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Social dysfunction in mood disorders and schizophrenia: Clinical modulators in four independent samples

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ABSTRACT

Introduction: Social dysfunction is a common symptom of several neuropsychiatric disorders. However, only in the last few years research began to systematically investigate clinical aspects of this relevant outcome. Interestingly, its distribution and link with other clinical variables is still unclear. This study investigated social dysfunction in 4 different cohorts of patients affected by mood disorders and schizophrenia to evaluate 1) the degree of social dysfunction in these populations; 2) the associations among social dysfunction and socio-demographic and psychopathological features. *Methods*: Data from 4 independent studies (CATIE, GSRD ES1, ES2 and ES3, STAR*D, STEP-BD) were investigated. Behavioural and affective indicators of social dysfunction were derived and operationalized from scales or questionnaire items related to the interaction with relatives, friends and significant people in patients affected by schizophrenia (N = 765) and mood disorders (N = 2278 + 1954 + 1829). In particular the social dysfunction indicator was derived from Sheehan Disability Scale (SDS) for GSRD sample, from the Work and Social Adjustment Scale (WSAS) for STAR*D sample, from the Life-Range of Impaired Functioning Tool (LRIFT) for STEP-BD sample, and from the Quality of Life Scale (QOLS) for CATIE sample. The distribution of social dysfunction was described and association with socio-demographic and psychopathological characteristics were analysed. *Results*: Social dysfunction indicators showed a broad distribution in all samples investigated. Consistently across studies, social dysfunction was associated with higher psychopathological severity (all samples except CATIE) and suicide risk (GSRD ES1 and ES2, STAR*D, and STEP-BD) that explain up to 47% of the variance, but also to lower education level (GSRD ES2, STAR*D, CATIE, and STEP-BD), poorer professional/work status (GSRD ES2 and ES3, STAR*D, CATIE, and STEP-BD), marital status (STAR*D and CATIE), age (younger age in GSRD ES1 and STAR*D, older age in CATIE), higher BMI (GSRD ES2 and ES3, and STEP-BD), and smoking (GSRD ES2 and ES3). *Conclusion*: Our results demonstrated that a significant percentage of patients affected by both mood disorders and schizophrenia shows relevant social dysfunction. Social dysfunction is related, but not completely explained by psychopathological severity. In several patients, it tends to persist also during remission state. Socio-demographic and lifestyle factors were also found to play a role and should therefore be taken into consideration in further studies investigating social dysfunction.

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1. Introduction

Social functioning is fundamental for human wellbeing and survival (Eisenberger and Cole, 2012). Consistently, social dysfunction has been repeatedly associated with severe health outcomes and premature mortality (Eisenberger and Cole, 2012; Holt-Lunstad et al., 2015). Social functioning is sustained by a number of complex neurobiological processes, which form together the so-called "social brain" (Porcelli et al., 2018). Unfortunately, such complexity is associated with a high susceptibility to several pathogenic noxae, as demonstrated by the repeated observations of social dysfunction in a number of neuropsychiatric disorders (Porcelli et al., 2018; Cacioppo et al., 2014). As a matter of fact, although social dysfunction is a distinctive feature of neuropsychiatric disorders such as autism spectrum disorders (ASD) and Hikikomori Syndrome (Barak and Feng, 2016; Li and Wong, 2015), it has also been observed in several other neuropsychiatric conditions. Among them is schizophrenia (SCZ), where various social impairments have been reported since the first descriptions of the disorder (e.g., Addington and Addington, 2008; Green et al., 2015), but it is common also in mood disorders (Kupferberg et al., 2016; Van Rheenen and Rossell, 2014), anxiety disorders (Plana et al., 2014), eating disorders (Caglar-Nazali et al., 2014), borderline and antisocial personality disorders (Beeney et al., 2015; Jeung and Herpertz, 2014; Cotter et al., 2018), and Alzheimer's disease and other dementias (Dickerson, 2015; Havins et al., 2012). Taking into account these observations, it has been hypothesized that social dysfunction may represent a trans-diagnostic symptomatology domain (Cotter et al., 2018; Gur and Gur, 2016) which is sustained by pathogenic processes affecting the social brain, that are partially independent from the other consequences of the affecting disorder (Porcelli et al., 2018). Undoubtedly, social dysfunction as a whole is a complex phenotype, which is influenced clearly by impairments in social cognition (i.e. the ensemble of mental operations that underlie social interactions, including perceiving, interpreting, and generating responses to the intentions, dispositions, and behaviours of others Green et al., 2015; Gur and Gur, 2016; Fett et al., 2011), but also by socio-demographic (e.g., family, work, financial situation, education, etc.) and psychological (e.g., character and temperament) factors and by basic domain deficits, such as neurocognitive impairments (Porcelli et al., 2018; Van Der Wee et al., 2018). Therefore, in order to investigate this aspect in clinical studies, social dysfunction should be assessed with specific instruments together with a detailed assessment of socio-demographic, cognitive, and psychopathological features (Van Der Wee et al., 2018; Green et al., 2018; Kas et al., 2017). Indeed, a detailed knowledge of the various factors that contribute to determine social dysfunction might allow to identify the neurobiological substrates of social functioning, paving the way for the development of novel, targeted treatments (Porcelli et al., 2018). Nonetheless, until recent years, social functioning has been mainly investigated in the context of more general functioning evaluation, through administered or self-report scales which investigated different aspects of global functioning together (e.g., Sheehan et al., 1996; Weissman et al., 1978; Mundt et al., 2002). Only in recent years, specific instruments aimed to assess social functioning and perceived social isolation have been developed and used in clinical settings (e.g., Cornwell and Waite, 2009; Priebe et al., 2008; Tyrer et al., 2005). Consequently, in the majority of studies performed so far, a specific measure of social functioning/dysfunction is lacking (e.g., De Silva et al., 2013; Hirschfeld et al., 2000). As a result, socio-demographic and psychopathological factors that modulate specifically social dysfunction are still largely unknown. Furthermore, studies investigating social dysfunction across different neuropsychiatric disorders are still few and not comparable (Cotter et al., 2018).

Taking into account these considerations, in the present study we aimed to investigate 1) the degree of social dysfunction; and 2) the socio-demographic and psychopathological characteristics associated with social dysfunction in four independent samples: two samples of major depressive disorder (MDD) patients; one sample of bipolar disorder (BD) patients and one sample of SCZ patients. To reach these aims, we derived and operationalized from the available assessments a specific indicator of social dysfunction, as detailed below. We decided to investigate these associations in three among the larger studies performed so far in MDD, BD and SCZ (respectively, the STAR*D, the STEP-BD, and the CATIE studies) and in three European MDD samples, which provided an overall assessment of socio-demographic and psychopathological features (i.e. the GSRD samples) (see methods section for detail).

2. Methods

2.1. Samples investigated

2.1.1. GSRD sample

The GSRD sample comprised three different subsamples, which were collected thanks to the European Group for the Study of Resistant Depression (GSRD) (Schosser et al., 2012). For all three original samples ethical approval was obtained from local research ethics committees.

2.1.1.1. European subsample 1 (ES1). The study design and population have been described elsewhere (Souery et al., 2007). In brief, in this cross-sectional study, recruitment of patients was performed from January 2000 until February 2004, based on consecutive ascertainment of depressed inpatients and outpatients in the specialist referral centers involved in the study. Inclusion criteria were 1) meeting criteria for a diagnosis of MDD according to DSM-IV criteria; 2) at least one adequate antidepressant trial received during the current or most recent depressive episode. Socio-demographic features were collected through a specific form at the inclusion. A 17-item Hamilton Rating Scale for Depression (HAMD-17) (Hamilton, 1967) score was obtained for each patient at inclusion. For 552 patients, the Sheehan Disability Scale (SDS) (Sheehan et al., 1996) was obtained as well. For the aim of the present study, only subjects with available SDS were considered.

2.1.1.2. European subsample 2 (ES2). 388 MDD patients were recruited in the context of a subsequent European multicenter project, lead by the GSRD as well, from January 2005 to December 2011. Inclusion and exclusion criteria have been previously described in detail (Souery et al., 2015). In brief, patients met DSM-IV TR criteria for a major depressive episode defined as moderate or severe as assessed by the Montgomery and Asberg Depression Rating Scale (MADRS) total score at baseline > 22 (Montgomery and Asberg, 1979). Patients entered a two- stage trial after the failure of at least one adequate antidepressant treatment (retrospectively assessed), firstly receiving a 6-week venlafaxine treatment and then, in case of non-response, a 6-week escitalopram treatment. Depressive symptoms were evaluated by MADRS and HAMD-21 at baseline and biweekly until week 12. Socio-demographic features were collected at inclusion through a specific form. The SDS was administered at inclusion as well (Sheehan et al., 1996). For the aim of the present study, only data at baseline were considered.

2.1.1.3. European subsample 3 (ES3). From 2011 to 2016, a further 1410 subjects affected by MDD were recruited in the context of the European multicenter project "Clinical and Biological Correlates of Resistant Depression and Related Phenotype (TRD3)" by the GSRD. Study design and study population were described elsewhere (Dold et al., 2018). Briefly, in this cross-sectional study subjects, aged 18 years and older who met the DSM-IV TR criteria for MDD were recruited by the specialist referral centers involved in the study. Subjects must have had at least one adequate previous antidepressant treatment for the current episode. The patients' socio-demographic, psychosocial, and clinical information were gathered within a detailed

clinical interview conducted by specifically trained psychiatrists and specific questionnaires, including SDS (cross-sectional data collection process Dold et al., 2018). For the aim of the present study, only subjects with available SDS were considered (n = 1338).

2.1.2. STAR*D sample

The Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study was performed to compare the efficacy and tolerability of various antidepressant therapies through four sequential treatment levels. Descriptions of the study design and study population are detailed elsewhere (Howland, 2008). Briefly, non-psychotic MDD (DSM-IV criteria) patients were enrolled from primary care or psychiatric outpatient clinics. Severity of depression was assessed using the 16-item Quick Inventory of Depressive Symptomatology-Clinician Rated (QIDS-C) (Trivedi et al., 2004) at baseline, weeks 2, 4, 6, 9, and 12. At baseline, psychopathological, clinical and demographic information were collected. Furthermore, a detailed assessment of global functioning was performed (for a detailed description see Yates et al., 2004), throughout the administration of the 12-item short form health survey (SF-12) (Ware et al., 1996), the Work and Social Adjustment Scale (WSAS) (Mundt et al., 2002), and the 16-item Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) (Endicott et al., 1993). All patients received citalopram in level 1. As depressive symptoms and global functioning were rated in level 1, for the aim of the present study only this level was considered.

2.1.3. STEP-BD sample

The Systematic Treatment Enhancement Program for Bipolar disorder (STEP-BD) study is one of the largest clinical prospective trial including bipolar patients to date (Sachs et al., 2003). STEP-BD was a prospective study, performed to develop and expand knowledge on the management and treatment of BD and evaluate the longitudinal outcome of the disease. STEP-BD applied a hybrid design to collect longitudinal data as patients make transitions between naturalistic studies and randomized clinical trials (Sachs et al., 2003). Description of the study design and study population are detailed elsewhere (Sachs et al., 2003; Kogan et al., 2004). In brief, patients older than 15 years of age, affected by bipolar disorder type I or II, cyclothymia, bipolar disorder NOS, or schizoaffective disorder, bipolar subtype were recruited. Exclusion criteria are minimal, and include unwillingness or inability to comply with study assessments, inability to give informed consent, or need for inpatient detoxification at the time of enrolment (Sachs et al., 2003). For the aim of the present study, only data at the entry were considered.

2.1.4. CATIE sample

The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia study is a large, 18-month, National Institute of Mental Health-funded, randomized controlled trial designed to compare the outcome of 1 conventional antipsychotic medication and 4 s-generation antipsychotic medications. The study baseline visit occurred within 21 days of the screening visit. Eligible participants were initially randomized to olanzapine, risperidone, ziprasidone, quetiapine, or perphenazine under double-blind conditions and received treatments for up to 18 months or until treatment was discontinued for any reason. At baseline, the patients' socio-demographic, psychosocial, and clinical information were gathered throughout a detailed assessment, including the Quality of Life Scale (QOLS) (Heinrichs et al., 1984) (for detail see Swartz et al., 2003). More information about the study design and study population can be found elsewhere (Stroup et al., 2003). For the aim of the present study, only baseline data were considered.

2.2. Indicators of social dysfunction

Social dysfunction is a common symptom of several neuropsychiatric disorders. However, only very recently systematic evaluations of social functioning were implemented, the most part of studies performed so far lacking any specific assessments. Consistently, specific measures of social dysfunction were also missing in the datasets investigated in the present study. Therefore, different indicators of social dysfunction were derived and operationalized for each dataset from available clinical scale and demographic information after a careful evaluation performed by three researchers (S.P., E.M.P and A.S.). The evaluation was based on the selections of the available items that specifically assessed social interactions with relatives, friends and other significant people. Conversely, the items focusing on work/school functioning were excluded because it has been hypothesized that the two functions are characterized by different motivational drivers (Pedersen et al., 2017; Thandi et al., 2017; Tchanturia et al., 2013). When possible, the same indicator was selected from the different datasets in order to increase as much as possible comparability across the different populations. Each social dysfunction indicator was standardized accordingly with the following formula (original value - mean/SD) and used as main outcome of interest.

2.2.1. GSRD sample

For all the three subsamples included in GSRD sample, the SDS was available (Sheehan et al., 1996). The SDS is a self-report scale which assesses on a ten-point scale how much the symptoms have disrupted 1) patient's work/school work; 2) patient's social life/leisure activities; and 3) patient's family life/home responsibilities. According to the developers' instructions, the three items may be summed into a single dimensional measure of global functional impairment that ranges from 0 (unimpaired) to 30 (highly impaired). Patients who score 5 on any of the three scales likely have a significant functional impairment. For the aim of the present study, we combined the scores of item 2 and item 3 into a unique measure of social dysfunction, ranging from 0 (unimpaired) to 20 points (highly impaired).

2.2.2. STAR*D sample

For the STAR*D sample, the WSAS (Mundt et al., 2002) was identified as the most informative scale to derive an operationalized indicator of social dysfunction. WSAS is a self-report scale which assesses on an eight-point scale 5 items investigating the patient's ability to do certain day-to-day tasks in his or her life. For the aim of the present study, we combined the scores of item 3 (“Social activities impaired: Because of my depression, my social leisure activities (with other people, such as parties, bars, clubs, outings, visits, dating, home entertainment) are impaired”) and item 5 (“Close relationships impaired: Because of my depression, my ability to form and maintain close relationships with others, including those I live with is impaired”) into a unique measure of social dysfunction, ranging from 0 (unimpaired) to 16 points (highly impaired).

2.2.3. STEP-BD sample

For the STEP-BD sample, the Life-Range of Impaired Functioning Tool (LRIFT) (Leon et al., 1999) was selected as the most informative scale to derive and operationalize an indicator of social dysfunction. The LRIFT was specifically developed to assess functional impairment in different areas, such as work, interpersonal relations, satisfaction, and recreation. LRIFT is a clinical administrated scale which assesses on a five-point scale (in the version modified for the STEP-BD study) functional impairment. For the aim of the present study, we combined the scores of item 2c (“Interpersonal relations with other relatives”) and item 2d (“Interpersonal relations with friends”) into a unique measure of social dysfunction, ranging from 2 (unimpaired) to 10 points (highly impaired).

2.2.4. CATIE sample

For the CATIE sample, the Quality of Life Scale (QOLS) - “Interpersonal relations” category (Heinrichs et al., 1984) was selected as indicator of social dysfunction. The QOLS is a 21-item scale, ranging

from 0 (highest impairment) to 6 (almost normal), which was developed to assess deficit symptoms in schizophrenia. The category "Interpersonal relations" (items 2–8) assesses various aspects of interpersonal and social experience, although many items go beyond rating amount of frequency of social contact to such complex judgment as capacity for intimacy, active versus passive participation, and withdrawal tendencies (Heinrichs et al., 1984). This implies a greater risk of bias due to the subjective nature of the assessment compared to other scales. For the purpose of this study, we used as social dysfunction indicator the mean of the 9 items of the QOLS "Interpersonal relations" category, as suggested by previous studies (Bhalla et al., 2018), ranging from 0 (unimpaired) to 6 (highly impaired).

For the present study, only subjects with available data about social functioning were considered. These data were available for 2278 MDD patients in the GSRD sample, for 1954 MDD patients in the STAR*D sample, for 765 SCZ patients in the CATIE sample, and for 1829 BD patients in the STEP-BD sample. Thus, overall, we included for analysis 6826 subjects affected by MDD, BD, and SCZ.

2.3. Statistical analysis

Socio-demographic and clinical characteristics were described using chi-square statistics for categorical variables and analysis of variance (ANOVA) for continuous variables. In order to investigate the associations with social dysfunction indicators, simple regressions were used for continuous variables and ANOVA for categorical variables. Further, bivariate associations of social dysfunction indicators with socio-demographic and clinical features adjusted for psychopathology severity (i.e., HAMD, MADRS or PANSS total scores) were investigated through multiple linear regressions or analyses of covariance (ANCOVAS). These analyses were performed in the total samples and in the remitted/less severe subsamples. Remitted subsamples were available for GSRD ES1 and ES2 samples (remission has been defined as to have HAMD-21 score lower than 13, i.e. absence of major depressive episode Hamilton, 1967), for STEP-BD sample (remission has been defined as to have MADRS score lower than 7 and MRS score lower than 15, i.e. absence of both major depressive episode and manic/mixed episode Montgomery and Asberg, 1979; Young et al., 1978), and for CATIE sample (remission defined as PANSS score lower than 60, i.e. absence of clinical relevant symptoms Kay et al., 1987). For GSRD ES2 and STAR*D samples remitted patients were not available. Thus, we decided to perform an exploratory analysis on the less-severe patients subsamples, defined as to have HAMD-17 score lower than 19 for both samples (i.e. patients with a moderate depressive episode Hamilton, 1967). Finally, multiple linear regression analyses were also conducted to investigate the variance explained of social dysfunction indicators by continuous and categorical variables. All p values were 2-tailed and statistical significance was set at the standard level of $p = .05$. Statistical analyses were conducted using STATISTICA software package (StatSoft, Inc. Tulsa, OK, USA).

3. Results

3.1. Descriptive analysis of social dysfunction indicators across different samples

Socio-demographic and psychopathological features of the samples under investigation were described elsewhere (Souery et al., 2007; Souery et al., 2015; Dold et al., 2018; Miller et al., 2018; Gaynes et al., 2009; Bowden et al., 2012) and shown in Supplementary Table 1.

3.2. Social dysfunction indicators distribution by psychopathology severity

The distributions of social dysfunction indicators in each sample are showed in Fig. 1. For each dataset, we showed the distribution in the total sample, in the sub-sample of less-severe patients, and in the sub-sample of remitted patients (see Fig. 1). Of note, as previously stated, for GSRD ES2 and STAR*D samples, remitted patients (i.e. the subsample of patients who achieved symptomatology remission, as detailed below) were not available. As expected, in all mood disorder samples, social dysfunction indicators showed more impairment in non-remitted patients as compared to less severe and to remitted patients (all $p < .001$, data not shown). Counter-intuitively, in SCZ sample (CATIE) social dysfunction indicators showed more impairment in remitted patients as compared to non-remitted patients ($p < .001$).

Furthermore, the percentage of patients with severe social dysfunction was different across the diagnostic groups. In particular, in the ES1 sample (MDD) patients with severe social dysfunction were 313 (65.07%) in the total sample and 66 (41.51%) in the remitted subsample; in the ES2 sample (MDD) patients with severe social dysfunction were 233 (60.05%) in the total sample and 25 (31.25%) in the less-severe subsample; in the ES3 sample (MDD) patients with severe social dysfunction were 498 (54.78%) in the total sample and 61 (29.76%) in the remitted subsample; in the STAR*D sample (MDD) patients with severe social dysfunction were 907 (46.46%) in the total sample and 120 (27.52%) in the less-severe subsample; in the STEP-BD sample (BD) patients with severe social dysfunction were 139 (7.6%) in the total sample and 18 (4.47%) in the remitted subsample; in the CATIE sample (SCZ) patients with severe social dysfunction were 34 (4.47%) in the total sample and 17 (11.49%) in the remitted subsample.

3.3. Associations among social dysfunction indicators and socio-demographic and psychopathological features

We investigated in each sample whether social dysfunction indicators were associated with available socio-demographic and psychopathological features. Various nominal associations were found in each dataset (for detail, see Table 1). As expected, in all datasets social dysfunction indicators were associated with psychopathological severity (all $p < .001$), as measured by the available psychometric scales. Therefore, we repeated the analyses 1) adding the psychopathological severity score as covariate and 2) in the remitted/less severe patients only (defined by the scores at psychometric scales, as detailed below) in each dataset. Finally, we performed various multiple linear regression analyses to investigate the variance explained of social dysfunction indicators by the identified predictors in each dataset.

Here below, the associations found in these analyses were detailed for each sample (a summary of the associations found is showed in Table 2 and detailed in Supplementary Table 2).

3.3.1. GSRD sample

3.3.1.1. ES1 sub-sample. In the ES1 sub-sample, higher social dysfunction (SDS Item 2 + Item 3) was associated with higher HAMD-21 total score ($p < .001$), younger age ($p = .02$), higher suicide risk ($p < .001$), anxiety disorder co-morbidity ($p < .001$), benzodiazepines co-treatment ($p = .009$), and antipsychotic drug augmentation ($p = .03$).

Adjusting for HAMD-21 total score, social dysfunction was still associated with higher suicide risk ($p = .02$) and antipsychotic drug augmentation ($p = .04$). Considering together HAMD-21 total score and age in a multiple regression analysis, younger age was still associated with social dysfunction ($p = .02$).

In the remitted patients of the ES1 sub-sample (i.e., patients with HAMD-21 < 13), social dysfunction was associated with higher HAMD-21 total score ($p = .002$), younger age ($p = .04$), higher suicide risk ($p = .005$), and anxiety disorder co-morbidity ($p = .008$).

In ES1 sub-sample, the best fitting model included the variables HAMD-21 total score, age, suicide risk, benzodiazepines co-treatment, and antipsychotic drug augmentation. It explained the 23% of the variance of social dysfunction indicator ($F = 22.65$, $df = 6$, $p < .001$).

3.3.1.2. ES2 sub-sample. In the ES2 sub-sample, social dysfunction (SDS

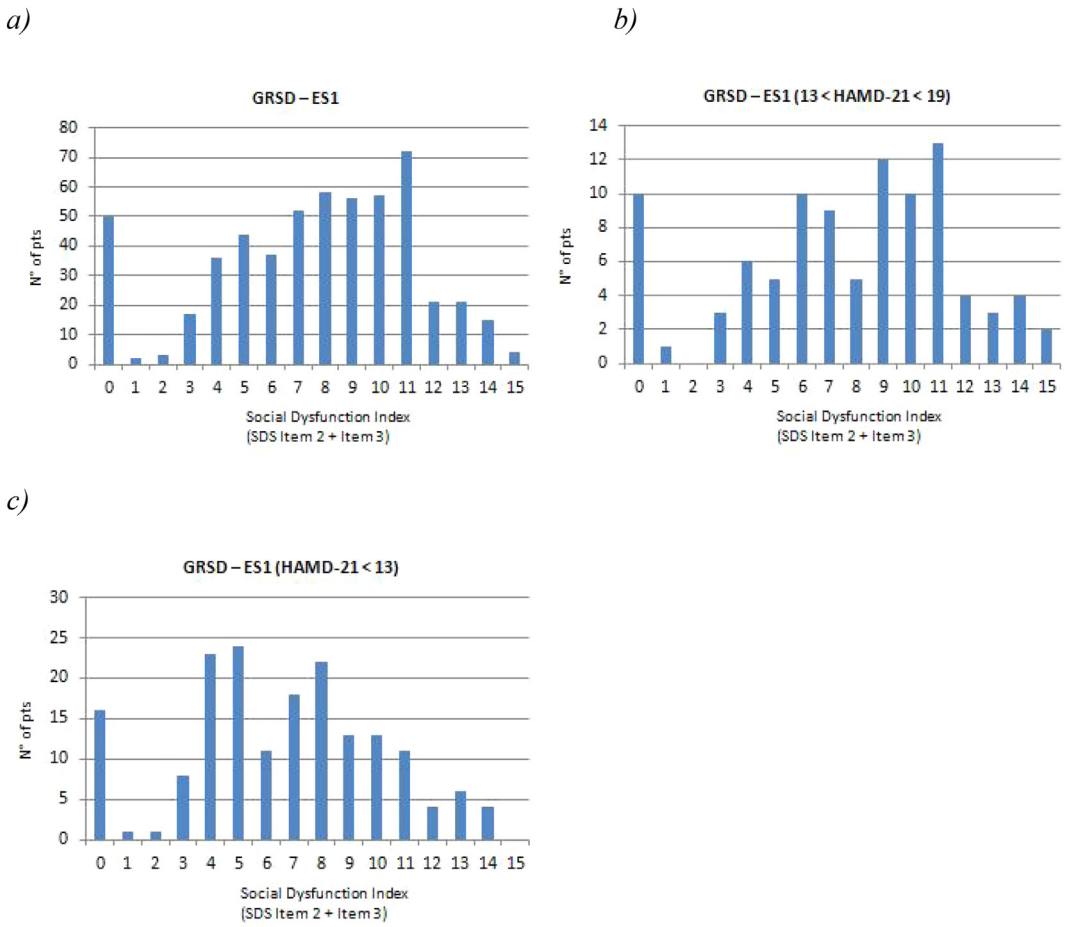

Fig. 1. Social Dysfunction (SD) Indicators distribution in the different datasets.

Item 2 + Item 3) was associated with higher HAMD-21 total score ($p < .001$), lower educational level ($p < .001$), lower income ($p = .002$), poorer professional work ($p < .001$), poorer professional status ($p < .001$), presence of melancholic features of depressive episode ($p < .001$), higher suicide risk ($p = .046$), smoke habit ($p = .002$), and higher BMI ($p = .035$).

Adjusting for HAMD-21 total score, social dysfunction was still associated with lower educational level ($p < .001$), lower income ($p = .006$), poorer professional work ($p < .001$), poorer professional status ($p = .006$), and smoke habit ($p = .002$). Considering together HAMD-21 total score and BMI in a multiple regression analysis, higher BMI was still associated with the social dysfunction ($p = .09$).

In patients with moderate severity of the ES2 sub-sample (i.e., patients with HAMD-17 < 19), social dysfunction was associated only with the presence of melancholic features of depressive episode ($p < .001$).

In the ES2 sub-sample, the best fitting model included the variables HAMD-21 total score, educational level, main source of income, smoke habit, suicide risk, and BMI. It explained the 47% of the variance of social dysfunction indicator ($F = 1.64$, $df = 101$, $p = .002$).

3.3.1.3. ES3 sub-sample. In the ES3 sub-sample, social dysfunction (SDS

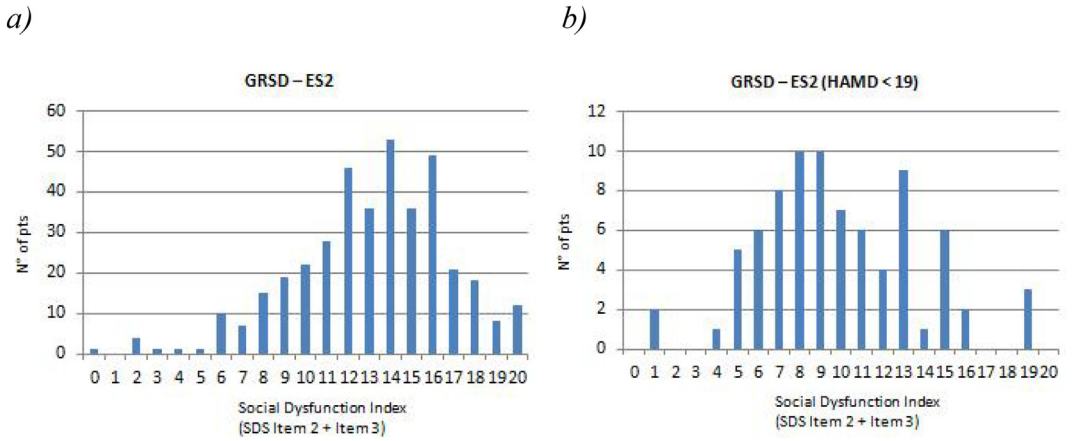

Fig. 1. (*continued*)

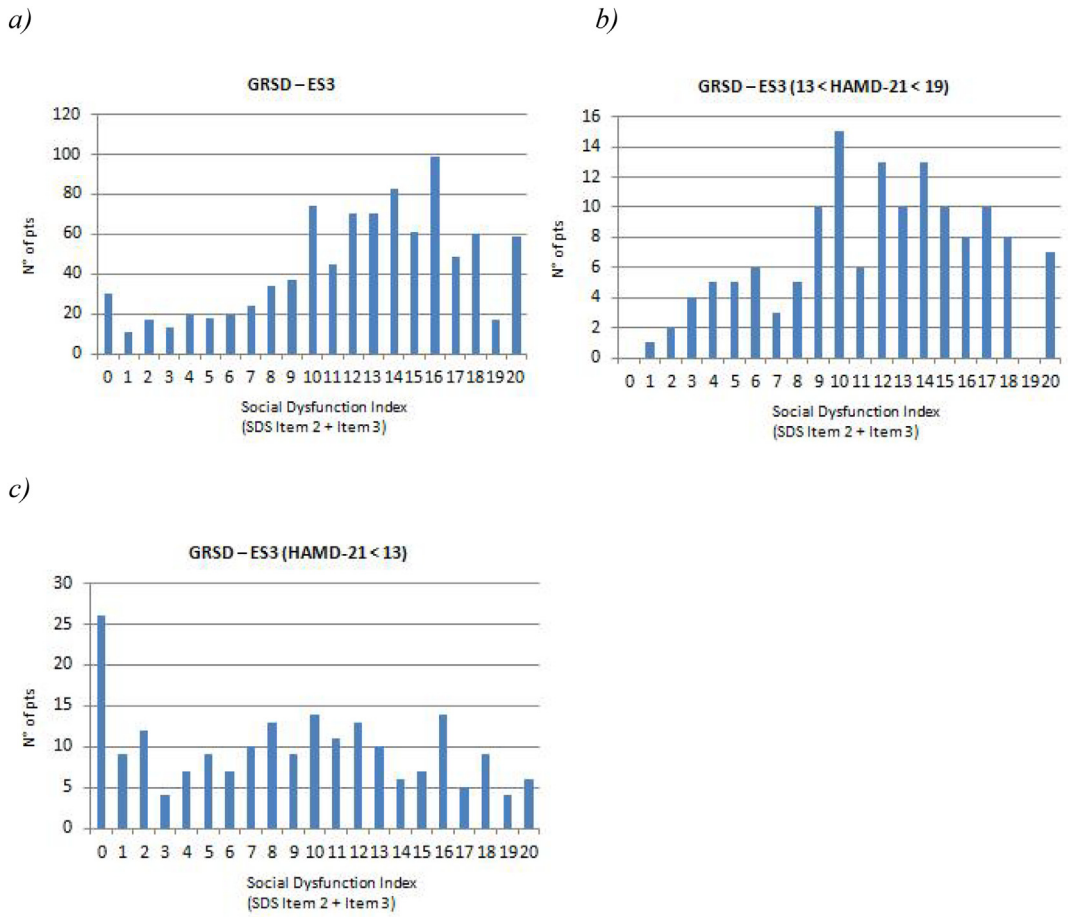

Fig. 1. (*continued*)

Item 2 + Item 3) was associated with higher HAMD-21 total score ($p < .001$), lower income ($p = .017$), poorer professional work ($p = .005$), benzodiazepines co-treatment ($p < .001$), antipsychotic drug augmentation ($p < .001$), smoke habit ($p = .001$), and higher BMI ($p < .001$).

Adjusting for HAMD-21 total score, social dysfunction was still associated with poorer professional work ($p < .001$), benzodiazepines co-treatment ($p < .001$), antipsychotic drug augmentation ($p < .001$), and smoke habit ($p = .001$). Considering together HAMD-21 total score and BMI in a multiple regression analysis, higher BMI was still associated with social dysfunction ($p < .001$).

In the remitted patients of the ES3 sub-sample (i.e., patients with HAMD-21 < 13), social dysfunction was associated with higher HAMD21 total score ($p < .001$), lower income ($p = .044$), poorer professional work ($p = .019$), benzodiazepines co-treatment ($p = .04$), antipsychotic drug augmentation ($p = .013$), and higher BMI ($p = .003$).

In the ES3 sub-sample, the best fitting model included the variables HAMD-21 total score, main source of income, smoke habit, benzodiazepines co-treatment, antipsychotic drug augmentation, and BMI. It explained the 34% of the variance of social dysfunction indicator ($F = 7.73$, df = 54, $p < .001$).

3.3.2. STAR*D sample

In the STAR*D sample, social dysfunction (WSAS Item 3 + Item 5) was associated with higher HAMD-17 total score ($p < .001$), younger age ($p = .004$), lower education (yrs) and educational degree ($p = .004$ and .02, respectively), marital status (Cohabitant/ Married patients showed lower social dysfunction) ($p < .001$), poorer professional status ($p < .001$), and higher suicide risk ($p < .001$).

Adjusting for HAMD-17 total score, social dysfunction was still associated with marital status ($p < .001$), poorer professional status ($p < .001$), and higher suicide risk ($p < .001$). Considering together HAMD-17 total score and age in a multiple regression analysis, younger age was still associated with social dysfunction ($p < .001$).

In the sub-sample of patients with moderate severity (i.e., patients with HAMD-17 < 19), social dysfunction was associated with higher HAMD-17 total score ($p < .001$), marital status ($p = .009$), and higher suicide risk ($p = .008$).

In the STAR*D sample, the best fitting model included the variables HAMD-17 total score, age, marital status, professional status, and suicide risk level. It explained the 15% of the variance of social dysfunction indicator ($F = 5.03$, df = 66, $p < .001$).

3.3.3. STEP-BD sample

In the STEP-BD sample, social dysfunction (LRIFT Item 2c + Item 2d) was associated with higher MADRS total score ($p < .001$) and higher Mania Rating Scale (MRS) (Young et al., 1978) total score ($p < .001$), lower educational degree ($p < .001$), poorer professional status ($p < .001$), higher suicide risk ($p < .001$), higher BMI ($p < .001$), and medical co-morbidities ($p = .026$).

Adjusting for MADRS total score, social dysfunction was still associated with lower educational degree ($p = .003$), poorer professional status ($p = .007$), and medical co-morbidities ($p = .002$). Considering together MADRS total score and BMI in a multiple regression analysis, higher BMI was still associated with social dysfunction ($p < .001$).

In the remitted sub-sample (i.e., patients with MADRS < 7 and MRS < 15), social dysfunction was associated with higher MADRS total score ($p < .001$), lower educational degree ($p < .001$), poorer professional status ($p = .026$), and smoking habit ($p = .001$).

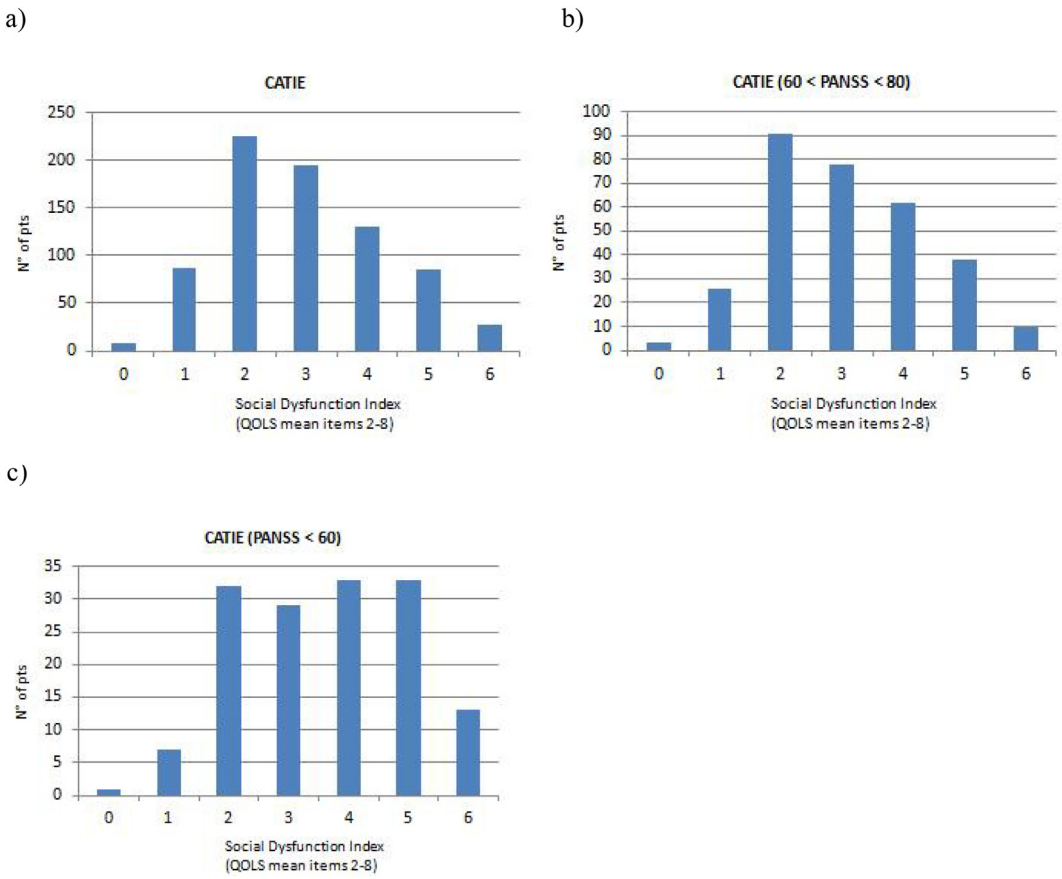

Fig. 1. (*continued*)

In the STEP-BD, the best fitting model included the variables MADRS total score, MRS total score, BMI, medical co-morbidities, smoke habit, suicide risk, educational degree, and professional status. It explained the 24% of the variance of social dysfunction indicator ($F = 2.17$, df = 158, $p < .001$).

3.3.4. CATIE sample

In the CATIE sample, social dysfunction (mean of the QOLS items 2–9 "Interpersonal relations" category) was associated with higher PANSS total score ($p < .001$), older age ($p = .008$), lower education ($p < .001$), unemployment ($p < .001$), and marital status (Cohabitant/Married patients showed lower social dysfunction) ($p < .001$). Adjusting for PANSS total score, the associations with social dysfunction were confirmed (unemployment, $p = .002$; marital status, $p < .001$). Considering together PANSS total score and both age and education years in a multiple regression analysis, older age and lower education were still associated with social dysfunction (respectively, $p = .002$ and .001).

In the remitted sub-sample (i.e., patients with PANSS < 60), social dysfunction was associated with lower education (yrs) ($p = .01$), marital status (Cohabitant/Married patients showed lower social dysfunction) ($p = .004$), and unemployment ($p = .01$).

In the CATIE sample, the best fitting model included the variables PANSS total score, marital status, education years, age, and professional work. It explained the 19% of the variance of social dysfunction indicator ($F = 15.79$, df = 11, $p < .001$).

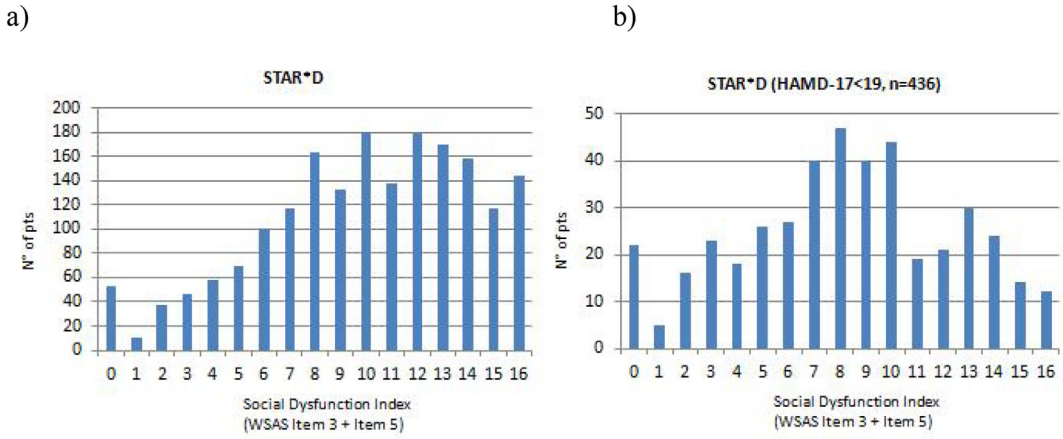

Fig. 1. (*continued*)

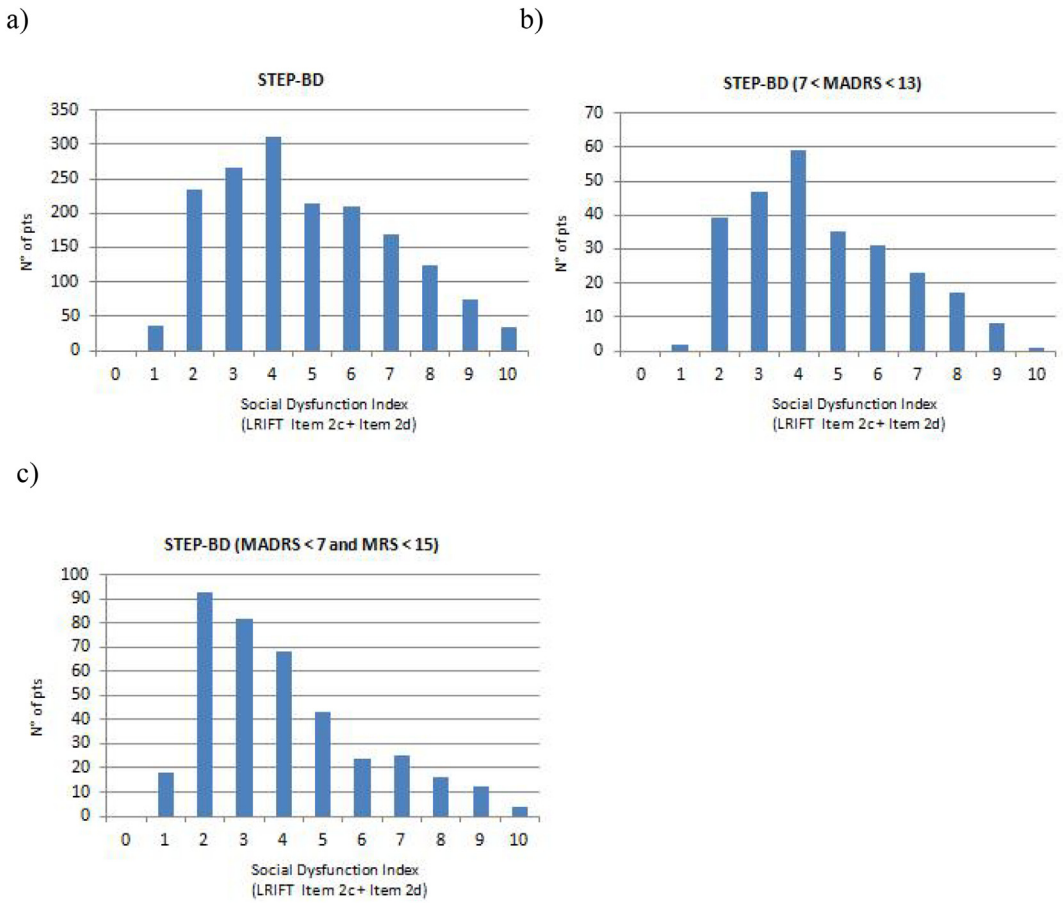

Fig. 1. (*continued*)

4. Discussion

In the present study social dysfunction indicators reflecting interactions with relatives, friends and other significant people showed a broad distribution in all the samples investigated, ranging from absence to severe social dysfunction (see Fig. 1). This result is consistent with literature data (Kupferberg et al., 2016; Green et al., 2018; Rossi et al., 2016) and suggests social dysfunction as a partially independent transdiagnostic domain (Porcelli et al., 2018; Gur and Gur, 2016). Furthermore, when we repeated the analysis in the remitted or in less severe patient sub-samples in each dataset, we found that the percentage of mood disorder patients with severe social dysfunction was lower compared to the whole samples, but not absent. Counter-intuitively, in the SCZ sample, we found an higher percentage of patients with severe social dysfunction in the remitted sample, compared to the whole one. This result suggests that social dysfunction depends on psychiatric symptom severity; however, since in several cases severe social dysfunction persisted also in the remission state, particularly in SCZ, social dysfunction may have other drivers. Consistent with our results, a wide range of social dysfunction and persistence during remission were reported in patients with MDD, BD (Kupferberg et al., 2016; Saito et al., 2017; Rhebergen et al., 2010) and SCZ (Rossi et al., 2016; Velthorst et al., 2017). Of note, the criteria used for identify the remitted subsample in SCZ (i.e. PANSS total score $<$ 60) may be questionable (e.g., Van Os et al., 2006), since it likely identify patients with residual predominant negative symptoms, rather than remitted one, partially justifying our counter-intuitively result.

Further, the percentage of patients with severe social dysfunction was different across the diagnostic groups. This percentage was lower in SCZ and in BD patients compared to MDD patients. Interestingly, this finding is opposite to literature data which show how SCZ and BD patients have often more severe social dysfunction compared to MDD patients (Heslin et al., 2016; Yasuyama et al., 2017). This inconsistency may be due to the self-report nature of some instruments we used to derive the social dysfunction indicators. Indeed, these instruments may caught the subjective experience of social dysfunction (i.e. loneliness, perceived social support, etc.) rather than objective aspects of social dysfunction (e.g., social network size, social cognition assessed with tasks, etc.) (see for example Porcelli et al., 2018; Van Der Wee et al., 2018). More severe social dysfunction scores based on subjective experience have been observed to a greater extent in MDD than in SCZ and BD (Kupferberg et al., 2016; Matthews et al., 2016; Poradowska-Trzos et al., 2007; Eglit et al., 2018), partially supporting our findings. Furthermore, the QOLS "Interpersonal relations" category (items 2–9) – used to assess social dysfunction in the CATIE sample – included many items which go beyond rating amount of frequency of social contact to such complex judgment as capacity for intimacy, active versus passive participation, and withdrawal tendencies (Heinrichs et al., 1984). This implies a greater risk of bias due to the subjective nature of the assessment compared to other scales. Furthermore, raters may involuntary assess these aspects of social dysfunction comparing patients to SCZ population, rather than with the normal population, partially justifying the low rate of high social dysfunction found in the sample.

When considering the associations among social dysfunction indicators and socio-demographic factors, we observed some interesting associations.

First, in four independent datasets higher *educational level* was associated with lower social dysfunction. This association persists also when weighting for psychopathological severity in three datasets (STEP-BD, CATIE and ES2) and it was found also in remitted patients in STEP-BD and CATIE (Table 2). Although education level has been previously associated with social cognitive processes (Irene Ingeborg

Table 1
Associations among social functioning indicators and socio-demographic and psychopathological features.

1.1GSRD sample (MDD patients)

GSRD sample				
	ES1	ES2	ES3	
Social functioning indicator	SDS Item 2 + Item 3			Effect
Age	**$r = -0.11$** **$p = .024$**	$r = 0.08$ $p = .12$	$r = -0.03$ $p = .37$	↑ age = ↓ SD[a]
Sex	$t = 1.93$ $p = .054$	$t = -0.70$ $p = .48$	$t = -0.19$ $p = .84$	
Educational level (EL)	F = 0.54 p = .70	**F = 4.18** **$p = .0004$**	F = 0.54 $p = .70$	↑ ED = ↓ SD
Psychopathology Severity Scale (PSS) (HAMD-21)	**$r = 0.36$** **$p < .001$**	**$r = 0.40$** **$p < .001$**	**$r = 0.50$** **$p < .001$**	↑ PSS = ↑ SD
Marital status	F = 1.28 $p = .27$	F = 1.64 $p = .16$	F = 1.86 $p = .11$	
Housing condition		F = 0.98 $p = .43$	F = 2.21 $p = .051$	
Main source of income (INC)		**F = 3.94** **$p = .002$**	**F = 2.77** **$p = .017$**	↑ INC = ↓ SD
Professional Work (PW)		**F = 4.34** **$p = .00005$**	**F = 2.73** **$p = .005$**	↑ PW = ↓ SD
Professional Status (PS)		**F = 3.52** **$p = .0006$**	F = 1.733 $p = .09$	↑ PS = ↓ SD
No of child	F = 2.47 $p = .06$		F = 1.41 $p = .24$	
Ethnicity	F = 1.32 $p = .27$	F = 0.93 $p = .98$	F = 0.38 $p = .77$	
Melancholic features (MF) of depressive episode	F = 1.81 $p = .18$	**F = 16.24** **F = 0.00007**		↑ MF = ↑ SD
Suicide risk (SR)	**F = 41.45** **$p < .001$**	**F = 3.99** **$p = .046$**		↑ SR = ↑ SD
Anxiety disorder co-morbidity (ADC)	**F = 12.85** **$p = .0004$**			↑ ADC = ↑ SD
Benzodiazepines co-treatment (BC)	**F = 6.88** **$p = .009$**		**F = 30.91** **$p < .001$**	↑ BC = ↑ SD
Antipsychotic drug augmentation (AA)	**F = 4.54** **$p = .03$**		**F = 28.19** **$p < .001$**	↑ AA = ↑ SD
Smoking habit (SH)	F = 2.51 $p = .11$	**F = 10** **$p = .0017$**	**F = 10.25** **$p = .0014$**	↑ SH = ↑ SD
BMI		**$r = 0.1086$** **$p = .035$**	**$r = 0.1466$** **$p < .001$**	↑ BMI = ↑ SD
Variance explained of SD by the best fitting model	23%	47%	34%	

1.2STAR*D sample (MDD patients).

STAR*D sample		
Social functioning indicator	WSAS Item 3 + Item 5	Effect
Age	**$r = -0.067$** **$p = .004$**	↑ age = ↓ SD[a]
Sex	$t = -0.63$ $p = .53$	
Education (yrs)	**$r = -0.067$** **$p = .004$**	↑ Edu. = ↓ SD
Educational degree (ED)	**F = 2.51** **$p = .02$**	↑ ED = ↓ SD
Psychopathology Severity Scale (PSS) (HAMD-17)	**$r = 0.31$** **$p < .001$**	↑ PSS = ↑ SD
Marital status	**F = 8.28** **$p < .001$**	Never Married = ↑ SD
Housing condition	F = 1.83 $p = .14$	Alone = ↑ SD
Professional status (PS)	**F = 10.99** **$p < .001$**	↑ PS = ↓ SD

Table 1 (*continued*)

1.2STAR*D sample (MDD patients).

STAR*D sample		
Social functioning indicator	WSAS Item 3 + Item 5	Effect
Suicide Risk level (SR)	**F = 30.94** **$p < .001$**	↑ SR = ↑ SD
Variance explained of SD by the best fitting model	15%	

1.3STEP-BD sample (BD patients).

STEP-BD sample			
Social functioning indicator	LRIFT Item 2c + Item 2d		Effect
Age	$r = -0.03$ $p = .23$		↑ age = ↓ SD[a]
Sex	$t = 0.22$ $p = .83$		
Educational degree (ED)	**F = 5.65** **$p < .001$**		↑ ED = ↓ SD
Psychopathological Severity Scale (PSS)	MADRS	**$r = 0.30$** **$p < .001$**	↑ PSS = ↑ SD
	MRS	**$r = 0.13$** **$p < .001$**	↑ PSS = ↑ SD
Marital status	F = 0.78 $p = .46$		
Housing condition	F = 1.65 $p = .20$		
Professional status (PS)	**F = 4.84** **$p = .00006$**		↑ PS = ↓ SD
Suicide Risk (SR)	**F = 31.40** **$p < .0001$**		↑ SR = ↑ SD
Smoking habit	F = 3.79 $p = .052$		
BMI	**$r = 0.1157$** **$p < .001$**		↑ BMI = ↑ SD
Medical co-morbidities (MC)	**F = 4.95** **$p = .026$**		↑ MC = ↑ SD
Psychosocial problems	F = 1.40 $p = .24$		
Variance explained of SD by the best fitting model	24%		

1.4CATIE sample (SCZ patients)

CATIE sample		
Social functioning indicator	QOL Inter_rel (mean Item 2–9)	Effect
Age	**$r = -0.09$** **$p = .008$**	↑ Age = ↑ SD[a]
Sex	$t = 0.68$ $p = .50$	
Ethnicity	F = 0.01 $p = .99$	
Education (E_yrs)	**$r = 0.14$** **$p < .001$**	↑ E_yrs = ↓ SD[a]
Psychopathology Severity Scale (PSS) (PANSS)	**$r = -0.36$** **$p < .001$**	↑ PSS = ↑ SD[a]
Marital status	**F = 9.95** **$p < .001$**	Married = ↓ SD[a]
Professional work	**F = 12.43** **$p < .001$**	Unemploy. = ↑ SD[a]
Variance explained of SD by the best fitting model	**19%**	

[a]SD = social dysfunction.
Associations found in the different samples are in bold.

Table 2
Summary of the associations found among social functioning indicators and socio-demographic and psychopathological features.

Sample (social functioning indicator)	Psychopathological features associated	Socio-demographic features associated	Associations found in the sub-sample of remitted/less severe patients
ES1 (SDS Item 2 + Item 3)	✓ HAMD-21 total score ✓ **Suicide risk**[a] ✓ Anxiety disorder co-morbidity ✓ Benzodiazepines co-treatment ✓ **Antipsychotic drug augmentation**	✓ **Age**	✓ HAMD-21 total score ✓ Suicide risk ✓ Anxiety disorder co-morbidity ✓ Age
ES2 (SDS Item 2 + Item 3)	✓ HAMD-21 total score ✓ Suicide risk ✓ Melancholic features	✓ **Educational level** ✓ **Main source of income** ✓ **Professional work** ✓ **Professional status** ✓ **Smoking habit** ✓ **BMI**	✓ Melancholic features
ES3 (SDS Item 2 + Item 3)	✓ HAMD-21 total score ✓ **Benzodiazepines co-treatment** ✓ **Antipsychotic drug augmentation**	✓ Main source of income ✓ **Professional work** ✓ **Smoking habit** ✓ **BMI**	✓ HAMD-21 total score ✓ Main source of income ✓ Professional work ✓ Benzodiazepines co-treatment ✓ Antipsychotic drug augmentation ✓ BMI
STAR*D (WSAS Item 3 + Item 5)	✓ HAMD-17 total score ✓ **Suicide risk level**	✓ **Age** ✓ Education (yrs) ✓ Educational degree ✓ **Marital status** ✓ **Professional status**	✓ HAMD-17 total score ✓ Marital status ✓ Suicide risk level
STEP-BD (LRIFT Item 2c + Item 2d)	✓ MADRS total score ✓ MRS total score ✓ Suicide risk	✓ **Educational degree** ✓ **Professional status** ✓ **BMI** ✓ **Medical co-morbidities**	✓ Educational degree ✓ MADRS total score ✓ Professional status ✓ Smoking habit
CATIE (QOL Inter_rel mean Item 2–9)	✓ PANSS total score	✓ **Age** ✓ **Education (yrs)** ✓ **Marital status** ✓ **Professional work**	✓ Education (yrs) ✓ Marital status ✓ Professional work

[a] In bold associations which survived adding psychopathological severity scale score as covariate.

van Driel et al., 2016), to the best of our knowledge it has not been previously associated with the domain of social functioning dealing with interactions with relatives, friends and other significant people (Saito et al., 2017; Galderisi et al., 2014). However, premorbid IQ (Saito et al., 2017) and neurocognitive processes (Galderisi et al., 2014; Bowie et al., 2008) have been repeatedly associated with a broader domain profiles of social functioning in the real world (Fett et al., 2011; Kalin et al., 2015). Since education level may be partly due to both premorbid IQ and neurocognitive performances, the associations found in the present study may reflect association between social functioning and neurocognitive performances. However, considering the positive effect of education on IQ (Lager et al., 2017), education itself may be directly correlated with social functioning. Thus, education level should be considered as a potential contributing factor in the level of social functioning.

Second, in five independent datasets (ES2, ES3, STAR*D, CATIE and STEP-BD) higher *professional/work status* has been associated with better social functioning, also when weighting for psychopathological severity. Consistently, in three dataset (STEP-BD, CATIE and ES3) this association was confirmed also in the remitted sub-sample (Table 2). Overall, unemployed patients showed a greater social dysfunction compared to the others. Despite this association could be explained by the consequent lower financial availability of these patients for social leisure activities, also the kind of job seems to play a role. Indeed, among the employed patients, low rank employees showed a greater social dysfunction compared to patients that are self-employed or that hold high-rank jobs (e.g., managers). It could be hypothesized that both financial availability and working time (or its flexibility) play a relevant role in the modulation of social functioning (see for example Mandelli et al., 2019). On the other hand, pre-existing social dysfunction may cause employment barriers, limiting the possibility to achieve better job positions (e.g., Himle et al., 2014). Furthermore, in two independent datasets (STAR*D and CATIE) to be married has been associated with lower social dysfunction. This result supports a role of a co-habitant partner in sustaining social functioning and quality of life overall, as reported by previous studies (e.g., Ran et al., 2017; Carlson and Kail, 2018). Obviously, this finding may also reflect that patients with higher social functioning could more easily find and maintain a relationship with a partner.

Third, *age* was found associated with social dysfunction in three datasets (ES1, CATIE and STAR*D) with younger patients showing higher degree of social dysfunction in mood disorder samples also when weighting for psychopathological severity. In the ES1 dataset this association was confirmed also in the remitted sub-sample (Table 2). Although this result may seem counterintuitive, we suggest that earlier pathophysiological processes may had greatly impacted on social functioning (Bernaras et al., 2018) whose normal profile is general more articulated than later in life (Marcum, 2013). On the other hand, in CATIE older age was associated with greater social dysfunction. This could be explained by the natural course of SCZ, which is often characterized by a progressive predominance of negative symptoms in older age (e.g., Mucci et al., 2017; Dollfus and Lyne, 2017).

Fourth, some measures of physical health were found associated with social functioning, with higher social dysfunction associated with *higher Body Mass Index (BMI)* in three datasets (ES2, ES3, and STEP-BD), *smoking habit* in two datasets (ES2 and ES3) and *medical co-morbidities* in STEP-BD dataset, also when weighting for psychopathology severity (see Table 2). Despite medical co-morbidities and overweight/obesity may intuitively impact on social functioning (Hofmann, 2016; Tamura et al., 2017; Krahn, 2011), it has also been demonstrated that social dysfunction impacts negatively on global health (Eisenberger and Cole, 2012), overweight/obesity (Serlachius et al., 2016) and smoking habit (Kim, 2018). Despite smoking is common in patients affected by psychiatric disorders (Ziedonis et al., 2008), the relationship between smoking and psychopathology is still not clear (Mathew et al., 2017; Fluharty et al., 2017). Nonetheless, it could be hypothesized that social

dysfunction may contribute to maintain this habit through the lack of social support, which is a factor contributing to successful smoking cessation (e.g., Creswell et al., 2015). Moreover, obesity seems to impact also on some neurocognitive processes (e.g., Mora et al., 2017) that may be involved also in the social brain functioning (e.g., attention and working memory) (Porcelli et al., 2018; Gilmour et al., 2018). Therefore, the associations found in our study were consistent with literature data, although the casual relationships between social dysfunction and both health and dangerous habit are still to be elucidated in detail.

Finally, as initially mentioned, we found that psychopathology severity modulates social functioning in all the investigated datasets. This is not surprising, taking into account that social dysfunction has been recognized as a relevant component of both MDD and SCZ clinical severity and it is listed among their DSM-V diagnostic criteria (Association AP, 2013). Nonetheless, the variance of social dysfunction indicators explained by psychopathological severity ranged from 12% to 29.2% in our samples, suggesting that the impact of symptoms on social functioning is significant but in some measures limited. When pooling both psychopathological severity and socio-demographic factors described above in a unified model, the variance of social functioning explained increased to 15–47%. Our results are consistent with previous literature, where only a percentage of real-world social functioning was explained by complex models that included various measures of symptoms, cognition, social cognition, and socio-demographic data (Fett et al., 2011; Bowie et al., 2008; Kalin et al., 2015). Therefore, although a number of psychopathological, cognitive, and socio-demographic factors may modulate social functioning, other elements, that still need to be identified, likely play a relevant role in causing social dysfunction (Ehnvall et al., 2014; Eisenberger, 2012; Holt et al., 2015). Thus, further studies are needed to investigate the other determinants of social functioning in both health subjects and neuropsychiatric patients (Kas et al., 2017; Kas et al., 2018). Clearly, these studies should carefully consider the factors already associated with social functioning in order to weight their effects, which could mask other associations (Porcelli et al., 2018).

A specific attention deserves the association between social functioning and *suicide risk* that was found in four datasets (ES1, ES2, STAR*D, and STEP-BD), which persists in two datasets (ES1 and STAR*D) also when weighting for psychopathological severity. Although a causal relationship cannot be derived from cross-sectional studies, our result underline the higher risk of suicide in patients with relevant social dysfunction, as already reported in literature (Heikkinen et al., 1993). Finally, in two dataset (ES1 and ES2) social dysfunction was associated with both benzodiazepines and antipsychotic co-treatments. Accordingly with literature data (Lugoboni et al., 2014; Park et al., 2016), it could be hypothesized that these drugs modulate social functioning, probably through their sedative and extra-pyramidal side effects.

4.1. Strengths and limitations of the study

Several limitations are present in our study. Despite the inclusion of 6826 patients affected by MDD, BD and SCZ from four different independent databases, most of the findings reported in the present work will require further studies to confirm the conclusions we proposed. For example, further studies are needed to better define (a) the role of education as critical moderator for social functioning, (b) the role of psychopathological, cognitive, and socio-demographic factors on social dysfunction in MDD, BD and SCZ patients, (c) the relevance of emotional biases in self-assessment of social functioning in MDD, (d) the more marked effects observed in younger age in mood disorders, probably reflecting a different age-dependent normal social functioning and a stronger impact of psychiatric disorders in adolescents. Recently, an example of this kind of studies has been developed: the PRISM project. PRISM is a European founded project that aim to investigate the determinants of social functioning across different neuropsychiatric disorders, applying a deep phenotyping which allows to assess several biological parameters, together with real-life indicators of social functioning and with a careful assessment of possible socio-demographic and psychopathological confounders (Kas et al., 2018; Bilderbeck et al., 2018). We identified other limitations. First, our analyses were cross-sectional, thereby not allowing causal inferences that require longitudinal observations, as previously underlined. Second, the use of derived and operationalized indicator of social dysfunction could be questionable, since post-hoc and not directly validated for the purpose. Third, since they were derived from different scales developed for different purposes, the comparability across the different indicator of social dysfunction is limited. Nonetheless, all the items selected from the different instruments assess the interactions with relatives, friends and other significant people, allowing a certain degree of comparison. Furthermore, the instruments selected are often self-reported and validation with objective outcomes (i.e. number of friends, contacts per day, social activities, etc.) of social functioning are lacking in the most part of datasets investigated. However, as stated above, also clinician-rated assessment of social functioning (e.g., QOLS “Interpersonal relations” category) may be affected by bias due to the subjective nature of the assessment. Fourth, these indicators were restricted to assess social interaction with friends, relatives and significant people, excluding work/school attendance and not addressing all the other aspects of social functions. Fifth, the use of different social dysfunction indicators across the samples limits the possibility of comparison between diagnoses. Sixth, we perform exploratory analysis on remitted patients only in four datasets, since for two datasets (STAR*D and GSRD ES2) these patients were not available. Further, as stated above, the remission criteria used for the SCZ sample (CATIE), may be questionable, since they are based on the total score of PANSS, possibly leading to a selection of a sub-sample of patients with predominant residual negative symptoms, rather than remitted patients. Finally, since our analyses were all hypothesis-driven and performed in 6 different datasets, we decided to not apply any statistical correction, setting the statistical significance at the standard level of $p < .05$. We are aware that our choice may increase the risk of false positive findings, but the comparison of results across different dataset mitigates this possibility.

4.2. Conclusion

In conclusion, this study demonstrated that a significant percentage patients affected by MDD, BD and SCZ show relevant social dysfunction. Social dysfunction is importantly related to but not completely explained by psychopathological severity since in some patients it persists during remission. Socio-demographic factors such as age, education level, professional work/status, marital status, medical co-morbidities, and smoking are associated with social functioning and should be taken into account in further studies investigating social dysfunction.

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Disclaimer

This publication reflects only the author's views and neither the IMI 2 JU nor EFPIA nor the European Commission are liable for any use that may be made of the information contained therein.

Declaration of Competing Interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pnpbp.2019.109835.

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