non-selective (anxiolytics, e.g. benzodiazepines), recent laboratory work suggests that pharmacological agents can be applied much more specifically, to selectively target unwanted or disabling traumatic memories. Two *modi operandi* have already been identified. We might be able to pharmacologically boost memory for corrective exposure experiences, e.g. by administering D-cycloserine during or right after exposure treatment (Hofmann *et al.*, 2012a; Vervliet, 2008). Alternatively, we might diminish the emotional loading of trauma memory directly, e.g. through administration of propranolol during retrieval of the trauma memory, which interferes with subsequent reconsolidation (Kindt *et al.*, 2009).

Laboratory results suggest that the latter is more effective in preventing return of fear than pharmacological enhancement of exposure learning (Soeter and Kindt, 2010; but see Haaker *et al.*, 2013, for a promising approach that involves administration of L-DOPA during extinction learning to make extinction less context-specific). However, the exact boundary conditions for fear memory reconsolidation blockade in humans are still being determined (e.g. Bos *et al.*, 2012; Sevenster *et al.*, 2012, 2013). Also, the evidence for clinical effectiveness is limited to a single study so far (Brunet *et al.*, 2008). Similar approaches are being tested in the context of addiction (Sorg, 2012; Taylor *et al.*, 2009); however, those addiction interventions have yet to be tested in humans. Increased understanding and integration of formal (psychological) and material (biological) explanations for mental disorders will likely strengthen this development and allow similar integrative psychopharmacological approaches to the treatment of other forms of psychopathology to be developed in the future.

Increasing external validity of psychological models for mental disorders

Psychopathology research relies progressively more on experimental laboratory paradigms to evaluate or model specific endophenotypes of mental disorders. One of the great advantages of an experimental model is that the obtained results are well-controlled (i.e. they have strong internal validity), but the main disadvantage is the uncertainty whether these solid results actually tell us something about the disorder being modeled (questionable external validity). This issue has received some attention at the rise of experimental models in psychology research (Abramson and Seligman, 1977), but interest has waned afterwards. In contrast, the issue has remained a primary focus in

neuropsychopharmacology research that makes widespread use of animal models.

Generally, three different criteria of validity are outlined in this literature (e.g. Willner, 1991). Face validity refers to the phenomenological similarity between behaviours in the model and symptoms of the disorder. It is the easiest but also the weakest criterion to assess, as face validity is neither sufficient nor necessary for a model to have good external validity. Predictive validity requires that the behaviour in the model reacts to known treatments of the disorder. Accordingly, good predictive validity is particularly important if we are to use laboratory models to evaluate the effectiveness of novel interventions; without predictive validity, effectiveness of the intervention in our laboratory model is of little relevance for treatment of the actual disorder. Construct validity is based on a homology between the theories underlying the behaviour in the model and the disorder. Typically, construct validity is achieved by recreating the etiological factors of the disorder in the model. Of note, models can never mimic entire disorders, but only components of (symptoms) disorders. This is in line with the broader evolution from mental disorders to endophenotypes as units of analysis. Good construct validity of a model, even if partial, is vital if the model is to genuinely increase our understanding of the psychological processes that underlie mental disorders.

In human experimental psychopathology, a fourth aspect of external validity that is arguably of importance is diagnostic validity, that is, the extent to which the experimental model is able to distinguish between clinical and non-clinical populations (Vervliet and Raes, 2012; see also Emmelkamp *et al.*, 2014). In a dimensional perspective, diagnostic validity also requires that the model can distinguish within sub-clinical groups between individuals situated at different levels of a particular dimension. For instance, to have good external validity, a test of autobiographical memory specificity should ideally not only differentiate between depressed and non-depressed individuals but also between non-depressed individuals with low mood and normal mood. This issue relates to the use of weak situations as opposed to strong situations in dimensional models of psychopathology discussed earlier.

Validity testing is never complete, but should be an integral and explicit part of a continuous research program – more than is current practice in experimental psychopathology research. Further examinations of the mechanism underlying the model will influence the construct validity of the model and/or the theory of the disorder itself. Further screenings of known and experimental treatments will influence the predictive validity of the model and possibly result in treatment innovations.

Conclusions: current strengths, critical needs and gaps regarding psychological theories and models of mental disorders from a cognitive perspective

Great progress has been made over the past decades in explaining and modeling mental disorders from a psychological perspective. Recent evolutions towards accounting for mental disorders in terms of dimensional, transdiagnostic endophenotypes are promising – the work is far from finished, exiting times for the understanding and treatment of psychopathology are ahead. We are confident that increased attention to development of weak situation paradigms and assessment of external validity of psychological models, along with increased integration of kinds of explanation, will further enhance our understanding of mental disorders and ultimately help to develop more powerful interventions for prevention and treatment.

Research on mental disorders and psychological interventions can profit from a number of strengths and opportunities conveyed by the current European and international research context:

- In basic behavioural science and research, there already is a strong drive away from the study of disorder-specific psychological characteristics and processes and towards the study of component processes that potentially underlie a range of disorders and clinical and sub-clinical states in a dimensional fashion (see Goschke, 2014). Europe is at the forefront of this evolution and can benefit from the presence of a considerable number of strong and impactful experimental psychopathology groups.
- The current controversy over the revision of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association (APA) (2013)) has opened a window of opportunity to initiate an even stronger push towards research directed at component processes and cognitive endophenotypes that cut across diagnostic entities and classes (see also the recent decision by the National Institute of Mental Health [NIMH] to no longer support research project that are guided exclusively by DSM criteria).
- At the same time, there is increasing convergence between biomedical and psychological approaches to psychopathology, resulting in an increased emphasis to integrate the various biopsychosocial factors that promote and maintain psychological problems and mental disorders. Such integration is ever more crucial for the development of integrated behavioural science interventions (e.g. targeting core component psychological

processes of mental disorder with pharmacological agents such as Yohimbine, D-cycloserine, propranolol, L-DOPA, etc.).

However, in order to capitalize on those developments, it is vital that a number of critical needs and gaps are addressed in future research:

- It will be clear from the above that further basic research is needed into the mental processes that underlie normal and abnormal behaviour, as a constant source for the development of novel, more targeted interventions.
- It is equally important to maintain strong ties between basic psychological science and clinical intervention research; the history of psychology shows that the strongest progress in the treatment of psychological problems and mental disorders has been made when interventions were tailored closely to progress in basic behavioural science. A strong divide between basic psychological research and clinical research should therefore be avoided. Basic researchers should be encouraged to consider the clinical implications and applications of their work; clinical scientists should equally be encouraged to remain updated about the latest developments in basic science and to press basic scientists to attend to clinical problems.
- There is a great need to improve on our understanding of the validity of various laboratory models for (component processes of) psychopathology, taking into account the various criteria for validity of laboratory models that have been developed in biomedical research. A more systematic and multi-faceted assessment of the validity of basic science models of psychopathology should allow to better decide how relevant basic science findings are to clinical application.
- Integration of psychological and pharmacological interventions may bear great promise for the treatment of some aspects of psychopathology (particularly disordered memory processes); however, much more knowledge is needed on the exact boundary conditions for pharmacological intervention on specific psychological processes. Increased knowledge along those lines should help pave the way for interventions that in an intelligent, science-based way combine psychological and biomedical techniques. So not just the standard "let's do some combined psychotherapy and psychopharmacology", but the development of interventions that combine the specificity of psychological interventions (targeting specific behaviours, cognitions, emotions) with the directness and power of biomedical interventions.
- Much more than is now the case, targeted interventions need to be developed that are process-specific (and non-disorder-specific) rather than disorder-specific (and non-process-specific, as is now often the case). The development of such interventions that can improve basic disordered processes will necessitate a new kind of clinical trials that are not disorder-specific but evaluate the effect of interventions in the general population (or a subset of the general population that displays an impairment in a given transdiagnostic component process, e.g. people with planning problems, working memory impairments, elevated impulsivity, reduced cognitive control, excessive rumination, or such), irrespective of a specific mental disorder. Indeed, taking the cognitive processes framework seriously implies gradually moving away from trials in very specific diagnostic populations that typically employ highly selected samples and exclude all comorbidity.
- The above should not be taken to indicate that there is no longer a need to improve our understanding of the effectiveness and mechanisms of action of existing psychological interventions. While the development of novel treatments and interventions that target specific clinical and sub-clinical deficits in component processes across the general population indeed requires a new kind of intervention studies, the status of such interventions is likely to remain somewhat experimental for the years to come. We cannot afford to meanwhile drop pace on the evaluation and refinement of more traditional interventions, some of which have proven extremely valuable and highly effective (if perhaps limited in diagnostic scope).
- In summary, in parallel to traditional intervention research, we need clinical trials that evaluate population-wide interventions that aim to remedy deficits in specific component processes in those people that exhibit deficits, irrespective of psychiatric diagnosis.

Psychological treatment research – time to reboot?

Against the background of the previous considerations regarding psychological theories and models of mental disorders from a cognitive perspective one may ask the question, whether time has come to reboot psychotherapy research altogether? Psychotherapy is rooted in many different traditions, conceptual models and "schools of thinking", ranging from theoretically-based approaches such as psychodynamic therapy to more experimentally-based psychological interventions such as cognitive-

behaviour therapy (CBT). Psychotherapy has become a well-founded field of science with specific theories and models, research targets, methods and procedures. However, there is a clear lack of conceptual frameworks that bring together the wide variety of findings, models and perspectives, and the breadth of research is almost incapable to follow-up for both researchers and clinicians. Attempts to develop common overarching integrative frameworks such as proposals for empirically-based "psychological therapies" or a "unified treatment" have not solved the problem.

Unfortunately, this incoherent picture has sometimes created confusion to policy makers and the public as with regard to the scientific status of psychotherapy. The following section summarizes the state-of-the-art in psychotherapy treatment research – focusing on needs and gaps in psychotherapy research on anxiety-related disorders as an example. We highlight "component analyses" to define optimally core ingredients and identify mechanisms of change, efficacy and effectiveness of psychotherapy, as well as translational issues (including dissemination and transfer). Given the established efficacy and benefits of psychotherapy and CBT in particular, we argue that time has come for concerted action to overcome the current fragmentation between theory-based and evidence-based approaches by focusing on empirically supported principles of change, targeting relevant processes rather than being focused on distinct diagnostic categories.

State-of-the-art in psychotherapy research: the lack of comprehensive conceptual frameworks

There is a well-known chiasm between science and practice of psychotherapy (Beutler, 2009) that goes far beyond the notorious translational issues and the issue of dissemination. Psychotherapy is rooted in many different traditions, conceptual models and "schools of thinking", ranging from theoretically-based approaches such as psychodynamic therapy to more experimentally-based psychological interventions such as CBT. The fast and exponential growth of our knowledge about the brain and the neural and neurobiological underpinnings of behaviour, cognition and affect make it difficult even for scientists to keep up with the state-of-the-art and hardly impossible for clinicians. There is a clear lack of conceptual frameworks that bring together the wide variety of findings, models and perspectives. Attempts to develop common overarching integrative frameworks such as proposals for empirically-based "psychological therapies" or a "unified treatment" (Barlow *et al.*, 2004) have not solved the problem. Unfortunately, this incoherent picture has sometimes created confusion to policy-makers and the public as with regard to the scientific status of psychotherapy.

Yet, it is also important to highlight that psychotherapy in many areas has become a well-founded field of science with specific theories and models, research targets, methods and procedures, typically fitting three major paradigms: (1) psychodynamic (Barber *et al.*, 2013); (2) humanistic-experiential (Elliott *et al.*, 2013); and (3) cognitive-behavioural (Emmelkamp, 2013). Each paradigm can generate specific psychological treatments (i.e. clinical protocols), often flexible manualized (i.e. especially in cognitive-behavioural approach), for specific clinical problems (one or more for each problem). Such well-defined psychological treatments, primarily CBT approaches, have become established first-line treatments for many mental disorders with effect sizes that are at least as good as those established in state-of-the-art randomized clinical drug trials. For this position paper we define psychotherapy as "a science-based psychological health care technology for treating mental disorders and mental health problems, including somatic diseases with significant psychological components, by psychological means". Essential components are (i) reliance on evidence-based structured and planned interactional process between a therapist and patient, and (ii) use of psychological methods and techniques. Within this frame and given the basic position papers by Goschke (2014) and Wittchen *et al.* (2014) that have highlighted already some key issues for a science-based strategy, we focus on three domains of psychotherapy treatment: (a) efficacy and effectiveness of psychotherapy, (b) component analyses to identify core ingredients and mechanisms of change, and (c) translational issues (including dissemination and transfer).

Efficacy and effectiveness of psychotherapy

Strengths

There is little doubt from a scientific perspective that psychotherapy according to this definition is effective, highly beneficial and cost-effective for a wide range of mental disorders and health conditions (see for example Health Technology Assessment reviews; Roth and Fonagy, 1996), such as anxiety, stress and trauma-related disorders, depressive and somatoform and pain disorders, personality disorder, substance use disorders and behavioural addictions, eating disorders and a number of childhood disorders. For all these disorders, various variants of CBT

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have been established in clinical randomized trials. There is also strong evidence for the efficacy of CBT and other psychotherapeutic methods, at least as an adjuvant treatment, for psychotic and bipolar disorder (Hutton and Taylor, 2013; van der Gaag *et al.*, 2012; Jones *et al.*, 2012a; Jones *et al.*, 2012b). Further psychotherapy is established for a wide range of somatic diseases and a range of health conditions for which behavioural factors play a significant role in the initiation, maintenance and rehabilitation such as cancer (e.g. Fors *et al.*, 2011) cardiovascular disease (e.g. Gulliksson *et al.*, 2011), metabolic disease and obesity (e.g. Grilo *et al.*, 2012), and fibromyalgia (Kashikar-Zuck *et al.*, 2012).

Further, multiple systems are in place that regularly evaluate evidence-based psychological therapy. The most representative might be (1) the National Institute for Health and Clinical Excellence Guidelines (NICE Guidelines; http://www.nice.org.uk), (2) the American Psychological Association (APA/Division 12/Society for Science of Clinical Psychology/SSCP; http://www.div12.org/PsychologicalTreatments/index.html), and (3) Cochrane Reviews (http://www.cochrane.org). Among the psychological treatments promoted by these international systems, those coming from the CBT paradigm are currently the best represented. Therefore, many example and analyses made to understand how we can advance the psychotherapy field will be mainly focused on CBT.

Problems

Against this overwhelming level of evidence there are however some notable problems. First, current systems of evaluating evidence-based psychotherapy focus on data supporting (psycho)therapeutic packages, while neglecting the degree of empirical support for the theoretical basis of these packages. To delineate core ingredients and to identify mechanisms of action and therapeutic change, David and Montgomery (2011) proposed a new grid system (see Table 1) for the evaluation of evidence-based psychotherapy.

They propose nine categories, resulting from levels of evidence regarding two factors: (1) theory/mechanisms of change and (2) interventions (i.e. therapeutic package) derived from that theory. Of note, the proposed categories are not static, but based on the progress of research, allowing one form of psychotherapy to move from one category to another.

Second, often psychotherapy research lacks cost-effectiveness analyses. Therefore, even if a psychological treatment could show strong efficacy and/or effectiveness, due to high costs it might never be assimilated in real clinical practice.

Therefore future research should take into account the efficacy/effectiveness of psychological treatments, evidence for the underlying theory of change, and cost-effectiveness.

Open questions, needs and gaps

Although there is a wealth of studies that are based on high standards regarding design, methods and date analyses (e.g. Lambert, 2013), there is a lack of programmatic research that takes into account the validity of its underlying theory, the outcome of the intervention and cost-effectiveness considerations.

(1) *On the theoretical and mechanisms of change level* it should be emphasized that this level does not necessarily refer to the aetio-pathogenic mechanism that have led to expression of the disorder or condition, but more generally to the assumed mechanism of change in the psychotherapeutic approach under study. Mediation and moderation analyses are typically involved in this kind of analysis. The hypothesized mediators and/or moderators should be specified in advance, based on scientific clinical theories. The specific role of "placebo conditions" (Kirsch, 1990) as well as non-specific factors such as therapeutic alliance (Wampold, 2001) in psychotherapy should be emphasized. For example, placebo, as described here, may have an effect on the outcome, though involving different mechanisms as the active ingredient under study. This may cause a logical problem – what could then be an adequate control/placebo condition? A solution would be to instead focus on comparative designs: what is the active ingredient/mechanism to positively affect the outcome?

(2) *On the outcome level*, analyses focus on the impact that a specific intervention has on a specific outcome or on a spectrum of outcomes (e.g. clinical conditions). The quality of the outcome analysis depends on the level of outcome specification:

   (a) *Complex analyses of the outcome*: In order to have a comprehensive understanding of the outcome and impact, the following assessment domains should be mandatory: (i) the clinical symptomatology (i.e. including primary and secondary symptom or diagnostic outcomes); (ii) the general level of distress; and (iii) the social functioning and quality of life to understand how the clinical condition(s) and/or interventions impact the real life of our clients

   (b) *Multidimensional operationalization of the outcome*: The measures by which the outcome is operationalized must have good psychometric properties and be representative, allowing international comparisons. Further,

Table 1. Psychotherapies classification framework: categories I–IX (adapted from David and Montgomery, 2011)

Therapeutic package	Theory		
	Well-supported[b]	Equivocal – no, preliminary, or mixed data[c]	Strong-contradictory evidence[d]
Well-supported[a]	Category I	Category II	Category V
Equivocal – no, preliminary or mixed data[c]	Category III	Category IV	Category VII
Strong-contradictory evidence[d]	Category VI	Category VIII	Category IX

[a]Well-supported therapeutic packages are defined as those with randomized clinical trial (or equivalent) evidence of their efficacy (absolute, relative, and/or specific) and/or effectiveness; "well-supported" within this framework means that it has been empirically supported in at least two rigorous studies, by two different investigators or investigating teams.
[b]Well-supported theories are defined as those with evidence based on (1) correlational and experimental studies and/or (2) component analyses, patient × treatment interactions, and/or mediation/moderation analyses in complex clinical trials; thus, the theory can be tested independent of its therapeutic package (e.g. in correlational and experimental studies) and/or during a complex clinical trial; "well-supported" within this framework means that it has been empirically supported in at least two rigorous studies, by two different investigators or investigating teams.
[c]Equivocal evidence for therapeutic package and/or theory means *no* (data not yet collected), *preliminary* (there is collected data, be them supporting or contradictory, but do not fit the minimum standards), or *mixed data* (there is both supporting and contradictory evidence).
[d]Strong-contradictory evidence for therapeutic package and/or theory means that it has been empirically invalidated in at least two rigorous studies, by two different investigators or investigating teams.
Note: Red indicates pseudoscientifically-oriented psychotherapies (POPs); the core of POPs (dark red) is represented by Category IX. Green signifies scientifically-oriented psychotherapies (SOPs); the core of SOPs (dark green) is represented by Category I. Depending on the progress of research, a form of psychotherapy could move from one category to another; and thus, one can plan a programmatic research to evaluate and/or to stimulate the progress of a certain therapeutic approach.

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assessment of outcome should allow measuring various levels, i.e. cognitive, affective, behavioural, and physiological/biological level by including self-report, objective psychobiological and physical behavioural measures, informants report, in addition to clinical judgement;

(c) *Efficacy*: Use of specific measures that inform how well the psychotherapeutic intervention works under well-controlled conditions that preserve a high internal validity. The data should be analysed at various levels, i.e. statistical significance; effect sizes; and clinical significance (e.g. by using normative comparisons).

(d) *Effectiveness*: Use of measures that inform about how well a psychotherapy intervention works under real ecological conditions that preserve a high level of general validity.

(e) *Follow-up analyses*: It should be an internationally accepted standard to evaluate the effects of psychotherapy not only post-treatment but also at medium and long-term follow-up. Studies should define core constructs of remission, relapse and recurrence and should investigate moderators influencing long-term outcome.

(f) *Trial registers*: As it is mandatory for drug trials, the design of any psychotherapy outcome study, including primary and secondary outcome measures, moderators and mediators of outcome and number of participants to be recruited should be submitted and made public before the start of the study in a clinical trial register such as www.clinicaltrials.gov.

(3) C*ost-effectiveness considerations* should be incorporated as a standard, because even the best treatment with known mechanism of action is unlikely to be used, if it is too expensive (Sava *et al.*, 2009).

Having defined and accept these three major needs, more specific steps should be taken in order to fill the gaps:

- *Exploiting basic experimental research to characterize commonalities and differences across disorders and optimize core active ingredients of psychotherapy*. Despite its claim as being scientifically based, current CBT manuals are not entirely consistent with novel basic and clinical research (i.e. neural underpinnings, fear circuitries, (epi-)genetic factors, developmental pathways, dynamic role of learning, extinction, avoidance, safety behaviour, etc. Arch and Craske, 2009; Etkin and Wager, 2007; Gloster *et al.*, 2011; Kircher *et al.*, 2012). Emotional responses like fear and anxiety are grounded in "complex systems" that feeds back to sensory systems, heightening vigilance and information gathering (if a threat is expected or detected), and importantly, prompting for example defensive reflexive, autonomic, and motor responses that in evolutionary history acted directly to counter threats and escape punishments (Arch and Craske, 2009). Comparative research across different forms of mental disorders is necessary to detect such core aspects of dysfunctions shared by all disorders versus disorder-specific features (Domschke and Deckert, 2012; Etkin and Wager, 2007; Haber and Rauch, 2010; Lueken *et al.*, 2011) and to inform how therapeutic interventions can be optimized. A better understanding of the basic mechanisms of mental disorders and their personal variations will guide the translational agenda of how evidence-based psychotherapy can be procedurally optimized, for example to reduce more effectively dysfunctional patterns of fear, anxiety and avoidance. Such research will also inform when to intervene best with what component (i.e. timing of interventions, add-on modules, comorbidity issues). Here, there is a clear need of research in truly clinical samples or even clinical cohort samples, rather than in (psychology) students with heightened scores on a questionnaire.
- *Moderators and mediators of change*. Although CBT is the most effective psychological treatment, there is considerable room for improvement. Thus, there is a clear need to figure out how these treatments work and what accounts for the variability in outcomes. Unfortunately, few studies have measured the proposed mechanisms during treatment so it is unclear whether change in the supposed mediator preceded change in the outcome. For example, although most therapists hold that change in cognitions is responsible for effects achieved with CBT, there is still a surprisingly small number of studies that have directly tested for cognitive mediation (e.g. Meyerbröker *et al.*, 2013). Further, most of the studies that focused on mediators of treatment outcome failed to assess that the mediator changed before the improvement occurred, meaning it was not possible to test questions of temporality, a critical component of mediation (Teachman, 2013). More rigorous designs are needed to investigate mediators of treatment outcome. Current findings are inconclusive. Further, little is known about the similarities, differences and specificity of the change processes across treatment modalities and paradigms (e.g. cognitive therapy versus behaviour therapy versus interpersonal psychotherapy versus psychodynamic therapy).
- *Endo-phenotypes relevant for treatment choice and treatment response*. Our knowledge about relevant endo-phenotypes and respective neurobiological, psychological and behavioural markers could more reliably

guide clinicians' treatment choice and improve the prediction of treatment outcome if these variables were studied in the context of psychotherapy. Despite substantial knowledge regarding family genetic factors and the role of adverse early childhood in the expression of many mental disorders, little is known how such constellations affect the course and outcome of psychological interventions. For example, even for patients suffering from PTSD following repeated or chronic interpersonal trauma, such as sexual of physical abuse in childhood (type II trauma), there has been little research on the efficacy of treatment outcome. PTSD following type II trauma is considered to be more difficult to treat than PTSD following single event trauma; because of the assumed more pronounced neurobiological long-term effects as well as a particularly complex symptom presentation. In such constellations, treatments that are purely focused on trauma processing as stand-alone treatment may be insufficient and require additional components targeting emotion regulation difficulties, dissociation and interpersonal problems. For example, some have therefore suggested that treatment of PTSD following type II trauma should consist of two phases: acute problems, emotion regulation difficulties and interpersonal problems are addressed in the first phase ("stabilization") and then trauma-focused therapy is provided in the second phase (Cloitre *et al.*, 2010). Although there is promising evidence for the effects of stabilization followed by trauma-focused exposure there is a clear need for well controlled studies in this area (Neuner, 2012).

- *Treatment fidelity*. Given that in psychotherapy appropriate choice of evidence-based psychological interventions, as well as their dose and timing is critical, relatively few studies have systematically examined the degree and the role of therapists' adherence to the treatment protocol. This failure significantly limits the degree to which one can make causal inferences about the specific effects attributable to a particular treatment component. Psychotherapy component research should systematically examine and provide evidence to what degree therapist adhere to the treatment protocol and when, what type of individual modification might be allowed (for example due to patients comorbid conditions, or life events accruing during treatment) without threatening the integrity of the research.
- *Pharmacological agents*. Psychopharmacotherapy is an established effective first-line treatment in many mental disorders. Twenty to 45% of treated patients depending on diagnosis or country asking for psychotherapy present with some form of past and/or concurrent medication. A number of studies have investigated the combination of psychotherapy with anti-depressant drugs or tranquilizers, but generally such pharmacotherapy did not enhance the effects of evidence-based psychotherapy as stand-alone treatment (e.g. Forand *et al.*, 2013). Given the unfavorable cost-effectiveness ratio of combined treatment approaches, there is an urgent need to answer this unresolved issue and to investigate the moderator role of concurrent therapies. There is little systematic research about how such medication affects psychotherapy and what clinicians and researchers should do in such situations. Unresolved core questions are (i) Do past or only concomitant medication affect treatment response and the mechanism of action? What type and pattern of medication has an impact? (ii) How frequent are particular patient constellations: Is the patient a non- or partial-responder associated with appropriate or inappropriate psychopharmacotherapy? Would the patient profit more from stopping or changing (optimizing) medication? Has the patient remitted under medications, wants to stop after continuation/maintenance therapy, but experiences recurrence of symptoms or relapse? Currently, tapering off medication before inclusion or keeping the medication constant (combination treatment) are the two major options, providing no further or more specific guidance.
- *Routine outcome monitoring*. There is a clear need of research into routine outcome monitoring as a mean of investigating the accountability of treatments, therapists and treatment centers. Very few research has yet been done into the effects of implementing these systems in clinical practice. There is some evidence that providing therapist with systematic feedback about progress of individual patients on session by session basis is more effective than providing no feedback (Lambert, 2007). In other studies, however, feedback about improvement or deterioration did not lead to enhancement of treatment outcome or even to deterioration, but in these studies feedback was less regularly and less systematically provided (de Jong *et al.*, 2012). Studies need to investigate the optimal timing of feedback, and which patient, therapist and treatment factors moderate the results of providing systematic feedback to therapists about patient progress and deterioration. Apart from providing feedback, routine outcome monitoring can also be used within mental health organizations to compare successful and less successful therapists in order to provide additional training to the latter.
- *Reducing barriers in translating state-of-the-art treatments into clinical practice*. Although effective psychological

treatments (CBT) exist for many disorders, treatment rates are low (Wittchen *et al.*, 2011) and are characterized by long time lapses (typically decades) between disorder onset and treatment (Gustavsson *et al.*, 2011; Wang *et al.*, 2005; Wittchen *et al.*, 2011). Among the few treated, drug and particularly psychotherapy treatment are frequently inadequate or inappropriate. State-of-the-art "CBT" as studied in controlled clinical trials (randomized controlled trials) are rarely applied, despite short- and long-term effect sizes that are larger than for other treatments of mental disorders. When applied, treatment characteristics in routine care typically do not match the randomized controlled trial manual specification or treatment guidelines in terms of type, length and content. The reasons for this unfortunate situation are only partly understood despite promising suggestions on how to change the situation (Crawcour *et al.*, 2012). Increasing the "ecological validity" and clinical utility of CBT programmes by avoiding overly selective inclusion criteria and diagnostic fragmentation might provide guidance on how to deal with comorbid conditions, prior or concomitant drug treatment and with patients not achieving full remission.

Is there a need to advance CBT for anxiety-related disorders?

State-of-the-art in CBT research on anxiety disorders

Using the anxiety-related disorders and CBT as their first-line treatment as an example, we outline in greater detail the specific needs and gaps in psychotherapy research. CBT is the established first line treatment for all kinds of anxiety disorders (Emmelkamp, 2013; Olatunji *et al.*, 2010) and exposure-based CBT is probably the best investigated psychotherapy technique for all anxiety disorder-related conditions (Neudeck and Wittchen, 2012). Exposure consists basically of techniques that expose patients in various ways (i.e. *in vitro*, *in vivo*), or in virtual reality (Meyerbröker and Emmelkamp, 2010) to feared situations. Cognitive psychotherapists acknowledge the value of exposure as an important element in cognitive therapy (e.g. Clark, 1999). Similarly, also in recent CBT-extensions like acceptance-based approaches (acceptance and commitment therapy) exposure is considered as an important component of therapy (Orsillo *et al.*, 2004). Several studies have provided supportive evidence for the role of habituation in exposure therapy, as self-reported fear and physiological arousal showing a declining trend across exposures, consistent with habituation. Results of studies investigating whether within session habituation and between session habituation are associated with outcome are however inconclusive. The success of exposure *in vivo* has also been explained by the acquisition of novel, disconfirmatory evidence, which weakens the catastrophic cognitions. From this perspective, exposure is viewed as a critical intervention through which catastrophic cognitions may be challenged. Although also "pure" cognitive therapy is wide-spread, there are very few methodological-sound data to show that cognitive therapy enhances the effects of pure exposure as stand-alone treatment. Interestingly, exposure was equally effective in promoting cognitive change as exposure plus cognitive therapy in participants with specific phobias, which does not support the idea that cognitions have to be explicitly challenged to elicit cognitive change in exposure treatment (Emmelkamp, 2013).

Reviews and meta-analyses for panic disorder and agoraphobia (Mitte, 2005a; Sánchez-Meca *et al.*, 2010) indicate that exposure *in vivo* has a substantial effect size for agoraphobic symptoms. A total of 60 to 80% of all treated agoraphobics significantly benefit from exposure. Thus, exposure has become the gold standard treatment of agoraphobic patients. Exposure not only leads to a reduction of anxiety and avoidance, but also to a reduction of panic attacks and a reduction of negative self-statements (e.g. Meyerbröker *et al.*, 2013). There is convincing evidence that cognitive therapy dealing with misinterpretations of bodily sensations is highly effective in reducing panic attacks. However, this does not necessarily lead to a reduction of the avoidance behaviour in severe agoraphobic patients. In agoraphobia, exposure-based interventions are usually superior to cognitive interventions (e.g. Emmelkamp, 2004; Moscovitch *et al.*, 2009; Sánchez-Meca *et al.*, 2010). There is little evidence that additional components (e.g. cognitive restructuring, breathing retraining) do increase outcomes above exposure alone (e.g. Craske *et al.*, 1997; Öst *et al.*, 2004). Also interpersonal therapy is less effective than CBT in patients with panic disorder and agoraphobia (Vos *et al.*, 2012). It is important that the therapist guides the exposure *in vivo* practice. In a large randomized controlled trial (Gloster *et al.*, 2011) therapist-guided exposure was more effective than exposure without therapist guidance both in reducing number of panic attacks, avoidance behaviour and improvement of global functioning.

Similar findings were summarized for other anxiety disorders like Social Anxiety Disorder. A meta-analysis of 32 randomized controlled trials found that CBT outperformed waitlist ($d = 0.86$) across outcome domains and at follow-up (Powers *et al.*, 2008). No significant difference was found between combined treatment (exposure with cognitive therapy) and exposure or cognitive methods alone. It is interesting to note that while not significantly different,

exposure methods produced the largest controlled effect size relative to cognitive or combined. In addition, exposure and cognitive methods showed significant improvement on both behavioural and cognitive measures. Similar encouraging results were found for Internet-based treatments for social phobia (see Gallego and Emmelkamp, 2012).

In this domain of CBT research we also see a wide range of studies that link psychotherapy efficacy research with the domain of experimental psychopathology, such as implicit processes reflected in attentional bias towards threat. Cognitive bias modification procedures systematically change patterns of selective attention and selective interpretation. Based on cognitive theories, for example for social anxiety which hold that socially anxious individuals selectively attend to social threat cues, it is assumed that changing these biases by attention bias modification will lead to positive changes in anxiety. Over the course of many trials, participants are expected to implicitly learn to attend selectively to non-threatening stimuli rather than threatening stimuli. These studies showed that anxious individuals are no faster to respond to probes replacing threat cues than to non-threat cues, but they are slower to respond to probes that are opposite to threat cues relative to non-threat cues. A series of primarily laboratory-based studies found attention bias modification in socially anxious participants to lead to reduced anxiety (Hakamata *et al.*, 2010). In a randomized controlled trial of Carlbring *et al.* (2012), this procedure was applied through the Internet, but the positive effects of attention bias training from previous studies could not be replicated in clinically socially anxious individuals. Also in other clinically relevant studies results of attention bias training were very limited (Emmelkamp, 2012). So there is no robust evidence that attention training is of clinical value. Also here, there is a clear need for studies with real clinical patients instead of using "normal" populations with an enhanced score on a questionnaire.

Exposure *in vivo* and response prevention are effective with a substantial number of obsessive-compulsive patients as well, resulting in large effect sizes (Eddy *et al.*, 2004; Fisher and Wells, 2005; Rosa-Alcazar *et al.*, 2008). In contrast to the study of patients with agoraphobia (Gloster *et al.*, 2011) results of controlled studies found therapist controlled and self-controlled exposure equally effective in obsessive-compulsive disorder (OCD) (e.g. van Oppen *et al.*, 2010). A number of studies have compared cognitive therapy based on the cognitive appraisal model with exposure and response prevention and results suggest that both treatments are about equally effective (e.g. Belloch *et al.*, 2008). Interestingly, exposure *in vivo* and response prevention leads to comparable cognitive changes as cognitive therapy. Unfortunately, studies into the long-term effects of cognitive therapy for OCD are lacking.

In PTSD, two different types of psychological treatments have been found to be effective, namely trauma-focused cognitive-behavioural treatment (TF-CBT) on the one hand and eye movement desensitization and reprocessing (EMDR) on the other hand (e.g. Bisson *et al.*, 2007; Powers *et al.*, 2010). Combining cognitive therapy with exposure did not result in added value above exposure alone (e.g. Foa *et al.*, 2005). Interestingly, exposure led to cognitive change without formal cognitive therapy (Foa and Rauch, 2004; Paunovic and Öst, 2001). There is also considerable evidence that other trauma-focused therapies, i.e. narrative exposure therapy and structured writing therapy are also effective (van Emmerik *et al.*, 2008; Robjant and Fazel, 2010).

In recent years a number of studies have been conducted that investigated the effectiveness of various CBT packages targeting various putative core mechanisms involved in patients with generalized anxiety disorder (GAD) by using cognitive and exposure-based principles. Depending on the theoretical assumptions there are three general approaches: (i) that target primarily a reduction of the excessive psychophysiological activation characteristic of GAD by means of relaxation procedures; (ii) that target primarily change of the GAD-specific worrying process by cognitive techniques; (iii) that emphasize exposure and behavioural activation. Most evidence-based treatments for GAD include a complex package of treatment strategies aimed to target the cognitive, behavioural, and emotional processes thought to underlie pathological worry processes and thus all approaches show some overlap in at least some the intervention components. The CBT packages of Borkovec *et al.* (2004) and Dugas and Robichaud (2006) have been found effective in a number of controlled studies in terms of symptom reduction for anxiety as well as worry (e.g. Covin *et al.*, 2008; Gould *et al.*, 2004; Mitte, 2005b). More recent evidence also revealed that exposure based CBT is effective. Interpersonal emotion focused therapy did not enhance the effects of the standard CBT approach (Newman *et al.*, 2011a). Further, these CBT packages were significantly superior to psychodynamic therapy on worrying, trait-anxiety and depressed mood (Leichsenring *et al.*, 2009) and to non-directive therapy (Gosselin *et al.*, 2006). In sum, CBT treatment packages have been found to be effective in GAD. However, as these multi-component packages both include a number of different strategies, it remains unclear which of these is responsible for the observed effects.

Problems in CBT research

The role of comorbidity

One of the problems associated with drawing conclusions based on randomized controlled trials is that often strict inclusion and exclusion criteria are used that exclude patients with comorbid psychiatric (Axis-I and Axis-II) disorders, restricting the clinical utility of findings seriously. Given that most patients with anxiety (and other disorders) meet diagnostic criteria for more than one disorder, this seriously limits conclusions to be drawn on the basis of such academic efficacy studies. Exclusion of these patients will affect the external validity of such clinical studies. Previous studies concluded that the percentage of participants excluded by these criteria ranged between 50 and 80%, suggesting that clinical trials exclude a substantial proportion of patients with other disorders (Hoertel *et al.*, 2012). Systematic research is needed to provide guidance what targets and procedures should be chosen in patients with comorbidity. Restricted evidence from temporally primary anxiety disorder with comorbid anxiety disorders and other comorbid complications strongly suggests that exclusively treating anxiety, without any specific focus on comorbid conditions, is associated with improvement of major depressive disorders with effect sizes that are as large in depression-specific CBT. However, similar evidence is lacking for many other comorbid patterns.

Cognitive enhancers

Standard pharmacotherapy for anxiety disorders includes selective serotonin reuptake inhibitors, tricyclic antidepressants and benzodiazepines. These treatments have an acute but transient effect on anxiety. Anxiety often recurs upon treatment discontinuation. A highly interesting recent development is research into the effects of cognitive enhancers on the speed of habituation/extinction in exposure-based therapies (Vervliet *et al.*, 2013). Research on the role of so-called "cognitive enhancers" is prompted by the growing evidence on fear extinction being weakened by antagonists of the glutamate receptors in the amygdala and evidence for D-cycloserine to enhance extinction in animal studies. Examples of these novel pharmacological enhancers include D-cycloserine, and Yohimbine hydrochloride. Although there are some studies demonstrating that D-cycloserine (Bontempo *et al.*, 2012; Norberg *et al.*, 2008) and Yohimbine hydrochloride (Powers *et al.*, 2009) may indeed enhance extinction in exposure therapy, results of other studies are negative (e.g. Storch *et al.*, 2007; Litz *et al.*, 2012; Meyerbröker *et al.*, 2013). Further studies are needed to investigate the potential of cognitive enhancers in the context of exposure therapies.

Major advances and strengths of CBT and psychotherapy research regarding anxiety and related problems

There is considerable evidence that CBT and exposure-based CBT in particular are highly effective psychotherapeutic treatment tools for most anxiety disorders (including OCD and PTSD), with particularly strong evidence for efficacy in specific phobias, agoraphobia, social anxiety and OCD.

Although the field of anxiety-related disorders is the most advanced, we see similar strong evidence for the effectiveness of CBT for depression and bipolar disorder, somatoform disorder, and the majority of other mental disorders (Emmelkamp, 2013; Hollon and Beck, 2013; Hollon and Ponniah, 2010).

Similar strong levels of evidence are currently lacking for personality disorders (Emmelkamp and Kamphuis, 2007), psychotic disorders (e.g. Jones *et al.*, 2012a) as well as the application of psychotherapeutic methods targeting somatic disease conditions (Smith and Williams, 2013; Sabaté, 2003).

In terms of active components there seems to be some consensus – at least for anxiety disorders, that exposure interventions are a core component and that in most cases, adding cognitive components does not enhance the outcome, because exposure seems to lead on its own to improvement in anxiety and cognitive changes. It is noteworthy though that exposure therapy has undergone a number of transformations. Significant changes in its administration are related to advances in the areas of cognition, fear learning and fear extinction, neuroscience and more recently acceptance-based approaches (Wolitzky-Taylor *et al.*, 2012; Gloster *et al.*, 2012). Each of these have resulted in further shifts in the conceptualization and optimized delivery of CBT and exposure as science-based models of clinical practice.

It seems important to highlight particularly, that recent psychotherapy research has been using more comprehensive research approaches, combining experimental basic investigations with clinical trial methodology to develop a better understanding of the active ingredients as well as mechanism of action of CBT, including effects of epi-(genetic) factors as well as neuroimaging changes in the neural fear and anxiety circuitries.

It should be noted, that in addition to psychotherapy research on targeted established diagnostic groups, there is also an increasing (yet not fully evaluated) trend towards

the development of integrated treatments and integrated cross-cutting principles in psychotherapy.

Open questions, needs and gaps, and concluding remarks

CBT is established as a highly effective treatment method, though it remains yet to be elucidated why it works. Further, we need to acknowledge substantial rates of relapse or recurrence, and also of non-responders. From that, there is a need to better understand why CBT works, what are the underlying mechanisms and of note what are moderators and mediators of these mechanisms. More precisely, questions in this regard are:

(1) *Why are CBT methods effective?* Such research should understand the mechanisms of action and the mechanism of therapeutic change in relation to specified diagnostic groups, specified core aetiological and pathogenic processes and the specific theoretical assumptions under study.
(2) *Which factors and mechanisms are diagnosis-specific* and which are shared or common factors that apply to a wider scope of clinical problems and diagnoses?
(3) *What is the role of individual variation?* Are there specific endo-phenotypes that allow optimization of choice and allocation of interventions to specific patient characteristics? Although psychotherapy – by its very nature is personalized – there is at this point little knowledge about which neurobiological, psychological and behavioural markers may be relevant to improve outcomes.
(4) Given the complex aetiologies of mental disorders, *when, why and how can combined strategies* of drug and psychological interventions be beneficial, respectively when are they not providing additional positive effects.
(5) There is a clear need of *further research into cognitive-enhancers* in the context of exposure-based therapies.
(6) Given the many sufferers of personality disorders and the lack of robust evidence for specific psychological treatments of most personality disorders there is a clear need for c*oncerted action of therapists of different orientations* to evaluate comprehensive treatment protocols in randomized controlled trials.
(7) How can the *notorious gap between research into experimental psychopathology and evidence-based psychotherapy in clinical routine settings* be closed? There is a clear need for experimental psychopathology research in real patients rather than in "normal" students.

Given the established efficacy and benefits of psychotherapy and CBT a particular time has come for concerted action to overcome the current fragmentation of research areas and fields. There is already at this point in the European Union (EU) a substantial, though fragmented, knowledge base regarding basic and applied psychotherapy research in many mental disorders. Appraising the state-of-the-art and existing expertise it seems timely to launch a comprehensive research agenda with clinical trials, basic and translational projects within an overall population-based developmental framework covering all ages, instead of a smaller-scale, narrow research agenda. A number of current developments may turn out to be particularly fruitful in the future to substantially advance our understanding of mental disorders and the way psychotherapy might help to reduce the burden. These include the suggestion to focus more on empirically supported principles of change rather than specific treatment packages for specific disorders (Harvey *et al.*, 2004). Future treatments may therefore focus more on targeting relevant processes rather than on distinct diagnostic categories. Although it remains to be tested whether these approaches result in more effective interventions, it appears that they may help to overcome some of the dichotomies between theory-based and evidence-based approaches in the current literature.

Psychotherapy research in children and adolescents

During the course of development, a substantial number of children and adolescents come to suffer from serious mental health problems and mental disorders. Epidemiological research has indicated that before the age of 18 up to one third of youth meet the full criteria of a psychiatric disorder at some point in time (Costello *et al.*, 2003; Wittchen *et al.*, 2011), with the most frequently diagnosed problems being emotional disorders such as anxiety disorders and depression, and behavioural disorders such as ADHD, oppositional-defiant disorder (ODD), conduct disorder (CD), and substance use disorders. A significant proportion of these children and adolescents are referred to clinical services for treatment of their problems. Fortunately, the therapeutic arsenal for treating childhood psychopathology has expanded markedly in the past few decades, and even better a number of evidence-based interventions have been identified. In this brief section, we provide an overview of the state-of-the-art of current psychotherapeutic programmes for children and adolescents with mental health problems. Limitations and gaps in the research on psychotherapy for youths are highlighted, which are translated into a research plan for moving this field forward.

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State-of-the-art of psychological treatment in children and adolescents

Over the past 50 years, psychotherapy for children and adolescents has mushroomed (Weisz and Kazdin, 2010), and this advancement has shown itself in the development of standardized protocols of theoretically well-grounded interventions for most mental disorders that occur during childhood. A large number of controlled outcome studies have been published evaluating the efficacy of these interventions. In general this body of research has shown that psychotherapy for youth is indeed effective. Meta-analytic studies have demonstrated that children and adolescents who receive psychotherapy are far better off than those who are left untreated (Weisz *et al.*, 1998). In the meantime, it has also become clear that some therapies do better than others, thereby refuting the "Dodo bird verdict", that all psychotherapies, regardless of their specific components or theoretical underpinnings, produce equivalent outcomes. In general, available empirical evidence demonstrates that for most emotional and behavioural disorders in youth cognitive-behaviourally oriented therapies produce the best outcomes (March, 2009), and that the application of such interventions yields better results than care-as-usual approaches (Weisz and Gray, 2008).

Comprehensive reviews indicate that we now have a number of evidence-based interventions for children and adolescents with various types of mental problems (Barrett and Ollendick, 2004; Weisz and Kazdin, 2010). For example, it has become clear that treatments combining exposure and cognitive restructuring are effective for youth with anxiety disorders (including those that were previously regarded as difficult-to-treat such as OCD and PTSD). Interventions consisting of behavioural activation, cognitive restructuring, and interpersonal problem-solving work well with children and adolescents suffering from depression, and parent management training programmes evidently help parents to deal better with the difficult behaviours of youths with ADHD, ODD, and CD thereby reducing the symptomatology of these disruptive behaviour disorders. As noted earlier, most of these treatments are based on cognitive-behavioural principles, which have led some authors including a noted child psychiatrist, John March, to conclude that "The psychotherapy horse race is over: cognitive-behaviour therapy wins" (March, 2009, p. 173). Without any doubt, CBT with its direct, problem-focused, and methodological approach has caused a breakthrough in the effective treatment of mental disorders, including those of children and adolescents, and significant advances have been made.

Is the psychotherapy horse race really over?

From the beginning, CBT has been firmly grounded in research, which may have yielded significant advantages for its scientific substantiation. Meanwhile, a careful analysis of the outcome studies indicates that the evidence for CBTs of childhood disorders has been mainly obtained in university clinics that may not be truly representative of regular clinical settings, which are usually visited by more severely disturbed youth and families (Weisz and Gray, 2008). Studies are beginning to demonstrate that when being applied to disordered youth "in the real world," CBT are less effective than they are in research-based university settings. For example, CBT was shown to be effective in 75% of the children and adolescents with anxiety disorders in a university clinic, but produced a satisfactory treatment result in less than half of the youths referred to a routine outpatient treatment center (Bodden *et al.*, 2008). Disregarding the question whether this difference might be due to the fact that CBT might not be administered properly, client-related as well as clinician-related variables seem to account partially for this difference. For example, youth treated in regular clinical settings present with more severe problems and higher family adversity than youth in university settings. Further, clinicians working in regular clinical settings typically treat a broad array of problems and disorders, often within the same day, which hinders them in their effort to develop or use concentrated expertise in a single treatment for a single disorder (Weisz and Gray, 2008). Clearly, this underlines that further research evaluating the effectiveness of evidence-based psychotherapies in everyday clinical practice is urgently needed.

Although there is convincing evidence that some treatments, such as CBT, are more effective than other types of psychotherapy, it is also true that fairly little is known about the mediators of such successful interventions. For instance, cognitive-behaviour theorists view psychopathology as maladaptive behaviour and dysfunctional thinking that have been acquired via unfavorable learning experiences. Therefore, most cognitive-behavioural treatment packages that have been developed for various types of behavioural and emotional problems consist of a variety of techniques and procedures that may be helpful to correct faulty behaviour and cognition, in order to reduce the symptomatology of these childhood disorders. Therapy outcome studies, however, often do not include an assessment of potential mediating variables, and if they do, mediators are only measured at pre- and post-treatment. This approach does not make it possible to link treatment effects to specific elements of the treatment (Maric *et al.*, 2012). It has been

known for some time that a process analysis, which typically relies on the repeated assessment of symptoms and mediating variables, is the appropriate way for examining the processes underlying successful treatment (Judd and Kenny, 1981), but unfortunately this method is rarely applied. However, it is clear that research adopting this methodology would be highly valuable for further developing and refining psychotherapy for youth with mental disorders.

Such an approach would also provide an opportunity to investigate how effective various psychotherapies are for difficult-to-treat populations, including the offspring of parents with severe mental problems (e.g. substance use, psychosis), children and adolescents with learning problems, youths suffering from pervasive problems (e.g. mental retardation, autism spectrum disorders), children and adolescents exposed to physical and sexual abuse and neglect, and recalcitrant juvenile offenders. This would also relate to the important issue of studying treatment moderators – that is, identifying for whom these effective treatments work. So far, relatively little is known about why a certain type of psychotherapy is effective for one child but fails to produce a positive effect in another child. Research in this area has mainly focused on the examination of descriptive and demographic characteristics such as ethnicity, gender, family status, socioeconomic status, and comorbidity, but this has generally yielded disappointing results. It would certainly be an improvement to study more substantive variables associated with difficult-to-treat families and premature terminators of treatment (i.e. drop-outs). On the side of the child or adolescent, it seems relevant to focus on perturbations in personality development, and how they can be effectively handled in therapy. Obviously, interventions such as mentalization-based therapy (Allen and Fonagy, 2006) and schema-focused therapy (Young *et al.*, 2003) may be important candidates in this regard; however, it is extremely important that these psychotherapies be operationalized and translated into standardized protocols for young people so they can be subjected to scientific evaluation and scrutiny to determine if they meet the criteria of evidence-based treatments. On the side of the family, more attention could be devoted to emotion socialization practices of parents (Eisenberg *et al.*, 1998), and how such practices as emotion coaching can be promoted in psychotherapy of youth with various mental disorders as well as their parents.

Thus, while CBT certainly can be regarded as the primary evidence-based intervention for many of the emotional and behavioural symptoms in youth, it is also clear that a considerable proportion – up to 30% (Ollendick and King, 2012) – of children and adolescents do not respond adequately to this treatment approach, leaving room for improved or enhanced CBT interventions and perhaps other psychotherapies with different theoretical foundations. In other words, the psychotherapy race is only halfway and it seems too early to award the prizes.

Youths' and parents motivation for psychotherapy

Motivation is a critical precondition for (any) psychotherapy. Without motivation, it is highly unlikely that therapy will work and that therapeutic change will occur. Despite its logic, this common factor is often neglected. This is especially true for children and adolescents who often do not recognize the problematic nature of their emotional and/or behavioural symptoms (Kazdin, 2000). Most of the time, parents (and teachers) signal the problem and arrange the referral for psychological evaluation and help, which means that many of these youth "enter" psychotherapy unwillingly, without any clear goal, let alone motivation to participate in psychotherapy. Further, some parents – frequently those who are court-ordered or those who have serious (mental) problems themselves – are unaware of the fact that their child's development is at risk, which results in a hesitating collaboration with therapists and other clinicians. Finally, especially in the case of behavioural problems but also for many emotional problems, it may be necessary to change parenting behaviours in order to reduce child psychopathology, which of course requires explicit motivation from the parents as well. All these examples point out that it is highly recommended to check the motivation of both youth and parents, and if necessary begin treatment with motivational strategies before starting with the actual psychotherapy intervention. There is preliminary evidence to indicate that such a combined motivation–psychotherapy approach may be more effective than a method relying on psychotherapy alone (Chaffin *et al.*, 2011), but obviously more research on this topic is required.

Developmental psychopathology research as a firm basis

Research investigating the origins of mental disorders in children and adolescents is highly relevant for the (further) development of psychotherapeutic interventions targeting these problems. The widely adopted developmental psychopathology model offers important starting points in this respect. One core assumption of this model is that mental disorders are based on multiple and diverse etiological factors, some of which are genetically based while others are more linked to the environment. In most cases, different pathways may signal the need for different treatment modules to address these problems. For

instance, it is well-known that a difficult temperament of the child and a permissive, inconsistent parenting style may contribute to the development of conduct problems in young children, and that these difficulties can be adequately countered by means of a parent management training intervention. However, there is increasing evidence indicating that a subgroup of children and adolescents with conduct problems are characterized by callous-unemotional traits, which may require a more intensive psychotherapeutic approach that also addresses underlying faulty cognitions of these youth and the acquisition of empathy skills (Salekin *et al.*, 2010). A further tenet of the developmental psychopathology account is that the etiology of mental disorders should not only be approached from a risk/vulnerability perspective, but also from a protective or resilience standpoint. For instance, in the past years, executive functioning processes have been shown to help children and adolescents regulate their emotions and behaviour, and that the training and stimulation of such processes may be beneficial for youth with mental health problems. A good example is the Cogmed training that has been developed to remediate the working memory capacity of children and adolescents with ADHD (Klingberg *et al.*, 2005). Considerably more research evaluating the effects of such "positive" psychotherapy interventions is sorely needed and highly welcome. Another principle of the developmental psychopathology framework is that abnormal behaviour should be evaluated within the context of the age and/or developmental stage of the child. Within psychotherapy research there is a general tendency to "apply" a successful approach used with one age group to other age groups, without asking whether this type of intervention is appropriate for that developmental level. A case in point can be found in interventions that facilitate social interaction in youth with autism spectrum disorders. From a normative point of view, it seems appropriate to implement such treatments irrespective of the age of the child (Rogers, 2000). However, in clinical practice it is often noted that younger children with autism spectrum disorder are less hindered by deficits in social interactions and, in fact, that some of these young children have less desire for contact with other youth. Yet, when they reach adolescence, they may become more aware of their social problems and during this developmental stage connection with the peer group becomes increasingly important. As a result, motivation for psychotherapy will increase and social interaction treatment may be more indicated (see White *et al.*, 2010). Thus use of certain psychotherapeutic approaches could benefit from better timing that is strongly guided by research on the developmental manifestation of various emotional and behavioural problems.

Psychotherapy and the brain

In the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), a number of mental health problems that occur during childhood and adolescence are labelled as "neurodevelopmental disorders" (Andrews *et al.*, 2009; Arch and Craske, 2009). These problems, which include autism spectrum disorders, mental retardation, specific learning disorders, and social communication disorders, are primarily caused by impairment of the growth and development of the brain or central nervous system. Typically, youth with these disorders require long-term remediation and care, and during the course of development regularly appeal to psychotherapy. Such treatments can be effective as they improve daily functioning or alleviate a comorbid problem of these children, but are not capable of curing the core disorder, even though they sometimes specifically target a presumed pathogenic process (e.g. training theory-of-mind skills in autistic youth). Neurodevelopmental disorders are closely tied to a dysfunctional brain, and therefore cannot be fully repaired in psychotherapy. This is different for the more prevalent emotional and behavioural disorders, which – although also characterized by aberrant brain processes – are correctable by means of psychological interventions.

With the emergence of (functional) imaging techniques, it is now possible to directly study brain development, brain circuits, and physiological manifestations of emotional and cognitive processes, and to compare them for children with and without mental disorders. In the upcoming years developmental neuroscience will increasingly reveal the pathophysiology of neurodevelopmental as well as other emotional and behavioural disorders in children and adolescents (Nelson *et al.*, 2002). It will be the challenge for psychotherapy research to hitch on to this development by exploring whether and to what extent psychological interventions targeting these problems are able to modify aberrant developmental trajectories at a biological level. Some authors are very optimistic about this scientific endeavour. For example, March (2009) views psychopathology of children and adolescents as a set of dysregulated brain processes, which can be effectively corrected by using the appropriate combination of biological (pharmacotherapy) and psychological (psychotherapy) treatment modules. Obviously, this is an intriguing and important direction for future research in the domain of psychotherapy for youths with mental disorders.

Gaps in psychotherapy research in children and adolescents

This brief overview of the literature on psychotherapy for children and adolescents with mental disorders makes clear that substantial progress has been made with regard to the treatment of various types of behavioural and emotional problems in youths. However, a number of gaps and limitations in this research can be noted:

(1) In general, the quality of treatment outcome research in this field can be typified as good, but there is certainly room for improvement:
(2) To begin with, there is a paucity of studies examining mediators (why does this therapy work?) and moderators (for whom does it work?) of psychotherapies for youth with mental disorders.
(3) Furthermore, most of the research has focused on demonstrating the efficacy of these interventions in trials conducted in university clinics, but studies evaluating their effectiveness in everyday clinical settings and difficult-to-treat populations (e.g. mentally retarded youth, children and adolescents with autism spectrum disorders) are rare.
(4) Finally, although "no motivation – no therapeutic change" is an adage adopted by many clinicians and scientists, research examining the role of motivation in psychotherapy for children and adolescents as well as their parents can hardly be found.
(5) The majority of the youth suffering from behavioural and emotional disorders can be successfully treated by the available psychotherapeutic interventions, but a substantial minority does not respond to these evidence-based treatments.
(6) All human behaviour and so also abnormal behaviour is guided by brain processes, but at present we know too little about the aberrant processes underlying psychopathology in children and adolescents and in what way they can be changed by means of psychotherapy.

Needs

The earlier mentioned gaps also signal a number of needs that can be translated into a roadmap for scientific studies in the upcoming years. The following topics should be addressed during this empirical enterprise:

(1) Improvement of treatment outcome research by:
   - examining theoretically relevant mediating and moderating variables of evidence-based psychotherapies for youths with mental disorders;
   - evaluating the effectiveness of evidence-based psychotherapies for youths and parents who seek help in everyday clinical practice;
   - investigating the efficacy of psychotherapies in difficult-to-treat populations (e.g. mentally retarded youth, children and adolescents with autism spectrum disorders);
   - exploring the additional value of motivational techniques and strategies to increase the efficacy of psychotherapy for youths with mental disorders and their parents.
(2) Translating research into psychotherapy – new insights of ongoing developmental psychopathology research should be employed:
   - to further improve the efficacy of already effective psychotherapeutic interventions;
   - to develop new psychotherapy interventions targeting newly discovered vulnerability and protective factors of childhood psychopathology;
   - to develop more developmentally sensitive and appropriate treatment programmes.
(3) Linking psychotherapy to the brain – investments need to be made in developmental neuroscience research:
   - to establish the links between childhood psychopathology and aberrant processes in the developing brain;
   - to explore whether and to what extent these processes can be corrected and modified by means of psychotherapy.

Following this research roadmap will further improve and expand our psychotherapeutic arsenal for children and adolescents with mental disorders (and their families), which will ultimately help more youth in (re)finding a normative developmental track holding the prospect of a mentally healthy adulthood. As we have noted, much progress has been made; however, we assert that much remains to be done at this exciting juncture.

e-Health and innovation of mental health care

Psychological treatments are considered to be one of the most important interventions to contribute to a reduction of the disease burden of mental disorders. Most patients in Western countries prefer psychological treatment above pharmacological treatments (Kessing *et al.*, 2005; Raue *et al.*, 2009) and in several disorders, psychological treatments are as effective or more effective than pharmacological treatments (Cuijpers *et al.*, 2008b, 2009; Roshanaei-Moghaddam *et al.*, 2011; Mitte, 2005a, 2005b; Smith *et al.*, 2002). Psychological treatments have been well-developed in recent decades, and a number of evidence-based psychological treatments are currently

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available. However, these treatments have not been scaled up to the extent that they may help reduce the disease burden of mental disorders (Kazdin and Blase, 2011). Less than half of the people experiencing mental disorders receive treatment, and this is much lower in adolescents, older adults, people with lower socio-economic status, and people from ethnic minorities. Furthermore, the most dominant format in which psychotherapies are delivered is via individual face-to-face contact. This format is much more expensive and time-consuming than other formats, such as group therapies, guided self-help, and Internet-based treatments (Vos *et al.*, 2005). At the same time, most research shows that formats other than individual treatments can also be effective (Cuijpers *et al.*, 2010; Andersson, 2009; Andersson and Cuijpers, 2009; Smith *et al.*, 2011; Harrison *et al.*, 2011; Carroll and Rounsaville, 2010).

Furthermore, from the perspective of e-mental health the outcome of individual therapy might be enhanced by the implementation of new forms of technology-assisted clinical tools (e.g. self-help, virtual reality or minimal contact therapies) as well as psychometric feedback tools (e.g. patient-focused psychotherapy research) or internet tools (e.g. chat groups). e-Health can be defined as a "field in the intersection of medical informatics, public health and business, referring to health services and information delivered or enhanced through the Internet and related technologies" (Eysenbach, 2001). e-Mental health is the subfield of e-health that is focused on mental health problems.

There are several possibilities as to how research can contribute to a further reduction of the disease burden of mental disorders. This includes a shift in outcome research from a narrow focus on individual effects of treatments, towards a focus on the population at large and public health in general. In order to do this, it is necessary to develop and examine a portfolio of models to deliver psychological treatments and to examine these models from a public health point of view (Kazdin and Blase, 2011). In these models not only individual face-to-face psychotherapies with professional therapists should be included, but also other approaches, such as Internet-based treatments, treatments by non-professionals and para-professionals, self-help strategies, and media-based interventions. This is an important and promising area that may contribute to a reduction of the disease burden, an increase in coverage of treatment, and efficiency in Internet-based treatments. In the remaining sections of this position paper, we will describe this field, its potential and the possibilities of how research may contribute to this area.

State-of-the-art: Internet-based treatments for mental disorders, their advantages and disadvantages

It is now well-established in dozens of randomized controlled trials that Internet-based therapies are effective in the treatment of depression and anxiety disorders (Andrews *et al.*, 2010; Andersson and Cuijpers, 2009; Cuijpers *et al.*, 2009; Gallego & Emmelkamp, 2012; Hedman *et al.*, 2013), as well as for other mental health problems, such as sleep problems (Cheng and Dizon, 2012), pain (Buhrman *et al.*, 2004, 2011; Carpenter *et al.*, 2012), migraine (Trautmann and Kröner-Herwig, 2010; Sciamanna *et al.*, 2006; Devineni and Blanchard, 2005), bulimia (Pretorius *et al.*, 2009), fatigue (Nijhof *et al.*, 2012), pathological gambling (Carlbring and Smit, 2008), and alcohol problems (Blankers *et al.*, 2011; Riper *et al.*, 2008, 2011). Internet-based treatments can be seen as self-help interventions that are conducted through the Internet, which means that patients learn how to apply a psychological treatment to themselves (Andersson, 2009). Research also indicates that if there is some kind of human support (personal, by telephone, email or chat) for the patients available that the effects are larger. Internet-interventions without any form of support are not effective at all or have only small effects (Cuijpers *et al.*, 2011).

Internet-based therapies have several advantages and disadvantages. Important advantages are that it may save therapist time, reduce waiting lists, allow patients to work at their own pace, abolish the need to schedule appointments with a therapist, save travelling time, reduce the stigma of going to a therapist, and ease help for the hard of hearing, as self-help treatments typically work more with visual than auditory information. Another advantage is that it may be possible to reach populations with mental disorders who cannot be reached with other, more traditional forms of treatment. This is important because the majority of people with mental disorders do not receive any treatment at all due to the stigma of mental disorders, prejudices about therapists, lack of willingness to talk to strangers about personal problems, or physical obstacles such as walking problems or long distances. Furthermore, Internet-based therapies can quickly and automatically report patient progress and self-ratings and may be programmed to enhance patients' motivation by presenting a wide range of attractive audiovisual information with voices giving instructions in whichever gender, age, accent, language, and perhaps game format the patient prefers.

There are of course also potential drawbacks to the implementation of Internet-based treatments. One important issue involves the lack of appropriate diagnostic procedures when patients start working with an Internet program

without the involvement of a professional therapist (Ameringen *et al.*, 2010). Another concern is that patients do not apply the treatment in an appropriate fashion. Although this could result in the participant wasting time and energy, more importantly it might also result in the aggravation rather than the amelioration of symptoms. Another important issue is that the patient might not complete the course of therapy. For example, in an early study, it was found that only 50% of those who started with a bibliotherapy programme for phobia finished it (Rosen *et al.*, 1976). More recent studies show that open access to a website for mental disorders often results in drop-out rates of greater than 50% (Christensen *et al.*, 2006). Although there are no indications that the drop-out rates are higher in Internet-based treatments than in traditional psychotherapies, drop-out rates are considerably higher for Internet therapy without professional involvement. Side effects of Internet-based treatments have not been examined well, just as possible negative effects of psychotherapies in general.

Many researchers in Europe have a strong interest in Internet interventions. In May 2012, European researchers in this area founded the European Society for Research on Internet Interventions (ESRII; http://www.esrii.eu), in order to exchange new findings and collaborate in research and raising research funds. Ninety participants from 11 European countries came to this founding meeting.

Strategies to advance evidence-based Internet-based treatments: questions, gaps and needs

Overall we can distinguish four areas where future research might help to further develop and implement evidence-based Internet interventions:

(1) Application in routine care of the Internet-based treatments that have proven to be effective.
(2) Further development of newly developed and better Internet-based treatments.
(3) Research on the development and application of technological innovations, such as serious gaming, smartphones and ecological momentary assessments.
(4) Generic issues of dosage and feedback.

How can evidenced-based treatments be applied?

As indicated earlier, the efficacy of Internet-based treatments for common mental disorders has now been well established. The next step in this type of research is to conduct practice-oriented research on how this knowledge can be applied and its relative effectiveness in routine (mental) health care settings (Castonguay *et al.*, 2013). Internet-based interventions could be examined and tested in the following areas:

- *Prevention*. Especially in the field of indicated prevention (aimed at people with subthreshold symptoms not meeting formal diagnostic criteria for a mental disorder), Internet-interventions can be applied very well. These indicated preventive interventions are often simplifications of full treatments for mental disorders (Cuijpers *et al.*, 2005, 2008a). Because Internet-based treatments are automated versions of standard psychological treatments, and because the threshold to participate is low and costs are low, indicated prevention is an area where this type of intervention has promise.
- *Primary care*. Internet-based guided self-help can be very useful in the treatment of mental disorders in primary care. Because general practitioners are becoming less willing to prescribe antidepressive medication (because this has been found to be less effective in mild to moderate depression; Fournier *et al.*, 2010; Kirsch *et al.*, 2008), standardized Internet-based treatments can be an excellent alternative treatment for mild to moderate depression and anxiety disorders. First results of trials in this area are promising (Kessler *et al.*, 2009), but more research is needed.
- *Specialized mental health care*. Internet-based treatments can be useful in several ways in specialized mental health care, including immediate access while waiting for a first appointment (in order to reduce costs, number of face-to-face treatment sessions, and to speed up recovery), blended modules (in which patients work through Internet-based modules during face-to-face treatment), and relapse prevention modules. In this field some pilot projects are running, but more trials on (cost)effectiveness are needed (Andersson *et al.*, 2011; Warmerdam *et al.*, 2010).
- "*Independent*" *e-mental health services*. Because there is not always a need for personal contact between the patient and therapist, Internet-based treatments can be organized outside the traditional mental health care system. Some experiments have been conducted with such independent services, but more research is needed, especially because good referral methods to traditional mental health care are needed when Internet-based treatment does not result in sufficient improvement in the patient. These services may be more cost-effective than traditional services and may increase treatment rates in patients who currently do not receive treatment.

- *General medical settings*. Internet-based interventions can be useful in several other settings. Several trials have shown that these interventions can be used in general medical settings for patients with comorbid mental and somatic disorders (Van Bastelaar *et al.*, 2011; Kroenke *et al.*, 2010). Because many patients with mental health problems currently do not receive any treatment for their mental health problems, Internet-based screening and treatment may increase treatment rates, without strong increases in costs.
- *Other settings*. The fact that Internet-based treatments have been found to be effective can also be applied in several other settings where no or only very little research has been conducted until now, such as occupational settings and school settings.

Further development of new and better Internet-based treatments

Although Internet-based guided self-help treatments have been found to be effective, several important improvements are still possible and research in this area is highly likely to yield new applications.

One important research question is whether self-guided Internet-based treatments can be as effective as guided treatments. Until now the evidence clearly shows that self-guided treatments without any professional support are less effective than guided interventions. For example, in the field of depression it has been found that self-guided treatments have an effect size of $d = 0.28$, while guided self-help has an effect size of 0.61, which is comparable to the effects of face-to-face interventions for depression. However, this does not mean that self-guided treatment cannot become as effective as guided self-help interventions. For example, in a recent Australian trial it was found that self-guided treatment was as effective as guided self-help in specific conditions (Farrer *et al.*, 2011). It is also possible that, for example, better design of websites, or the use of mobile phones to support the traditional web-based intervention, may result in comparable effects without the use of professional support. If this improvement were possible, it would make the logistics of treatment planning much easier, because therapists would no longer be needed (for some patients with not too complex problems) receiving type of treatment.

Another important area of research concerns the logistical organization of Internet-based treatments. Although the effects of these treatments have now been well-established, it is not clear how many treatment sessions are needed, who can deliver the treatments (in the UK for example, low-intensity treatments are delivered by psychological well-being practitioners who have completed a 12-months training programme), how many treatment sessions are needed, and what the intensity should be.

Research in this area may also contribute considerably to our understanding of psychological treatments in general. Because it is logistically easier to conduct large randomized trials through the Internet than in traditional settings, research on working mechanisms, mediators and moderators can be stimulated considerably and may lead to more understanding and better focused psychological treatments in general. However, the intrinsic remoteness of participants in internet studies may result in less complete data.

Research on Internet-based treatments has focused mostly on common mental disorders, such as depression, anxiety disorders, addiction, and stress-related problems. Furthermore, most of these treatments have been based on CBT. However, it is now increasingly acknowledged that Internet-based treatments may also be useful in other mental disorders, such as bipolar disorders and psychotic disorders. Pilot projects and feasibility studies in this area could lead to an extension of the scope of these treatments. Furthermore, initial trials using other types of treatment (psychodynamic therapy, interpersonal psychotherapy; Andersson *et al.*, 2012) have been found to be successful as well, possibly leading to a further increase of treatment rates.

Research on cost-effectiveness is needed. Although initial studies in this field show promising results (Andersson *et al.*, 2011; Warmerdam *et al.*, 2010), further studies are needed to examine what the exact benefits of Internet-based treatments are in terms of cost-effectiveness ratios.

Research on technological innovations

Internet-based treatments have been developed as interventions that can be applied at a computer with Internet access. The technological developments are, however, moving very fast. The Internet can now be accessed easily through mobile phones, allowing the development of a new generation of Internet-based treatments. The first pilot projects are now running (for example the EU funded ICT4Depression project, in which a mobile application for depression is developed in which the sensors in the phone are used to support the intervention). Mobile applications offer new possibilities to increase access to Internet-based treatments, making these treatments easier to use, and using day-to-day information from the phone to improve treatments. More research can speed up developments in this area.

In line with the move from the traditional Internet to the mobile phone, the development of Ecological Momentary Assessment (EMA; Kaplan and Stone, 2013) will

become an interesting new tool for research on mental disorders in general. In EMA information from the sensors in the mobile phone (accelerometer, GPS, audio, contact with other phones) can be combined with personal information from the user (where are you, what are you doing, how is your mood, how did you sleep). This will allow examination of mental health problems in real time, and a move away from retrospective information about mental health towards actual assessment during day-to-day life. This will allow modeling of mental health problems on an individual level and may lead to new, personalized treatments of mental disorders.

There are several other technological developments that may have a considerable impact on mental health treatments:

- Telepsychiatry using television sets and allowing the provision of face-to-face treatments and support from a distance (without travelling). The technology is available but trials in the mental health field have hardly started yet.
- The development of avatars: together with the improved possibilities to recognize emotions through webcams, it may be possible to develop avatars which can replace human contact more and more.
- Virtual reality applications for mental disorders have been developed in several trials and may become more readily available.
- Serious gaming may give new possibilities to treat or help people with mental disorders who are not motivated to get engaged with traditional treatments (adolescents; people from lower socio-economic groups).
- Large computerized databases with patient information on characteristics and treatments received may be useful for the development of personalized treatments.

Mental health as a question of dosage and patient-focused research

Psychotherapy is successful for the majority of patients, but further research is needed focusing on how it can be improved for those people for whom it does not work. In the future the outcome of individual therapy might be enhanced by implementing new forms of technology-assisted clinical tools (e.g. virtual reality applications or minimal contact therapies) on one side and by supplementing the traditional treatment modalities by psychometric feedback tools (e.g. patient-focused psychotherapy research, quality management) or internet tools (e.g. chat groups) in preventing relapse (e.g. Lutz *et al.*, 2009; Newman *et al.*, 2011b).

The most efficacious amount of treatment sessions or therapist contact varies by disorder, level of the specific disorder, motivation, attrition and compliance (Newman *et al.*, 2011b). More research is needed on the question of how much therapy for which patient is enough (Barkham *et al.*, 2006). Instead of a specific package of treatment length (e.g. 10 sessions) for all patients, a more patient-specific approach about the amount of sessions depending on the needs of the patients seems to be necessary (Lutz *et al.*, 2009, 2011). Some patients might need more sessions than others and there is a lack of knowledge on moderating variables of treatment length (e.g. psychometric feedback on treatment progress, early response patients or therapist effects). This kind of knowledge can be seen as the basis for a stepped-care approach of treatment delivery (e.g. Clark *et al.*, 2009).

Crucially, research focusing on "real time" psychometric feedback over the course of treatment (supported by modern software tools as well as data entry systems like touch screens) has shown its effect on outcome and in developing patient-specific adjustments in treatment length, not only for adults but also for the treatment of children and youths (e.g. Bickman *et al.*, 2011). These kind of "real time" feedback systems lead to more treatment sessions and better final outcome for patients at risk for negative outcome and shorter treatments for early responders (e.g. Shimokawa *et al.*, 2010). Furthermore the large databases generated can be used for a more personalized treatment package based on predictive models of intake characteristics and early change information of patients (Lutz *et al.*, 2005).

Gaps and needs in research on e-mental health and innovation of mental health care: It is not clear when and how each of the treatment formats of psychological treatments (individual; group, family; guided self-help; Internet-based) is able to help better.

A shift in outcome research is needed towards more focus on reaching the right target groups, realizing effects in populations instead of individuals, reductions in disease burden and quality of life, and improvement of coverage of treatments.

For individual therapy generic issues of dosage and feedback with the aim of reducing treatment failures in the context of e-mental health should be further investigated.

A portfolio of models to deliver psychological treatments should be developed and methods to examine these models from a public health point of view.

More research on applying and implementing e-mental health tools and Internet-based treatment for mental disorders in several specific fields is needed:

- prevention of mental disorders and public health;
- treatment of mental disorders in primary care;
- treatment of mental disorders in specialized mental health care;
- general medical settings.

New and better Internet-based treatments should be developed:

- Comparative research on different treatment formats and unguided self-help can help in answering which treatment format helps best in which context.
- More research is needed on how and in which setting Internet-based treatments should be delivered.
- Research should not only be aimed at common mental disorders, but also at bipolar and psychotic disorders.
- Although there is already some research on cost-effectiveness of Internet-based treatment, this should be expanded to get a full overview of the benefits.

Technological innovations in e-mental health and Internet-based treatments can contribute considerably to the further development of these treatments:

- Research on the use of mobile applications may advance the field considerably.
- EMA is a promising new field that may have a large impact on Internet-based treatments but also on the field of psychology and psychiatry in general.
- More research in other new technologies is needed: the development of telepsychiatry, the development of Avatars as coaches in psychological interventions, virtual reality, and serious gaming.

Conclusions

Although psychological treatments have been well-developed in recent decades, they have not been scaled up to the extent that they may help reduce the disease burden of mental disorders sufficiently. In order to better contribute to a reduction in the disease burden of mental disorders, psychotherapy research has to move from a narrow clinical focus on individual patients to more public health strategies and treatments that can be applied more simply and more cost-effectively. One important option is to focus on Internet-based treatments and e-mental health tools (e.g. to support "real time" clinical decision-making to prevent treatment failure or relapse).

In this field, four broad research areas can be distinguished: (1) research on how to apply the knowledge in routine mental health care that Internet-based treatments are efficacious; (2) further development of existing Internet-based treatments; (3) the use of technological innovations, such as a move to the mobile phone, serious gaming (Merry *et al.*, 2012), and the use of Avatars, and (4) generic issues of dosage and feedback with the aim of reducing treatment failures. All this will lead us to more information not only about the common and specific effects of psychological treatments but also about the question of how much therapy for whom in which setting is necessary.

Acknowledgements

This article was generated as part of the activities of the group of leading European experts on psychological research and intervention, in order to provide an assessment of the state-of-the-art of research in different domains, identifying major advances and promising methods and pointing out gaps and problems which ought to be addressed in future research. A similar critical appraisal with partly similar conclusions is concurrently provided elsewhere (Schumann *et al.*, 2013) by the ROAMER workgroup "Biomedical research". Experts in both work groups have been selected for their academic excellence and for their competence in the different units of analysis needed to comprehensively characterize particular symptom domains. Their contributions do not aim to be systematic reviews of the field but rather provide a well-informed opinion of the authors involved. They also do not represent official statements of the ROAMER consortium, but are meant to inform the discussion on psychological research and intervention in mental disorders among interested stakeholders, including researchers, clinicians and funding bodies. Recommendations made in this issue will undergo a discussion and selection process within the ROAMER consortium, and contribute to a final roadmap, which integrates all aspects of mental health research. We thus hope to provide an informed and comprehensive overview of the current state of psychological research in mental health, as well as the challenges and advances ahead of us.

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Declaration of interest statement

The authors have no competing interests.

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