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Prevention of chronic PTSD with early cognitive behavioral therapy. A meta-analysis using mixed-effects modeling

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ABSTRACT

Post-traumatic stress disorder (PTSD) is of great interest to public health, due to the high burden it places on both the individual and society. We meta-analyzed randomized-controlled trials to examine the effectiveness of early trauma-focused cognitive-behavioral treatment (TFCBT) for preventing chronic PTSD. Systematic bibliographic research was undertaken to find relevant literature from on-line databases (Pubmed, PsycINFO, Psyndex, Medline). Using a mixed-effect approach, we calculated effect sizes (ES) for the PTSD diagnoses (main outcome) as well as PTSD and depressive symptoms (secondary outcomes), respectively. Calculations of ES from pre-intervention to first follow-up assessment were based on 10 studies. A moderate effect (ES = 0.54) was found for the main outcome, whereas ES for secondary outcomes were predominantly small (ES = 0.27–0.45). The ES for the main outcome decreased to small (ES = 0.34) from first follow-up to long-term follow-up assessment. The mean dropout rate was 16.7% pre- to post-treatment. There was evidence for the impact of moderators on different outcomes (e.g., the number of sessions on PTSD symptoms). Future studies should include survivors of other trauma types (e.g., burn injuries) rather than predominantly survivors of accidents and physical assault, and should compare early TFCBT with other interventions that previously demonstrated effectiveness.

Although most individuals are resilient in the face of traumatic events, or recover from acute stress reactions over time without any psychosocial or medical aid (according to Bonanno, Galea, Bucciarelli, & Vlahov, 2007; Norris, Tracy, & Galea, 2009, for example), other survivors develop a mental disorder during the first three months following the trauma, most commonly an acute stress disorder (ASD) at the first month post-trauma and/or an acute post-traumatic stress disorder (PTSD) by the end of the following two months. For ASD, prevalence rates vary from 6% in accident survivors (Bryant et al., 2008) to 59% in rape victims (Elklit & Christiansen, 2010), whereas acute PTSD rates range from 23% in accident survivors (Ehlers, Mayou, & Bryant, 1998) to 47% in rape victims (Brewin, Andrews, Rose, & Kirk, 1999). Considering that women more often than men are likely to develop posttraumatic stress symptoms, the prevalence rates are often found to be lower for both genders following incidents of a technical nature (i.e., accidents) as compared to events involving a human perpetrator (Wittchen, Gloster, Beesdo, Schönfeld, & Perkonigg, 2009).

Because the natural course of PTSD is mostly chronic (Wittchen et al., 2009), there is a high burden of disease for the individual and for society (Kessler, 2000). For example, PTSD is associated with suicidal thoughts and behaviors (Panagioti, Gooding, & Tarrier, 2012) and co-occurs with other mental disorders such as depression, anxiety, and substance-use disorders (Breslau et al., 1998; Perkonigg et al., 2005). In addition, lower quality of life (Olatunji, Cisler, & Tolin, 2007) and higher medical costs as well as work impairment (Greenberg et al., 1999) are found in individuals with PTSD compared to those with other anxiety disorders. For these reasons, we believe that there is an urgent need in public-health policy for psychosocial interventions to prevent chronic PTSD.

Recently, an international expert group recommended brief forms of trauma-focused cognitive-behavioral treatment (TFCBT) for adults with ASD or acute PTSD (Bisson et al., 2010). These early TFCBT approaches included psychoeducation, rationale for exposure, imaginal and in-vivo exposure, as well as homework assignments. Some, but not all TFCBT approaches integrate relaxation techniques, cognitive restructuring, and anxiety management. Limited evidence from randomized controlled trials (RCT) suggests

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that early TFCBT is effective in reducing subsequent PTSD. In previous meta-analyses (Kornør et al., 2008; NICE, 2005; Roberts, Kitchiner, Kenardy, & Bisson, 2009a, 2009b), the relative risk (treatment vs. control condition) for PTSD diagnosis varied between 0.40 [95% CI 0.16, 1.02] and 0.54 [95% CI 0.31, 0.95] at post-treatment as well as 0.36 [95% CI 0.17, 0.78] and 0.64 [95% CI 0.42, 0.99] at 3–6 months, respectively. In addition, there is limited evidence suggesting that anxiety and depression scores were more improved in the early TFCBT conditions compared to the control conditions. However, several limitations have to be taken into consideration. First, findings were based on a small study number ($k = 3$–5), in particular for meta-analyzing follow-up assessments (e.g., $k = 2$, Roberts et al., 2009a, 2009b). Second, the NICE (2005) meta-analysis included RCTs that examined TFCBT for individuals with chronic PTSD (more than 6 months after the traumatic event; Ehlers et al., 2003) or that did not use exposure techniques (Echeburúa, Corral, Sarasua, & Zubizarreta, 1996). Third, the Kornør et al. (2008) meta-analysis included studies that were conducted by only one research team (namely Bryant and colleagues). Lastly, in the Roberts et al. (2009a, 2009b) meta-analysis, data of three original studies were only included when participants met the ASD and acute PTSD diagnosis. Hence, excluding data of other participants made the assumption of randomization in the original studies invalid. Meanwhile, three new RCTs were published by independent research teams of different countries (from Germany: Freyth, Elsesser, Lohrmann, & Sartory, 2010; from the USA; Rothbaum et al., 2012; from Israel: Shalev et al., 2012), including at least a 3-months follow-up assessment. None of these RCTs were included in any of the aforementioned meta-analyses.

The aim of this meta-analytic review is: (a) to examine the effectiveness of early TFCBT from pre-treatment to follow-up assessment; and (b) to determine its long-term effectiveness on the number of diagnoses of chronic PTSD as well as c) on the severity of self- and expert-rated PTSD symptoms, and the number of self-rated depressive symptoms. We used hierarchical linear models (HLM) to account for the nested data structure encountered in meta-analyses. Compared to conventional analysis of data, this procedure provides a moderator with analyses as well as using Bayesian estimation of the overall effect size, both of which have been shown to be more appropriate in meta-analyses with a small number of studies (Castro & Gaviria, 2000). The structure of this paper follows the recommendations by the Meta-Analysis Reporting Standards (MARS; The American Psychological Association Publications and Communications Board Working Group on Journal Article Reporting Standards, 2008).

Method

Literature research and selection of studies

A systematic search was undertaken to find relevant literature from on-line databases (Pubmed, PsycINFO, Psyndex, Medline) using the following keywords: Acute stress disorder (ASD), Post-Traumatic Stress Disorder (PTSD), early intervention, trauma-focused therapy, prevention of PTSD, and acute PTSD. Additional papers were found through references in reviews and empirical studies, as well as by Internet search and contact with other research groups. Studies published up until the end of September 2012 were surveyed. The search was restricted to published randomized controlled studies. Included were those studies in which a) the adult patients who were treated and showed early post-traumatic symptoms after an event met criteria A of the DSM-IV (APA, 1994), or their symptoms fulfilled the criteria of the acute stress disorder, or fulfilled the criteria of acute PTSD in accordance with the DSM-IV (APA, 1994); b) early trauma-focused cognitive behavior therapy (early TFCBT) was initiated within 90 days post-trauma; c) a follow-up assessment at least 3 months post-treatment was included; d) the study could be obtained in English; e) the intervention group included more than 10 patients, since a sample size of $\geq$10 is recommended for adequate precision in calculating the effect-size variance (Hedges & Olkin, 1985); and f) the PTSD diagnosis was assessed at a minimum of 3-months follow-up using a standardized clinicians' rating. Early TFCBT was defined as an intervention of more than one session, including psychoeducation, rationale for exposure, imaginal and in-vivo exposure as well as homework assignments. The searching and selection procedures were done by two independent reviewers.[2] Disagreements with regard to inclusion or exclusion of a study were resolved by discussion with the authors (S. K., C. K.).

Study characteristics

An initial narrative synthesis was undertaken to describe the scope of the studies (sample sizes, frequency and type of traumatic events, duration of follow-up period, inclusion/exclusion criteria, percentage of dropouts, loss to follow-up, and patient and intervention characteristics). The data of the primary studies were extracted by two independent raters and checked by a second reviewer. Discrepancies with regard to the study characteristics were resolved by discussion with one of the authors (C. K.).

The literature has frequently shown how studies with low methodological quality tend to yield extreme results (e.g., MacLehose et al., 2000; Moher et al., 1998). Hence, the methodological quality of the primary studies was assessed using the checklist of Downs and Black (1998). The scale assesses the methodological quality with four subscales: reporting, external validity, internal validity, and power. The maximum number of points is 32 for RCTs. This instrument has high internal consistency (Kuder–Richardson-20 = 0.89), high test–re-test reliability ($r = 0.88$), and good inter-rater reliability ($r = 0.75$). To assess the inter-rater reliability of the scale, two postgraduate students in clinical psychology received 4 h of training in the use of the scale by one of the authors (C. K.). The students were blind (blackened text) to the investigators as well as to whether a given study was excluded. They rated the included studies and 25% of the excluded studies. Then the ratings were compared with those of one of the authors (C. K.). The inter-rater reliability for the quality assessment was assessed using intra-class correlation (ICC) coefficients for rater consistency in a two-way mixed model, with raters as fixed and studies as random factors.

Outcome measures

The primary outcome of the present meta-analysis was the diagnosis of PTSD, which was assessed by using any clinician-administered interview (i.e., *Clinician-Administered Posttraumatic Stress Disorder-Scale*, Blake et al., 1995; *PTSD Symptom Scale Interview-Version*, Foa, Riggs, Dancu, & Rothbaum, 1993; German version of the *Anxiety Disorders Interview Schedule* for DSM-IV, Schneider & Margraf, 2006) in the original studies. We also included the dropout-rates between pre- and post-intervention as a dichotomous outcome. Moreover, we used data from self-rating measures for assessing post-traumatic stress and depressive symptoms as continuous outcomes (i.e., the subscale *Avoidance* and the subscale *Intrusion* of the *Impact of Event Scale*, Horowitz, Wilner, & Alvarez, 1979; the *Posttraumatic Diagnostic Scale*, Foa, Cashman, Jaycox, and Perry (1997); the *Beck*

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