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Relationships between global assessment of functioning and other rating scales in clinical trials for schizophrenia

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ABSTRACT

The relationship between the Global Assessment of Functioning (GAF) with other scales in schizophrenia has rarely been investigated. A systematic literature search was conducted to identify articles that reported the GAF score together with scores in the Positive and Negative Syndrome Scale (PANSS), Clinical Global Impression (CGI) or Brief Psychiatric Rating Scale (BPRS), using MEDLINE, EMBASE and PsycINFO, with keywords of schizophrenia, clinical trial and global assessment of functioning (last search 30 June 2013). Correlational analyses with weighting by the study participant numbers across these rating scales were performed. In 40 clinical trials ($n=8000$) that reported cross-sectional data on the GAF and PANSS, a significant but modest correlation was noted (Pearson's $r=-0.401$, $p<0.0001$). Furthermore, a correlation between the GAF and CGI-severity (CGI-S) at study baseline in 38 studies ($n=11{,}315$) was robust ($r=-0.893$, $p<0.0001$). In longitudinal studies, changes in the GAF scores were negatively correlated with those in the PANSS as well as CGI-S scores ($p<0.0001$ for both). Data on the BPRS were all statistically significant although relatively scarce. While optimal degree of concordance is undetermined among psychiatric scales that are presumed to be measuring different but overlapping constructs, this study found significant correlations in the GAF and CGI-S or PANSS, both cross-sectionally and longitudinally. The GAF-CGI-S relationship was especially tighter, making it a reliable clinical indicator.

1. Introduction

Recently the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) eliminated the Global Assessment of Functioning (GAF) (American Psychiatric Association, 1994) because a single score from the GAF is unlikely to convey information to adequately assess diagnosis, severity of symptoms and diagnosis, dangerousness to self or others, and disability in social and self-care spheres, which are likely to vary independently over time, and because the GAF requires specific training to be used properly.

Nevertheless, global functioning in schizophrenia represents an important outcome and a heuristic endpoint in the real-world clinical practice since functional impairment is an obvious obstacle against social integration. Measuring this outcome is important from the viewpoint of any successful treatment aiming for remission and recovery (Lieberman et al., 2008). For that purpose, the GAF amongst others has been occasionally utilized (Suzuki, 2011). However, to the best of authors' knowledge, global functioning in schizophrenia has rarely been the primary outcome measure in clinical trials and its relationship with other commonly utilized rating scales has rarely been a topic of investigation.

"Measuring" outcome, frequently commenced with the existing rating scales, is of utmost importance to critically appraise the effect of any interventions including psychopharmacotherapy for schizophrenia. To address the gap in the literature, we examined the correlations between the GAF and other frequently recorded scales i.e., the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987), the Clinical Global Impression (CGI) (Guy, 1976) and the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1988) in clinical

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trials for schizophrenia, in order to shed light on their cross-sectional and longitudinal correlations and their robustness.

2. Materials and methods

A systematic literature search was conducted using Ovid MEDLINE(R) (1946-), PsycINFO (1806-), and Embase (1980-). Keywords were schizophrenia, clinical trial and global assessment of functioning. Articles that reported the GAF score as well as the scores in one or more of the following scales were sought: PANSS, CGI-Severity (CGI-S), and BPRS. The BPRS was restricted to the 18-item version and a scoring system of 0–6 was recalculated as 1–7 for consistency. The last search was conducted on 30 June 2013. Articles that did not allow exploration on the relationships between the GAF and the other scales, as well as studies that included patients with other diagnoses than schizophrenia in 50% or more instances were excluded.

Last-observation-carried forward (intention-to-treat) data were preferred to completer only (per protocol) data whenever available. The values of the scales were estimated from the figure if it was the only source of the data. The average scores in the respective rating scales within each study were obtained as follows. Assume the study with 3 treatment arms with the number of patients being A, B, and C, and the average score in a rating scale at baseline being X, Y and Z. In this instance, the overall score was calculated as X*〔A/(A+B+C)〕 plus Y*〔B/(A+B+C)〕plus Z*〔C/(A+B+C)〕. Then, in order to take into account the sample size of each study, the average score from each of the study was repeatedly entered by the number of the total participants in the EXCEL sheet in obtaining correlational values since individual data were unavailable. Degree of freedom was set at the study number minus 2.

Pearson's correlation coefficient was obtained to investigate the relationships between the baseline (i.e., cross-sectional) data on the GAF and the other scales. Also, longitudinal changes (i.e., pre-post delta data) in these assessment scales were correlated. Note that the higher the score in the GAF and the lower the score in the PANSS, CGI-S, and BPRS, the better the status of a patient. A p-value of <0.05 was considered statistically significant (two-tailed). Data were analyzed with EXCEL (year 2010 version) and figures were made with PRISM (version 5). Because of the totally noninvasive and anonymous nature of the study, no ethical approval from the institutional review board was sought.

3. Results

There were 132 articles from the initial list of 181 articles after exercising “remove duplicates” command. Among them, 41 articles did not provide data on both the GAF and at least one of the other scales, 20 articles studied non-schizophrenia or mixed populations in which schizophrenia patients represent a minority, 6 articles were duplicates, and full text was not obtainable for 4 (old non-English) articles. Thus, 61 studies were included in the present study.

There were 40 articles ($n=8000$) that provided cross-sectional data on the GAF and PANSS at study baseline or its equivalent. The mean score in the GAF was 49.8 while that of the PANSS was 76.9. A GAF score of 41–50 means serious symptoms (e.g., suicidal ideation, severe obsessional rituals, frequent shoplifting) or any serious impairment in social, occupational, or school functioning (e.g., no friends, unable to keep a job, cannot work) (American Psychiatric Association, 1994). In these studies, a correlation between the GAF and PANSS scores was modestly significant (Pearson's $r=-0.401$, $p<0.0001$), as depicted in Fig. 1.

In contrast, a highly significant negative correlation was found between the GAF and CGI-S scores in 38 studies with 11,315 patients (Pearson's $r=-0.893$, $p<0.0001$) (Fig. 2). The mean score in the GAF was 47.8 while that of the CGI-S was 4.41.

A longitudinal pre-post (i.e. delta) data on the GAF and PANSS was shown in Fig. 3 (32 studies, $n=7265$, $r=-0.848$, $p<0.0001$). In these studies, an average improvement of 8.6 in the GAF (increasing from the initial score of 49.6) and 14.8 in the PANSS (decreasing from the initial score of 77.8), was noted from study baseline to endpoint. When the PANSS data were interpreted as percent changes, the results were essentially similar (data not shown). Fig. 4 shows such data regarding the GAF and CGI-S (35 studies, $n=10,902$, $r=-0.891$, $p<0.0001$). Concerning these studies, an average gain of 14.2 in the

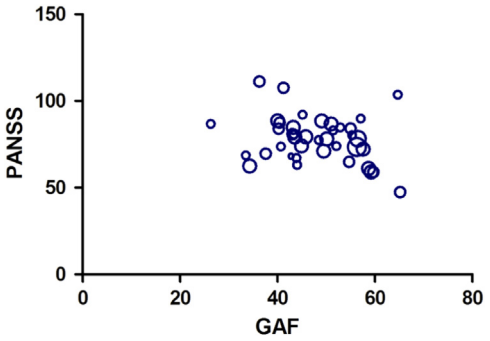

Fig. 1. Cross-sectional relationship between the GAF and the PANSS. There was a significant correlation between the GAF and the PANSS at study baseline (40 studies; $n=8000$; Pearson's $r=-0.401$, $p<0.0001$). The size of the circle is proportional to the log-transformed sample size of the study.

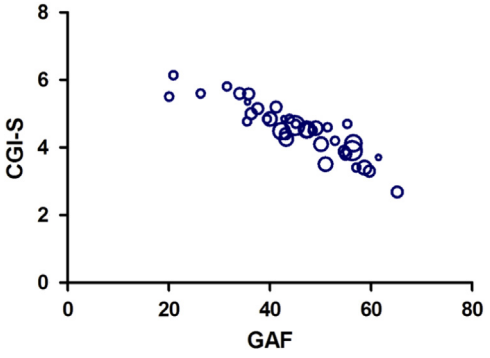

Fig. 2. Cross-sectional relationship between the GAF and the CGI-S. There was a significant correlation between the GAF and the CGI-S at study baseline (38 studies; $n=11,315$; Pearson's $r=-0.893$, $p<0.0001$).

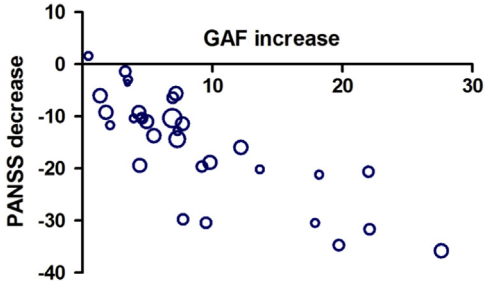

Fig. 3. Longitudinal relationship between changes in the GAF and the PANSS. There was a significant correlation between longitudinal changes in the GAF and the PANSS (32 studies; $n=7265$; Pearson's $r=-0.848$, $p<0.0001$).

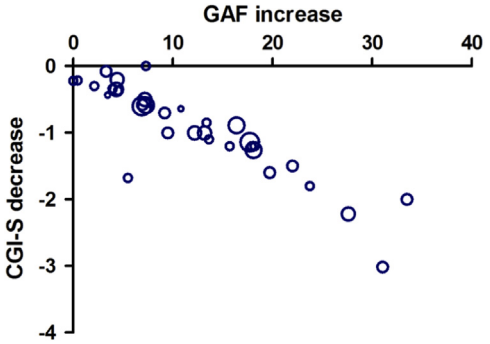

Fig. 4. Longitudinal relationship between changes in the GAF and the CGI-S. There was a significant correlation between longitudinal changes in the GAF and the CGI-S (35 studies; $n=10,902$; Pearson's $r=-0.924$, $p<0.0001$).