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Psychomotor agitation in subjects hospitalized for an acute exacerbation of Schizophrenia

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A B S T R A C T

The aims of this study were to establish the prevalence of moderate and severe psychomotor agitation in patients hospitalized for an active phase of schizophrenia, the associations between psychomotor agitation and patients' demographic and clinical variables, the intra-individual stability of the agitated/non-agitated dichotomy in independent psychotic breakdowns. The study was performed on a database relative to 630 inpatients hospitalized with a diagnosis of schizophrenia. Psychomotor agitation was measured with the Positive and Negative Syndrome Scale – Excited Component (PANSS-EC). Prevalence of moderate and severe psychomotor agitation was 40.5% and 23.7%, respectively. Non-agitated patients were older, with longer illness history and duration of untreated psychosis, were more frequently on antipsychotic medication, had lower incidence of recent use of substances, and functioned better before the index hospitalization than moderately and/or severely agitated patients. Non-agitated patients had lower scores for total PANSS and Emsley's positive and anxiety dimensions. Compared with the severely agitated group, non-agitated and moderately agitated patients scored more in Emsley's depression dimension. Poor functioning before index hospital admission, higher scores for negative subscale and Emsley's positive dimension and use of substances exerted an effect on risk of psychomotor agitation.

1. Introduction

Psychomotor agitation is a widespread, complex syndrome characterized by an appreciable increase in ideational, emotional, motor, and/or behavioural activity that may occur transdiagnostically in many psychiatric and non-psychiatric medical conditions (American Psychiatric Association, 2013; Garriga et al., 2016; Sacchetti et al., 2017). Its presence is common cause of persistent clinical concern, frequently imposes a significant burden on patients, families, caregivers and medical staff, detracts resources in health care systems and can be life-threatening to the patient and others when it escalates into aggressive variants (Abderhalden et al., 2007; Cardoso et al., 2005; Cots et al., 2016; Garriga et al., 2016; Peiró et al., 2004; Sacchetti et al., 2017; Stephens et al., 1999; Sugibayashi et al., 2014).

Given this unfavourable scenario, it is not surprising that the management of psychomotor agitation continues to be a topic of considerable interest as testified by the proliferation of systematic reviews, guidelines, and expert consensus papers (Allen et al., 2011, 2003; Garriga et al., 2016; Marder et al., 2007; National Collaborating Centre for Mental Health (UK), 2015; National Collaborating Centre for Nursing and Supportive Care (UK), 2005; Richmond et al., 2012; Sacchetti et al., 2017; Wilson et al., 2012; Zeller and Rhoades, 2010) and the recent ad hoc development of rapid-acting injectable second-generation antipsychotics and inhaled loxapine (Citrome and Volavka, 2014; Garriga et al., 2016; Nordstrom and Allen, 2013).

Therapeutic progress, however, has not been accompanied by improvement in knowledge of the pathophysiology of psychomotor agitation and profiling of patients affected by the syndrome. A number of obstacles have contributed to generate and maintain the gap. As highlighted previously, a major barrier lies in the fact that, because it is not a definite disorder but a complication of numerous clinical conditions, psychomotor agitation may be mediated by different, disease-specific mechanisms and pathways (Garriga et al., 2016; Sacchetti et al., 2017). Clearly, the possibility that the same individual may develop episodes of psychomotor agitation through distinct processes adds to the difficulty. In addition, the lack of a unitary definition of psychomotor agitation and the high number of measures to assess the syndrome are relevant confounders because they make comparison between studies difficult (Citrome and Volavka, 2014; Day, 1999; Garriga et al., 2016; Sacchetti et al., al.,2017; Sachs, 2006). The frequent use in the clinical debate of aggression and psychomotor agitation as synonyms, despite the fact that the former is only a partial component of the latter, is representative of this limitation. Furthermore, the list of obstacles is maximized by a common lack of control for a number of causal and moderating factors, in particular medication adherence, adequacy of the therapeutic plan and contingent clinical setting.

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This study was planned to improve our knowledge of some of these critical issues. In particular, the objective of the study was to analyse the prevalence of psychomotor agitation in patients with schizophrenia during an exacerbation of their disease and to identify the socio-demographic and clinical correlates of psychomotor agitation of different degrees of severity.

To this aim, a retrospective analysis of clinical charts was restricted at the start of an index hospital admission for an active phase of schizophrenia, the diagnosis was based on operational criteria, and a large number of socio-demographic and clinical variables were tested for putative associations with psychomotor agitation.

Access to data on a subsample of patients followed in two subsequent hospitalizations caused by a psychotic exacerbation has also given us the opportunity to assess whether, in the presence of similar clinical conditions, psychomotor agitation may constitute a recurrent complication.

2. Materials and methods

2.1. Study design

This is an exploratory, hypothesis-free, naturalistic, observational, retrospective study.

Data were obtained from a database of information derived from clinical charts of patients hospitalized for an active phase of schizophrenia at the Brescia University & Spedali Civili Psychiatric Clinic between 2006 and 2016. The Clinic, a 24 bed unit of a General Hospital, operates within the Lombardy Health Care System, serves a catchment area of about 350.000 inhabitants, and is functionally jointed with a number of in- and - out-patient facilities of the Psychiatric Unit n° 22 and 20 of the Department of Mental Health of the Spedali Civili Hospital, Brescia. In the Psychiatric Unit, the inpatient facilities include 20 beds for chronic patients, 35 beds dedicated to intensive rehabilitation, 32 beds located in Communities with a medium or low level of protection, and 19 social housing beds. The outpatient facilities consist of 3 Community Mental Health Services and 3 Day Centers for rehabilitation. During the 2006–2016 period, the Clinic has hospitalized a mean of 419 patients per year, with a bed occupation higher than 90%, while the Community psychiatric services have delivered a mean of about 30.000 visits per year. In agreement with Italian Health Care System, the Clinic is primarily responsible for all the acute psychiatric admissions for people living in its catchment area. The decision to hospitalize the patients has always been taken by psychiatrists performing their service at the hospital .

Individual patient data were entered in the database using routine procedures adopted at the Clinic and coded with a unique file number to ensure anonymity during the processing and data analyses and linking of information relative to independent hospital admissions.

2.2. Patients

In accordance with the naturalistic design of the study, the inclusion criteria were minimal: age between 16 and 70 years, a definite DSM-5 diagnosis of schizophrenia (American Psychiatric Association, 2013), absence of a diagnosis of a substance-related disorder at hospital admission, hospitalization due to an active psychotic phase (i.e. a condition that satisfied the DSM-5 criterion A for schizophrenia), a Clinical Global Impression-Severity Scale (CGI-S) (Guy, 1976) score ≥ 3, and administration of the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) within 2 days of admission in the Psychiatric Clinic.

Records stored before 2014 were re-analysed a posteriori to check the compatibility of the original DSM-IV-TR diagnosis of schizophrenia (American Psychiatric Association, 2000) with the DSM-5 criteria.

Patients initially entered in the database with a diagnosis of schizophreniform disorder were considered eligible only when the transition to schizophrenia was unequivocally proven in the following months.

Subjects entered in the subsample followed in two successive hospitalizations was also requested to have a 6-month at least interval between the two psychotic breakdown leading to hospitalization.

2.3. Assessments

Symptom severity was quantified with CGI-S and PANSS, which are administered routinely at the Psychiatric Clinic at admission, every week during hospitalization, and at discharge.

The storage of scores for each PANSS item allowed the use of an extended battery of measures, including total PANSS, the positive, negative, and general psychopathology subscales, and the seven PANSS dimensions emerged from a factor analytic study (Emsley et al., 2003). Given the explorative nature of the study and the primary objective of qualifying as much as possible patients with and without psychomotor agitation, it was judged acceptable the use of all the components of the extended PANSS-derived battery because, despite the common origin, the PANSS subscales and the Emsley's domains are not fully equivalent. The use of a backward stepwise selection that removes at each step the variable with the lower significant value further justifies this inclusive approach.

Psychomotor agitation was measured by extrapolating the PANSS scores for the five items (excitement, tension, hostility, uncooperativeness, and poor impulse control) included in the Positive and Negative Syndrome Scale – Excited Component (PANSS-EC) (Kay and Sevy, 1990; Lindenmayer et al., 2004). The adoption of this scale was justified by validations with other dedicated measures, extensive use in research and clinical settings (Baker et al., 2003; Breier et al., 2002; Garriga et al., 2016; Lesem et al., 2011; Marder, 2006; Montoya et al., 2011; Sacchetti et al., 2017; Sachs et al., 2007) and origin from PANSS that made possible the direct access to the information from the database. The PANSS-EC scores generated three categories of patients characterized by increasing levels of severity as follows (Montoya et al., 2011): < 14, without psychomotor agitation; 14–19, moderate psychomotor agitation; 20–35, severe psychomotor agitation.

Individual functioning in the year and the week before the index hospitalization was routinely assessed with the Global Assessment of Functioning (GAF) scale (American Psychiatric Association, 2000).

The age at onset was identified as the age of onset of active psychotic symptoms (Gasparotti et al., 2009). The time spent with illness and the duration of untreated psychosis were calculated by subtracting the age at disease onset from the age at index hospitalization and at the time of the first psychiatric contact with prescription of antipsychotic medications, respectively.

The patients were also subdivided as antipsychotic-naive, antipsychotic-free, or antipsychotic-treated, according to their status at the time of hospital admission. The label antipsychotic-free was applied to patients already treated with antipsychotic medications who, at the time of the index hospitalization, were not receiving for any reason the oral formulation by at least 4 weeks and/or had a 6-week or more delay in receiving the planned long-acting injectable antipsychotic.

Current psychiatric and medical comorbidities, a history of schizophrenia or related disorders in first-degree relatives, and recreational use of substances in the month before the hospitalization were investigated separately, together with the occurrence of obstetric complications and paternal age at the birth of the patient. The label recreational use of substances identified an use in absence of a definite DSM-5 substance-related disorder.

The data reported in the clinical records and included in the database had been collected through direct examination, detailed interviews with the patients, and critical review of all medical records available in the Clinic and associated Community Psychiatric Services. In some cases, the information had been supplemented by interviews with close relatives (Sacchetti et al., 2007) and the administration of a modified version of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First et al., 1996).