MEASURING CAPACITY TO CONSENT TO RESEARCH IN INDIAN SCHIZOPHRENIC PATIENTS WITH DEPRESSIVE SYMPTOMS

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ABSTRACT

BACKGROUND & OBJECTIVES

Depressive symptoms are commonly observed in schizophrenia. Around one-fourth of patients with schizophrenia meet criteria for a depressive disorder at some point of time in their lives. Schizophrenia can lead to impaired decision-making capacity resulting from delusions, lack of insight, impaired memory and mental flexibility. Moreover, depression can negatively influence concentration and abstract reasoning abilities, and also can be linked to nihilism and a decreased concern for personal well-being. Evaluating decisional capacity involves determining whether or not a patient/subject is psychologically or legally competent of making adequate decisions about research activities. The MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR) is a semi-structured interview format most extensively utilized by researchers for assessing the decision-making capacity of potential research subjects. Although the tool has expanded its global presence, little is known about its application in Indian schizophrenic patients with depressive symptoms. Therefore, the present study was designed to measure the decisional capacity to consent to research in Indian schizophrenic patients with depressive symptoms.

METHODS

Hundred patients aged 18–65 years with DSM-IV-TR diagnoses of schizophrenia participated in this study. Of these, 50 patients had depressive symptoms as defined by a score of ≥ 7 on the

Montgomery–Asberg Depression Rating Scale (MADRS). The patients were asked to pretend that they were potential candidates for a hypothetical trial involving an new antipsychotic drug, and their decisional capacity to consent to research was assessed using the MacCAT-CR.

RESULTS

The study results suggest that a majority of patients in both the schizophrenia and the schizophrenia with depressive symptoms groups demonstrated adequate understanding to consent to research. Schizophrenic patients with depressive symptoms showed weaker performance on all four abilities of decisional capacity in comparison to patients with schizophrenia, as measured by MacCAT-CR. This difference was statistically significant for 'understanding', 'appreciation' and 'reasoning' but not for 'expression of choice'.

CONCLUSION

These preliminary findings are among the first to illustrate the decision-making capacity to consent to research in Indian schizophrenic patients with depressive symptoms. Future work calls for larger samples to provide valuable information in this area.

KEY WORDS

schizophrenia/depressive symptoms/decisional capacity/competence/consent

BACKGROUND & OBJECTIVES

Schizophrenia is a long-term mental disorder that causes a range of different psychological symptoms like hallucinations, delusions, disorderly thoughts based on hallucinations or delusions and changes in behavior[1]. Several individuals with schizophrenia experience loneliness and social isolation, besides issues such as unemployment, low earnings and deterioration of physical health[2]. As a result, symptoms of depression may develop in people with schizophrenia. Furthermore, a study has shown that depressive symptoms are frequently observed in both men and women with schizophrenia, and do not appear to be merely a by-product of age, neuroleptics, family history, negative symptoms, or movement disorder[3].

In recent past, all areas of biomedical research have received reasonable attention from federal advisory bodies regarding the safety of human subjects. However, psychiatry research continues to be the topic of popular debate as mentally-ill individuals are prone to exploitation due to the effect of mental disorders on decision-making capacity (DMC) [4, 5]. For instance, people with schizophrenia may have an impaired DMC resulting from delusions, lack of insight, impaired memory and mental flexibility. Moreover, depression can negatively influence concentration and abstract reasoning abilities, and also can be linked to nihilism and a decreased concern for personal well-being[6].

Evaluating DMC involves determining whether or not a patient/subject is psychologically or legally competent of making adequate decisions about research activities[7]. Many significant advances have occurred in the structured tools intended for the assessment of DMC, but there still exists a need for further development and expansion of clinical evidence. The MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR) is a semi-structured interview format most extensively utilized by researchers for assessing the DMC of potential research subjects in all 4 commonly known dimensions of capacity to consent to research (understanding, appreciation, reasoning, and expression of a choice)[8]. Although the tool has expanded its global presence, little is known about its application in Indian schizophrenic patients with depressive symptoms. Therefore, the present study was designed to measure the decisional capacity to consent to research in Indian schizophrenic patients with depressive symptoms.

METHODS

PARTICIPANTS

Participants in this interview-based study conducted in the Department of Psychiatry, LTMG Sion Hospital, Mumbai, India, comprised of 100 patients aged 18–65 years with DSM-IV-TR diagnoses of schizophrenia. Of these, 50 patients had depressive symptoms as defined by a score of ≥ 7 on the Montgomery–Asberg Depression Rating Scale (MADRS) [9]. Patients with i) the presence of dementia, mental retardation or other organic brain damage, ii) any Axis-I psychiatric disorder other than schizophrenia according to the DSM-IV-TR diagnostic criteria, iii) serious and unstable medical conditions, and iv) current prolonged immobilization, formed a part of the study's exclusion criteria. Written informed consent was obtained from each patient after making them understand the study details. The study received favorable opinion from an independent Ethics Committee. After obtaining consent for the actual study, the investigator asked each patient to imagine that he/she was a potential candidate for another research study, and read through a comprehensive informed consent document for a hypothetical trial of a new drug for schizophrenia.

ASSESSMENT OF DMC

The MacCAT-CR format can be individualized to ask questions about a particular research project or, as in the case of this study, can describe a hypothetical project. In this study, the MacCAT-CR described a hypothetical clinical trial of a new drug for the treatment of schizophrenia. Selected information about the hypothetical study was disclosed, and a standard set of questions was asked to sample the participants' abilities.

All subjects in the study received the MacCAT-CR, an instrument used in the assessment of DMC to consent to research. This semi-structured interview provides subscale scores for four dimensions of DMC: understanding (range 0-26), appreciation (range 0-6), reasoning (range 0-8)

and expression of a choice (range 0-2). Questions for measuring 'understanding' comprised of 13 critical information elements concerning the study's purpose, methodology, benefits, risks, and alternatives (e.g., "What is the purpose of the research study explained to you?"). The three 'appreciation' questions revolved around subjects' beliefs about whether what they had been told truly applied to themselves, 1) "Do you think that you have been asked to participate in this study primarily for your benefit?"; 2) "As part of this study, do you think that you will visit your doctor as frequently as he/she thinks is best for your care?"; and 3) "What do you think would happen if you were to decide not to be in this study any longer?" Four questions for assessing 'reasoning' were based on subjects' abilities to compare research participation with other treatment options and to narrate the consequences of participation and nonparticipation on daily basis (e.g., "What is it that makes [the subject's chosen option] seem better than [the non-preferred options]?"). One choice question evaluated if the patient, without a doubt, could express a choice about participating in study. Higher total scores signify better performance.

RESULTS

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE PATIENTS

One hundred Indian schizophrenic patients aged 18–65 years with DSM-IV-TR diagnoses of schizophrenia participated in the study. Of these, 50 patients had depressive symptoms as defined by a score of ≥ 7 on the Montgomery–Asberg Depression Rating Scale (MADRS). Table 1 shows the demographic and clinical characteristics of the patients.

Table 1. Demographic and clinical characteristics of the patients

Particulars	**Schizophrenia (N= 50)**	**Schizophrenia with depressive symptoms (N=50)**	**ANOVA**
Mean Age in Years (S.D) (Range)	34.24 (14.008) (18-65yrs)	32.02 (11.631) (18-62yrs)	F= 0.743, df=1,98, p=0.391
Gender Male Female	 29 21	 24 26	χ^2= 1.004, df=1, p=0.316
Depression (total MADRS score) mean (S.D)	1.82 (1.600)	13.16 (4.287)	F= 307.045, df=1,98, p<0.01
MADRS, Montgomery–Asberg Depression Rating Scale.			

On the MADRS, the mean score for subjects with schizophrenia and depressive symptoms was higher than that of subjects with schizophrenia ($p<0.01$).

MACCAT-CR SCORE INTERPRETATIONS

Table 2 shows the performance of study subjects on the four decision-making abilities. Majority of the subjects in both groups were found to respond very well on the 42-point MacCAT-CR scale. Patients with schizophrenia had better overall scores than those with schizophrenia and depressive symptoms ($p<0.01$). On the 'understanding', 'appreciation' and 'reasoning' subscales, patients with schizophrenia scored higher than schizophrenic patients with depressive symptoms ($p<0.01$). The difference in mean scores for 'expression of choice' in both the groups was statistically non-significant ($p= 0.590$).

Table 2. Mean scores of patients on ability measures of the MacCAT-CR

Measure	Schizophrenia (N= 50)	Schizophrenia with depressive symptoms (N=50)	ANOVA
MacCAT-CR Score Total	39.96	29.16	F= 180.336, df=1,98, p<0.01
Understanding	25.52	20.28	F= 124.447, df=1,98, p<0.01
Appreciation	5.76	3.28	F= 217.753, df=1,98, p<0.01
Reasoning	6.82	3.86	F= 76.283, df=1,98, p<0.01
Expression of Choice	1.86	1.82	F= 0.293, df=1,98, p= 0.590

Table 3 shows relation between MacCAT-CR scores and the presence of depressive symptoms in study subjects ($p<0.01$).

Table 3. MAcCAT-CR scores relation with depressive symptoms

Presence of depressive symptoms	Mean rank	Findings
Yes (N= 50)	29.01	**U**= 175.500, z= -7.446, p <0.01
No (N= 50)	71.99	

DISCUSSION

Depressive symptoms are commonly observed in schizophrenia. Around one-fourth of patients with schizophrenia meet criteria for a depressive disorder at some point of time in their lives[10]. The presence of depressive symptoms in schizophrenia can possibly be linked with considerable distress, predominantly due to loss, grief and hopelessness.

Past research studies have established the fact that assessment of the schizophrenic patient's DMC to consent to research is a concern. Appelbaum and Grisso introduced MacCAT-CR, a semi-structured interview format that helps determine the capacity to provide informed consent [11-14]. Numerous studies involving schizophrenic patients and other patients have been carried out[15-17]. In this study, we aimed at measuring DMC to consent to research in schizophrenic patients with depressive symptoms.

Although the MacCAT-CR provides no optimal cutoff score for the establishment of capacity assessment, a National Institute of Mental Health-sponsored clinical trial called CATIE (Clinical Antipsychotic Trials in Intervention Effectiveness) used an 'understanding' score of 16 or higher on the 26-point subscale as an appropriate threshold for study randomization. The 'understanding' subscale was used to determine the threshold of DMC because 'understanding', in general, is highly associated with 'appreciation' and moderately with 'reasoning', and has the strongest psychometric properties of the three scales[18]. In support of this, the primary findings of our research suggest that a majority of patients in both the schizophrenia and the schizophrenia with depressive symptoms groups demonstrated adequate understanding to consent to research. Schizophrenic patients with depressive symptoms showed weaker performance on all four abilities of decisional capacity in comparison to patients with schizophrenia, as measured by MacCAT-CR. This difference was statistically significant for 'understanding', 'appreciation' and 'reasoning' but not for 'expression of choice'.

To our knowledge, these preliminary findings are among the first to illustrate the decision-making capacity to consent to research in Indian schizophrenic patients with depressive symptoms. Future work calls for larger samples to provide valuable information in this area.

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REFERENCES

1. Appelbaum P, Grisso T, Frank E, O'Donnell S, Kupfer D. Competence of depressed patients for consent to research. *Am J Psychiatry*. 1999; 156: 1380-1384.
2. Bosanac P, Castle D. Schizophrenia and depression. *MJA Open*. 2012; 1(4): 36-39.
3. Bonnie R. Research with cognitively impaired subjects: unfinished business in the regulation of human research. *Arch Gen Psychiatry*. 1997;54:105–11.
4. Candilis P, Geppert C, Fletcher K, Lidz C, Appelbaum P. Willingness of subjects with thought disorder to participate in research. *Schiz Bull*. 2006; 32 (1): 159-165.
5. Carpenter W, Gold J, Lahti A. Decisional capacity for informed consent in schizophrenia research. *Arch Gen Psychiatry*. 2000; 57: 533-538.
6. Cohen B, McGarvey E. Willingness and competence of depressed and schizophrenic inpatients to consent to research. *J Am Acad Psychiatry Law*. 2004; 32:134–43.
7. Decision-Making Capacity. Available from: www.ucsf.edu/lm/ethics/Content%20Pages/fast_fact_competence.htm, accessed on March 27, 2015.
8. Jeste D, Depp C, Palmer B. Magnitude of impairment in decisional capacity in people with schizophrenia compared to normal subjects: an overview. *Schiz Bull*. 2006; 32 (1): 121-128.
9. Kovnick J, Appelbaum P, Hoge S, Leadbetter R. Competence to consent to research among long-stay inpatients with chronic schizophrenia. *Psych Serv*. 2003; 54: 1247-52.
10. McDermott B, Gerbasi J, Quanbeck C, Scott C. Capacity of forensic patients to consent to research: the use of the MacCAT-CR. *J Am Acad Psychiatry Law*. 2005; 33: 229-307.
11. Moser D, Schultz S, Arndt S. Capacity to provide informed consent for participation in schizophrenia and HIV research. *Am J Psychiatry*. 2002; 159: 1201-1207.
12. Palmer B, Dunn L, Appelbaum P. Assessment of capacity to consent to research among older persons with schizophrenia, Alzheimer disease, or diabetes mellitus: comparison of a 3-item questionnaire with a comprehensive standardized capacity instrument. *Arch Gen Psychiatry*. 2005;62:726–733.

13. Ray G. Psychopathology and psychiatric disorders in neuropsychiatric patients. A Prospective Study. Available from: http://www.priory.com/psych/neuropsy.htm, accessed on April 15, 2015.

14. Siris S. Depression in schizophrenia: perspective in the era of "atypical" antipsychotic agents. *Am J Psychiatry*. 2000; 157: 1379-1389.

15. Schizophrenia. NHS Choices. Available from: www.nhs.uk/Conditions/Schizophrenia/Pages/introduction.aspx, accessed on March 24, 2015.

16. Stroup T, Appelbaum P, Hongbin G. Longitudinal consent-related abilities among research participants with schizophrenia: Results from the CATIE study. *Schizophr Res*. 2011; 130 (1-3): 47–52.

17. Vogel-Scibilia S. The controversy over challenge and discontinuation studies: perspective from a consumer-psychiatrist. *Biol Psychiatry*. 1999;46:1021–114.

18. Zisook S, McAdams L, Kuck J, Jude L, Jeste D. Depressive symptoms in schizophrenia. *Am J Psychiatry*. 1999;156(11):1736-43.