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Pretreatment biomarkers predicting PTSD psychotherapy outcomes: A systematic review

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ABSTRACT

Although our understanding of the relationship between posttraumatic stress disorder (PTSD), brain structure and function, neural networks, stress-related systems, and genetics is growing, there is considerably less attention given to which biological markers predict evidence-based PTSD psychotherapy outcomes. Our systematic PRISMA-informed review of 20 studies examined biomarkers as predictors of evidence-based PTSD psychotherapy outcomes. Results provide preliminary evidence that specific structural and functional neural systems (involved in information processing), glucocorticoid sensitivity and metabolism (part of the hypothalamic–pituitary–adrenal axis and the response to stress), heart rate (involved with fear habituation), gene methylation, and certain genotypes (associated with serotonin and glucocorticoids) predicted positive response to PTSD treatment. These pre-treatment biomarkers are associated with processes integral to PTSD treatment, such as those affecting fear learning and extinction, cognitive restructuring, information processing, emotional processing, and interoceptive monitoring. Identifying pre-treatment biomarkers that predict treatment response may offer insight into the mechanisms of psychological treatment, provide a foundation for improving the pharmaceutical augmentation of treatment, and inform treatment matching.

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Contents

1. Introduction 141
2. Methods 141
   2.1. Search strategy 141
   2.2. Study selection 141
   2.3. Data extraction 142
   2.4. Quality assessment 142
3. Results 143
   3.1. Search findings 143
   3.2. Systematic review 143
      3.2.1. Neuroanatomical/functional neuroimaging biomarkers 143
      3.2.2. Glucocorticoid biomarkers 148
      3.2.3. Electrodermal activity and heart rate 148
      3.2.4. Genetic biomarkers 149
4. Discussion 149

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4.1. Neuroanatomical/functional neuroimaging biomarkers 150
4.1.1. Neuroanatomical/functional neuroimaging biomarkers: discussion 150
4.1.2. Neuroanatomical/functional neuroimaging biomarkers: future directions 151
4.2. Glucocorticoid biomarkers 151
4.2.1. Glucocorticoid biomarkers: discussion 151
4.2.2. Glucocorticoid biomarkers: future directions 151
4.3. Electrodermal activity and heart rate biomarkers 151
4.3.1. Electrodermal activity and heart rate biomarkers: discussion 151
4.3.2. Electrodermal activity and heart rate biomarkers: future directions 152
4.4. Genetic biomarkers 152
4.4.1. Genetic biomarkers: discussion 152
4.4.2. Genetic biomarkers: future directions 152
4.5. Limitations 153
4.6. Future directions 153
Acknowledgements 153
References 153

1. Introduction

Over the past several decades, researchers have attempted to better understand the biological correlates of the development and maintenance of posttraumatic stress disorder (PTSD; see Michopoulos et al., 2015; Schmidt et al., 2013; Zoladz and Diamond, 2013, for a review). In particular, researchers have examined the role of brain structure and function, neural networks, stress-related systems (e.g., hypothalamic-pituitary-adrenal axis; HPA), and genetics. However, considerably less attention has been given to how these biological markers predict PTSD psychotherapy outcomes. Reviewing and synthesizing studies that identify pre-treatment biomarkers associated with PTSD psychotherapy outcomes may offer critical insight into the how treatment alleviates the pathophysiology of PTSD. Additionally, the use of objective markers in a clinical setting can address the limitations of self-report measures to better match individuals with treatments, tailor treatment for specific individuals, and improve overall treatment response rates (Schmidt et al., 2013).

The Institute of Medicine (IOM IoMCoToPSD, 2008), American Psychological Association (APA, 2013), and the VA/DoD Clinical Practice Guidelines for PTSD (2010) recognize several psychotherapies as evidence-based PTSD treatments. Of these, trauma-focused cognitive behavioral therapy (CBT), cognitive processing therapy (CPT), and prolonged exposure (PE) are recommended as front-line psychotherapies for PTSD. Eye movement desensitization and reprocessing (EMDR) is also considered an effective psychotherapy, but may be best understood as an exposure technique (Davidson and Parker, 2001).

There is a substantial body of literature that supports the use of these evidence-based treatments for PTSD; these interventions are associated with decreases in avoidance, re-experiencing, negative cognitions, and mood-related symptoms. However, partial and non-response rates to these treatments are sizable and can range from 20% to 60%, depending on the population and index trauma (Bisson et al., 2013; Schottenbauer et al., 2008; Van Minnen et al., 2002). Researchers have hypothesized that pre-treatment biomarkers (e.g., brain activity and morphology, physiological response, neuroendocrine response, genetics) may predict whether an individual responds to psychotherapy. Biological markers may be involved in underlying processes necessary for successful PTSD psychotherapy response, such as those affecting fear learning and extinction (Charney, 2014; Rauch et al., 2009; Rodrigues et al., 2009), cogntitive restructuring (Furmark et al., 2002), emotional processing (McGaugh, 2004; Roffman et al., 2005), and/or internal (interoceptive) monitoring (Craig, 2003).

The purpose of this study is to provide a systematic and informed review of research that examines pre-treatment biomarkers in predicting evidence-based PTSD psychotherapy outcomes. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Moher et al., 2009) to identify, select, and critically appraise relevant research while minimizing bias. The first section of our review summarizes the results reported for each biomarker category separately (i.e., neuroanatomical/functional neuroimaging, glucocorticoid, electrodermal/heart rate [HR], and genetic). In the second section we provide a critical discussion of the results, focusing on why specific biomarkers may predict PTSD treatment outcomes. Finally, we present recommendations for future research to help advance the field. An overarching goal was to provide a summary of the research in a format that is readily understood by researchers and clinicians who may not have a background in biology or neuroscience. Our examination reflects the most comprehensive and up-to-date review of the relationship between biomarkers and evidence-based PTSD treatment outcomes available.

2. Methods

2.1. Search strategy

All methods followed PRISMA guidelines to identify suitable publications. We did not include any date limitations on our search and utilized PsychINFO, PubMed/Medline, Web of Science, and PILOTS databases. Our first search was performed on December 9, 2014 across all databases and was repeated on October 28, 2015 and May 20, 2016 to ensure our review reflected the most up-to-date research. We used the following search terms at each time point: (CBT or therapy or EMDR or PE or Prolonged Exposure or CPT or Cognitive Processing Therapy or psychotherapy or cognitive behavior therapy or cognitive behavioral therapy or psychodynamic or meditation or yoga or mindfulness) AND (posttraumatic stress disorder or PTSD or post-traumatic stress disorder or posttraumatic stress disorder) AND (biomarker or biological marker or gene or brain imaging or neuroimaging or hormone or neuroendocrine or psychophysiology or imaging or endocrine or cortisol or heart rate or heart rate variability or fMRI or MRI or PET or fNIRS or SPECT or EEG or ERP or MEG or blood flow or blood volume or skin conductance or metabolites or galvanic skin response or startle or eye blink or EMG or pupillometry).

2.2. Study selection

During our December 2014 search, 3667 articles were found. On October 28, 2015 (searching December 10, 2014–October 28, 2015), 423 new articles were found. On May 30, 2016, a final search was