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Effects of online intervention for depression on mood and positive symptoms in schizophrenia☆

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ABSTRACT

Background: Depression is common in schizophrenia. Whereas the improvement of mood and self-esteem represents a subjective treatment priority for many patients, depression is rarely a primary target for clinical intervention. The present trial examined whether an online intervention for depression can ameliorate depressive symptoms in schizophrenia.
Methods: A total of 58 individuals with schizophrenia were invited to participate in an online survey which encompassed the *Center for Epidemiologic Studies-Depression Scale* (CES-D, primary outcome), the *Patient-Health-Questionnaire-9* (PHQ-9) and the *Paranoia Checklist*. Subsequently, telephone interviews were conducted to verify diagnostic status and assess symptoms (*Positive and Negative Syndrome Scale*, PANSS). Participants were randomized either to the experimental condition (online depression intervention) or to a waitlist control condition. Three months after inclusion, a reassessment was carried out (self-report and telephone interview blind for group condition). The trial was registered (registration: DRKS00007888).
Results: Participants in the treatment group showed a significant decline of depressive symptoms at a medium-to-large effect size, as assessed with the CES-D and the PANSS depression item, in comparison to the waitlist control group (completer (CC) and intention-to-treat analyses (ITT)). For the PHQ-9 (CC and ITT) and the PANSS distress subscale (CC only) significance was bordered at a medium effect size. Completion at the post-assessment after three months was 84%.
Discussion: Depression in schizophrenia is both underdiagnosed and undertreated. To reduce the large treatment gap in the disorder, low threshold strategies are urgently needed. Online treatment and bibliotherapy may represent valuable tools to address patients' needs beyond the treatment of the core positive syndrome.

1. Introduction

1.1. Depression in schizophrenia

Delusions and hallucinations (i.e., positive symptoms) are the defining features of psychosis and until recently represented the conventional target for the treatment of schizophrenia (Suzuki, 2011). In contrast, depressive symptoms in this disorder received comparatively little attention, presumably owing to historical and diagnostic reasons. Since Kraepelin (1899) who separated schizophrenia (then called dementia praecox) from affective disorders and more recently Schneider (1959) who confined the core of schizophrenia to positive features, depression is often regarded a negligible and secondary symptomatic feature of psychosis. Moreover, some phenomena that would be counted as depressive symptoms in other disorders are labeled as negative symptoms in schizophrenia (e.g., social withdrawal) or even receive distinct diagnostic terms once a diagnosis of schizophrenia has been determined (Burckhardt, 2012; Kuck et al., 1992). For example, a mental state dominated by affective numbness is usually termed melancholia in depression but anhedonia in psychosis. Similarly, lack of drive (depression) is commonly relabeled as avolition in schizophrenia and again counted as a negative symptom. This, along with the longstanding preoccupation that psychosis is not amenable to understanding (Jaspers, 1973; Walker, 1991), may have contributed to the relative neglect of treatment of depressive symptoms in psychosis in the past and to the poor transfer of available psychological treatment options against depression in patients with psychosis.

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1.2. Reasons why depression is an important treatment target in schizophrenia

A number of reasons exist why depressive symptoms deserve greater attention in the treatment of psychosis. First, beginning with Kasanin (1933), who coined the term *schizoaffective disorder*, clinicians increasingly acknowledge that affective symptoms coexist with psychosis. A review estimated that at least 50% of patients suffer from comorbid depression (Buckley et al., 2009), and many patients show single depressive symptoms such as low self-esteem (Freeman et al., 1998; Kesting and Lincoln, 2013; Moritz et al., 2010). Second, suicidality, a grave and life-threatening manifestation of depression, is frequent in psychosis and approximately 5% of patients commit suicide (Hor and Taylor, 2010). While some suicides are due to the influence of acoustic hallucinations, depression represents the best predictor for suicidality or self-harm behaviors in patients with schizophrenia (Fusar-Poli et al., 2014). Third, the implicit prevailing treatment paradigm posits that improving positive symptoms and insight will raise quality of life and reduce depression. Research suggests, however, that enhancement of insight can even paradoxically aggravate affective problems (Karow et al., 2008; Lincoln et al., 2007). Moreover, depression is not just a secondary consequence of having a severe mental disorder, it is also a frequent premorbid precursor of psychosis (Fusar-Poli et al., 2014). Fourth, depressive symptoms are often formulated by patients as their preferred target of treatment (Byrne et al., 2010; Hafner et al., 2013; Sterk et al., 2013; Moritz et al., in press-b).

1.3. Poor efficacy of available treatment

Notwithstanding the need to address depression in the therapy of psychosis as well as guidelines fostering psychotherapy in psychosis, many patients are still deprived of psychotherapy in general (Bechdolf and Klingberg, 2014; Shafran et al., 2009). If psychotherapy is sought at all, it often targets positive symptoms. Both pharmacological and psychological treatment approaches for psychosis are only partially effective in reducing depression. Antipsychotics yield a small effect size for the improvement of depressive symptoms in schizophrenia (Leucht et al., 2009). In fact, antipsychotic medication may even induce pharmacological depression (Naber and Karow, 2001). Augmentation with antidepressants has been shown ineffective for the treatment of depressive symptoms according to two meta-analyses (Kishi et al., 2013; Kishi and Iwata, 2014), underlining the need for non-pharmacological treatment options for depression in psychosis patients. Cognitive-behavioral therapy (CBT) yields a small to medium effect size (0.36) for the improvement of mood (Wykes et al., 2008).

1.4. The present study

The present study explored whether a generic online intervention for depression administered in a non-clinical setting can reduce depressive symptoms in patients with psychosis. We used a program called HelpID (developed by the novego AG) which is based on the CBT theoretical framework. Meta-analyses show that online interventions for depression exert a small-to-medium effect size in patients with depression when administered unguided (Cuijpers et al., 2011; Richards and Richardson, 2012, Johansson and Andersson, 2012).

Whether these effects also hold true for patients with comorbid depressive symptoms alongside other primary disorders, like obsessive-compulsive disorder, borderline personality disorder and schizophrenia, awaits to be established. While we hypothesize that HelpID will reduce depressive symptoms in psychosis, we were unable to make predictions with respect to the magnitude of the effect. Although self-help and online interventions have proven feasible in psychosis (Alvarez-Jimenez et al., 2014), a limiting factor could be that the online intervention under investigation is not adapted to the specific problems (e.g., stigma and self-stigma) and deficits (e.g., cognitive dysfunctions which may compromise translation of lessons/learning aims into everyday life) of psychotic patients. However, as patients with psychosis often do not receive specific treatment for depression, the potential of the program may be higher than in conventional (depression) populations who are usually not naïve about the contents of such programs. In line with this, the magnitude of the effect of online interventions for depression was moderate for a group of neurological patients in two recent studies of whom most had never received specific treatment for depression before (Fischer et al., 2015; Schröder et al., 2014). Based on the assumption that depressive symptoms and depression-related cognitions (e.g., worry thinking style, negative beliefs about the self, interpersonal sensitivity, sleep disturbance) play a causal role for the emergence of positive symptoms (Garety et al., 2001; Freeman and Garety, 2014; Lincoln et al., 2014), we also expected the treatment to impact on positive symptoms.

2. Method

2.1. Participants

Participants were primarily recruited via a database of former patients from the Department of Psychiatry and Psychotherapy at the University Medical Center Hamburg-Eppendorf (Germany, UKE). All former patients had previously given written informed consent to be re-contacted for future studies. While for most individuals a diagnosis of schizophrenia had been established on prior occasions, we additionally administered a diagnostic telephone interview as a precondition for participation. We also contacted high-quality Internet forums (e.g. moderated, conveying evidence-based information) devoted to schizophrenia as an additional source to recruit study participants. The following inclusion criteria applied: age between 18 and 65 years, willingness to participate in two anonymous (Internet-based) surveys as well as diagnostic telephone interviews that were scheduled three months apart, and a diagnosis of schizophrenia (as verified by telephone interview). Moreover, participants had to experience present subjective depressive symptoms and a willingness to undergo treatment for these symptoms (no formal cut-off was set). While presence of depressive symptoms was an explicit inclusion criterion, a diagnosis of major depression or dysthymic disorder was not. Severe suicidality led to exclusion. In these cases, participants were informed about help lines and treatment options. The trial was set up as an add-on intervention to care-as-usual: Participants were informed that the trial would not interfere with current treatments. For example, individuals were allowed to continue to take medication or see a physician.

Interested individuals were directed to the baseline survey via a weblink. The survey was set up using questback®, a software allowing to create online surveys. The study was anonymous (no name or postal address was requested; we did no store IP addresses were stored). Participants were informed that they would either immediately receive an online code allowing a free 3-month access to HelpID or would be allocated to a waitlist control condition. The latter group was promised full access to the program subsequent to the post-assessment (online survey and interview). Group allocation was carried out in random fashion subsequent to baseline assessment (i.e. following the interview) using an automated randomization plan with no stratification.

The trial was registered at the Internet Portal of the German Clinical Trials Register (DRKS; DRKS00007888). The DRKS was approved for the primary register in the WHO network and thus meets the requirements of the International Committee of Medical Journal Editors (ICMJE).

2.2. Procedure

On the first page of the baseline survey, the rationale of the study as well as exclusion criteria were summarized. All participants provided electronic informed consent. Multiple log-ins via the same computer were prevented by means of “cookies”. The survey consisted of the

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