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Review

Is good insight associated with depression among patients with schizophrenia? Systematic review and meta-analysis

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ABSTRACT

Among patients with schizophrenia, better insight may be associated with depression, but the findings on this issue are mixed. We examined the association between insight and depression in schizophrenia by conducting a systematic review and meta-analysis. The meta-analysis was based on 59 correlational studies and showed that global clinical insight was associated weakly, but significantly with depression (effect size r = 0.14), as were the insight into the mental disorder (r = 0.14), insight into symptoms (r = 0.14), and symptoms' attributions (r = 0.17). Conversely, neither insight into the social consequences of the disorder nor into the need for treatment was associated with symptoms of depression. Better cognitive insight was significantly associated with higher levels of depression. The exploratory meta-regression showed that methodological factors (e.g. the instrument used to assess depression and the phase of the illness) can significantly influence the magnitude of the association between insight and depression. Moreover, results from longitudinal studies suggest that the relation between insight and depression might be stronger than what is observed at the cross-sectional level. Finally, internalized stigma, illness perception, recovery attitudes, ruminative style, and premorbid adjustment seem to be relevant moderators and/or mediators of the association between insight and depression. In conclusion, literature indicates that among patients with schizophrenia, better insight is associated with higher levels of depressive symptoms. Thus, interventions aimed at promoting patients' insight should take into account the clinical implications of these findings.

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1. Introduction

Research has demonstrated that good insight is associated with the presence of depressive symptomatology among patients with schizophrenia; however, some conflicting results exist (Lincoln et al., 2007; Lysaker et al., 2013b). Lack of insight is a key feature in patients with schizophrenia and other psychotic disorders. It is generally regarded as a marker of illness severity and is associated with poor treatment compliance (Lincoln et al., 2007; Beck et al., 2011), poor clinical outcomes (Drake et al., 2007; Saravanan et al., 2010), and reduced long-term global functioning (Gharabawi et al., 2007; Lincoln et al., 2007). In line with these findings, improving patients' awareness into their illness is an important goal of clinical management and often leads to increased treatment adherence, improved clinical outcomes,

and better overall quality of life (Lincoln et al., 2007; Drake, 2008). Having good insight into schizophrenia, however, can also be paradoxically associated with negative subjective states related to depression (Lysaker et al., 2007), including demoralization (Cavelti et al., 2012b), decreased self-esteem (Staring et al., 2009), hopelessness (Lysaker et al., 2007; Misdrahi et al., 2014), and suicidal ideation (Barrett et al., 2010; Kao and Liu, 2011).

Overall, the studies that have examined the relation between insight and depression have yielded mixed results. Specifically, positive significant associations have been reported (Carroll et al., 1999; Mutsatsa et al., 2006; Konstantakopoulos et al., 2013), as well as non-significant (Palmer and Jeste, 2006; Kurtz and Tolman, 2011; Wang et al., 2011), and negative associations (Amador et al., 1993; Saeedi et al., 2007; Parellada et al., 2011; Riedel et al., 2012). Such inconsistencies may be related to several factors, including (1) the absence of a shared definition of depression comorbid with schizophrenia (Siris, 2000; Hausmann and Fleischhacker, 2002); (2) both insight and depression being assessed using instruments that possess different psychometric characteristics (Schwartz, 1998; Lincoln et al., 2007); and (3) study

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samples being examined in different clinical stages and phases of the illness, as both insight (Parellada et al., 2011; Comparelli et al., 2013) and depression (Chiappelli et al., 2014) have been shown to display state-related fluctuations that may have influenced their association. More than ten years have elapsed since the first meta-analysis on this topic (Mintz et al., 2003) and several studies have been published (Lysaker et al., 2013b). Thus, we conducted a comprehensive review on the association between insight and depression in patients with schizophrenia spectrum disorders.

2. Methods

We conducted: (1) a meta-analysis and meta-regression on the association between insight and depression, (2) a review of longitudinal studies and (3) a review of studies examining mediators or moderators of this association.

2.1. Search strategy

We searched Pubmed for relevant abstracts in English up to November 2013, with no past date restrictions. The search string was: [schizophr* AND (insight OR awareness) AND (depress* OR suicid*)]. The reference lists of original articles were searched for additional relevant citations.

2.2. Selection criteria

Two independent researchers (M.R. and A.C.) screened the retrieved citations adopting the following criteria for inclusion in the meta-analysis: (1) studies written in English; (2) studies reporting validated measures of insight and depression, where at least one had to be "multidimensional" (e.g. we excluded those reporting both insight and depression from items of the Positive and Negative Syndrome Scale); (3) study samples comprising at least 50% of patients with schizophrenia-spectrum disorders; and (4) studies reporting sufficient data to allow the calculation of an effect size for the association between insight and depression. If data was insufficient to calculate an effect size, we contacted the study corresponding author to retrieve such information.

For the reviews, we included all studies with longitudinal designs that analyzed: (1) repeated cross sectional associations between insight and depression; or (2) association between the changes of depression and insight along multiple time-points; or (3) prediction of levels of depression by levels of insight (or vice-versa) across multiple time-points. Lastly, we considered those studies that examined any factor's mediating or moderating role in the association between insight and depression, following widely used criteria (Baron and Kenny, 1986), or using Structural Equation Modeling (SEM) or Path Analysis (PA).

2.3. Data extraction and statistical analyses

For each study, we calculated the effect size of the association between levels of insight and depression. This was determined from the correlation index weighted for sample size. When studies did not report the values of correlation indices or other data, we computed an estimate from p, t or F values (Wilson and Lipsey, 2014). When non-significant associations were reported along with the direction of the effect, we used the lowest value of the 95% confidence interval of the mean effect size (Aleman et al., 2006). Effect sizes were calculated in such a way that a positive value represents a positive association between *better* insight and higher levels of depression. If studies reported that data on insight or depression was not normally distributed, the study was excluded from the meta-analysis.

First, we conducted a meta-analysis by grouping the effect sizes according to insight components. This method was chosen to summarize results obtained from different scales, similar to another previous work

on this topic (Mintz et al., 2003). However, given that domains of insight can be defined differently between different rating scales (Lincoln et al., 2007), we also conducted subgroup analyses dividing studies according to the rating scale for insight. All meta-analyses were performed with random effect models according to the DerSimonian and Laird method (DerSimonian and Laird, 1986), calculating both Q-statistics and I^2 as indicators of significance and entity of the heterogeneity.

In order to investigate causes of heterogeneity, we performed an exploratory meta-regression. Two researchers (M.R. and A.C.) coded study characteristics: year of publication, sample size, type of assessment for depression and insight, study sample mean age, percentage of females, diagnostic composition, percentage of patients treated with antipsychotics (AP), as well as severity of psychotic and depressive symptoms (z-scores). Illness stage was defined as early (first-episode schizophrenia or duration of illness lower than 2 years), intermediate (duration of illness between 2 and 10 years), and chronic (duration of illness longer than 10 years). Illness phase was defined as acute if patients were assessed within the first 4 weeks of AP treatment; post-acute: between 4 weeks and 6 months of AP; and stable: over 6 months of AP. Discordant ratings were solved by discussion.

We entered moderators in the regression model in two waves: a) publication year, type of assessment instruments for depression and insight, type of insight component assessed, and inclusion criteria related to the diagnosis and b) age, gender, length of illness, illness stage, phase, and severity of symptoms. We used the limit of less than one explanatory variable per 10 effect sizes and dropped nonsignificant predictors or those with 40% or more missing data. Improvements of the models were estimated from the decreases in the estimate of between-study variance (tau-squared). Finally, we tested data for publication bias, by visual inspection of funnel plots, Egger's tests and the trim and fill procedure. The STATA 12.0 package (StataCorp, College Station, Texas, USA) was used for all analyses.

3. Results

3.1. Search results and study characteristics

After the selection procedure (see Fig. 1), 59 studies were included (Amador et al., 1993; Collins et al., 1997; Sanz et al., 1998; Smith et al., 1998, 2000; Carroll et al., 1999; Moore et al., 1999; Kampman et al., 2002; Drake et al., 2004; Mintz et al., 2004; Pedrelli et al., 2004; Granholm et al., 2005; Kaiser et al., 2006; Mutsatsa et al., 2006; Palmer and Jeste, 2006; Schwartz-Stav et al., 2006; Simon et al., 2006; Sumich et al., 2006; Watson et al., 2006; Bell et al., 2007; Cooke et al., 2007; Saeedi et al., 2007; Warman et al., 2007; Karow et al., 2008; Roseman et al., 2008; Sitzer et al., 2008; Ulas et al., 2008; Yanos et al., 2008; Kruck et al., 2009; Mohamed et al., 2009; Staring et al., 2009; Barrett et al., 2010; Wiffen et al., 2010; Ayesa-Arriola et al., 2011; Engh et al., 2011; Kao and Liu, 2011; Kao et al., 2011; Kurtz and Tolman, 2011; Norman et al., 2011; Parellada et al., 2011; Wang et al., 2011; Ampalam et al., 2012; Birchwood et al., 2012; Cavelti et al., 2012b; Ekinci et al., 2012; Haug et al., 2012; Majadas et al., 2012; Pena et al., 2012; Romm et al., 2012; Sharaf et al., 2012; Vassileva and Milanova, 2012; Xiang et al., 2012; Innamorati et al., 2013; Konstantakopoulos et al., 2013; Raffard et al., 2013; Schrank et al., 2013; Sonmez et al., 2013; Tsai and Rosenheck, 2013; Thomas et al., 2014).

These studies were conducted on 9276 patients with a mean age of 35.2 years (SD = 9.0); 36.6% females (SD = 14.8) and 28.8% inpatients (SD = 42.3). Twenty studies included only patients diagnosed with schizophrenia or schizophreniform disorder, 26 included patients with schizoaffective disorder and 13 included also patients with affective psychoses. The average illness length was 140.23 months (SD = 94.5). In 25 studies, more than 90% of the participants were being treated with AP; whereas, two studies were on drug-naïve patients.

Nineteen studies evaluated insight using the Scale to Assess Unawareness of Mental Disorder (SUMD) (Amador et al., 1993), 7

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