



Decisional Capacity for Research in Schizophrenia: a Review

KEYWORDS

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ABSTRACT

Schizophrenia is a complex biochemical brain disorder that affects an individual's ability to differentiate real from unreal experiences. The vulnerability of individuals with schizophrenia to impaired decision-making capacity has resulted in ethical concerns regarding their involvement in research. In such persons, cognitive and emotional impairment may result in therapeutic misapprehension- the tendency to confuse clinical research participation with mental health treatment. Avoiding research involving patients is not a justified ethical response as it is also the right of all individuals to participate in research, to benefit from the best treatment, and to contribute to the establishment of best treatments. Several research studies have not only led to better outcomes for mental health conditions but also have had a significant impact on the quality of lives of individuals with mental illness and their families. This review summarises information available on the decisional capacity for research in schizophrenia

INTRODUCTION

For a valid informed consent, three requirements need to be considered. These are (1) the provider is accountable for providing key information on the nature and rationale of the proposed procedure, possible benefits and risks, options including no treatment, and voluntary withdrawal, (2) patients must have the opportunity to make decisions without force, (3) patients must be competent to make the treatment decision. Thus, an individual possessing the consent capacity may not be enrolled in a research without his / her consent and he / she may accept or refuse to participate without involvement or irrespective of a third-party consent. When the study subject is identified as incapable of giving a voluntary informed consent, a Legally Acceptable Representative (LAR) should provide the consent on behalf of the subject. Additionally, if consent is provided by the LAR, the potential subject must be informed of the consent and subject's objection, if any, should be considered (NBAC, 1998). The principle of informed consent in persons with incapacities is often undermined. However, some mental health providers feel that those with mental illness may have either no or selective impairment and could thus give informed consent.

Schizophrenia is a long-term mental disorder marked by the presence of distortions in perception, disorganization of thought, and weakening of motivation and emotional responsivity. Any of these elements of the illness, may reduce the decision-making capacity (DMC) in persons with schizophrenia (Carpenter *et al.*, 2000). Appelbaum and his colleagues (Appelbaum and Roth, 1982; Appelbaum and Grisso, 1988; Appelbaum and Grisso, 1995; Roberts, 1998) describe the fact that DMC consists of the ability to understand, appreciating the significance of the decision made, logical reasoning, and communicating a well-reasoned choice. This preliminary work has been employed by researchers who study the mentally ill to determine the impact or connection between mental illness and decision-making capabilities. Schizophrenia has an unpredictable course, so symptoms and functional impairment differ eventually.

ADVANCEMENT OF CAPACITY ASSESSMENT INSTRUMENTS

The progress of instruments to measure DMC has been important to the emergence of the capacity assessment field. In the 20th century, incapacity was evaluated on the basis of the presence of a diagnosis alone, and possibly some global indication of mental status. A critical conceptual and legal development shifted the focus from diagnosis to the key functional abilities relevant for specific capacity areas (Grisso, 2003). The emphasis on functional abilities stimulated the development of conceptually sound instruments to measure abilities related to decision making. These standardized capacity assessment instruments intend to improve the low reliability of more general clinical examinations (Markson *et al.*, 1994; Marson *et al.*, 1997; Rutman and Silberfeld, 1992) by focusing clinical evaluation on the most applicable functional skills. Numerous recent reviews summarize the characteristics and applications of different instruments (Moye *et al.*, 2006; Sturman, 2005).

The most commonly used instrument, the MacArthur Treatment Competence Assessment Tool for Clinical Research (MacCAT-CR), is designed to assess DMC in clinical research settings. Beginning with a description of the specific proposed clinical trial to potential participants, this semi-structured interview yields scores for the four commonly recognized dimensions of decisional capacity, namely, understanding (range 0-26 points), appreciation (range 0-6 points), reasoning (0-8 points), and expression of a choice (0-2 points). Each level is scored and a final score of 0-42 is computed. The instrument provides a comprehensive analysis of the subject's capacities and can be administered in 15-20 minutes (Appelbaum, 2006). Quantification of subjects' responses allows comparisons across subjects and subject groups and permits the MacCAT-CR to be used for screening individual participants. Since the MacCAT-CR was designed to be consistent with a basic maxim in the legal definition of competence, it has no established cutoff score for determination of capacity assessment. The MacCAT-CR has been used in several studies of consent capacity in patients with schizophrenia.

Since the development of the MacCAT-CR there have been attempts to develop more economical but still valid and reliable tests/ instruments for determining capacity to consent to research participation, predominantly for cognitively impaired individuals who may have limited ability to concentrate as a result of both physical and cognitive problems. Several shorter tools have been developed; however, their brevity limits their assessment to one or two components of the capacity construct, and thus limiting their role to screening rather than capacity determination (Saks *et al.*, 2002; Resnick *et al.*, 2007).

A five-item questionnaire known as the Evaluation to Sign Consent (ESC) intends to evaluate subject's understanding of key aspects of a study. Moser *et al.*, (2002) used both the ESC and MacCAT-CR in a study assessing the competence of patients with schizophrenia ($n = 25$) and HIV ($n = 25$). The ESC was able to identify those individuals who displayed poor understanding on the MacCAT-CR. However, the ESC does not evaluate appreciation, reasoning, or the capacity to evidence a choice. Therefore, the MacCAT-CR is better suited to disclose specific insufficiencies in a patient's capacity, which may then be addressed by researchers or health care practitioners (De Renzo *et al.*, 1998; Moser *et al.*, 2002).

The Aid to Capacity Evaluation (ACE) is a semi-structured test that allows clinicians to rate patients as: definitely incapable, probably incapable, probably capable, and definitely capable. Some advantages of the ACE include a short administration time (approximately 15 min) and the fact that it is customized to each patient's disorder/treatment. Though ACE has shown promise, it assesses only appreciation of disorder/treatment and understanding of informed consent, and requires further validation (Etschells *et al.*, 1999).

RESEARCH ON DECISION MAKING CAPACITY (DMC)

Many psychiatric researchers have challenged the assumption that persons with mental illness are at a higher risk of being exploited due to the effects of mental illnesses on DMC (Vogel-Scibilia, 1999; Bonnie, 1997). Others propose that there are those with mental illnesses who maintain considerable DMC and to single out this research group not only reinforces the social stigma of mental illness, but could hinder needed psychiatric research (Carpenter and Conley, 1999; Michels, 1999; Appelbaum, 1999).

Decision-Making Abilities in Patients with Schizophrenia

Some studies on decision-making abilities revealed that while patients with schizophrenia as a group had lower scores than those without neuropsychological impairment on DMC, they had higher performance than patients with dementia. The performance of patients with schizophrenia was highly inconsistent with a few patients performing at a level similar to the control participants. Poorer performance was most strongly linked with neuropsychological impairment. Cognitive ability was strongly associated with decisional capacity, while negative and disorganized symptoms were strongly associated with decreased decisional capacity.

In a pilot study (Grisso and Appelbaum, 1991), impairments in decision-making abilities were studied across three inpatient groups with schizophrenia or schizoaffective disorder, major depression or bipolar disorder, or ischemic heart disease, and one outpatient group with no major mental health or medical disorder. An instrument named 'Measuring Understanding of Disclosure' assessed individ-

ual understanding of typical information required for disclosure in informed consent for treatments involving medications. Each participant received one medical and one mental health standardized disclosure of informed consent form. Instrument was administered in three protocols: (a) uninterrupted with entire disclosure completed before asking standardized questions; (b) single-unit disclosure with a unit of informed consent presented and standardized questions immediately following each unit; (c) single-unit recognition with a unit of informed consent presented and participants then asked to identify after each unit if the four presented statements were similar to or different from the given information. There was a significant difference across the four groups on all three methods of administration. Generally, performance was better for all groups on the single-unit disclosure and recognition methods than on the uninterrupted disclosure. The schizophrenic group had significantly poorer understanding of informed consent disclosures about potential medication on both mental and medical illness forms on each of the protocols than the other groups. The researchers noted that the results did not support the generalized presumptions about decision-making abilities of those with schizophrenia. The schizophrenic participants had a considerable range of scores with some performing at a level similar to the means of the non-mentally ill participants. Findings suggested that poorer understanding may be greater in those with severe schizophrenic symptoms based on results of the Brief Psychiatric Rating Scale (BPRS).

Subsequently, a full-scale multi-centered study (Grisso and Appelbaum, 1995) was conducted with 498 similar participants. The study results were comparable to those of the pilot. Hospitalized patients with mental illness, predominantly those with schizophrenia, displayed deficits in DMC more often than the medically ill and control groups. Nevertheless, approximately 50 % of patients with schizophrenia performed well on all measures combined while a majority of them performed satisfactorily on any particular measure. Participants with more severe psychiatric symptoms, such as delusions and disorganized thinking, performed poorly. About three fourths of those with major depression performed well on all measures and demonstrated intermediate levels of DMC. The hospitalized medically ill patients performed almost on a level with those of the control group. The researchers concluded that mental illness does not necessarily impair DMC.

Stroup *et al.*, aimed to investigate whether research participants with schizophrenia maintain adequate consent-related abilities. They observed alterations in capacity to consent from enrollment to 6 and 18 months during the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study. Using the MacCAT-CR, they found that nearly all (96%) of the 1,158 participants with schizophrenia retained decisional capacity to consent during the CATIE study (Fischer *et al.*, 2013).

The ability to obtain informed consent in middle-aged and older persons (40 years of age or older) with schizophrenia may be more challenging as cognitive changes associated with aging may have an adverse impact on decision-making capacity (Palmer *et al.*, 2004). The researchers studied the range, stability, and correlates of DMC related to a hypothetical study of treatment with an atypical antipsychotic medication. The control group was asked to imagine they had the condition described in the disclosure form. Participants included 59 middle-aged and older outpatients (mean age of 50.2, SD= 6.8) with schizophrenia

or schizophrenia affective disorder and 38 control participants (mean age of 56.8, SD=9.2). The control group had significant positive correlations between cognitive abilities measured by total score of the Mattis Dementia Rating Scale (MDRS) and the MacCAT-CR reasoning measure and between the memory subscale score of the MDRS and the MacCAT-CR understanding measure. The MDRS memory subscale accounted for significant additional variance in the measure of understanding. The MDRS conceptualization subscale score accounted for significant additional variance in the measure of reasoning. The cognitive ability score of Abstraction/Cognitive Flexibility accounted for significant additional variance in the measure of expression of a choice. At a one-month follow-up, the test-retest correlations were highly significant for understanding, appreciation, reasoning, and expression of a choice. The researchers concluded that level of decisional making capacity was not associated with age or severity of psychology, but was strongly associated with cognitive test performance. The patients' decisional capacity remained stable during the one-month follow-up.

Candilis *et al.*, conducted a study involving 52 participants with schizophrenia of age 19-59 years so as to identify variables related to the willingness of subjects to participate in research that could be markers of participant vulnerability. The researchers asked the subjects to consider participation in a hypothetical trial of a new antibiotic versus standard treatment for a sore throat. When asked if they would choose to participate in the trial, 33 (63.5%) participants replied "yes," while 19 (36.5%) said "no." Participants with more education were more likely to indicate a willingness to take part in the trial. Willing and unwilling participants differed significantly on two of the reasons offered for their decision. Those who were willing to participate in the trial (1) scored higher in the understanding

and expressing a choice dimensions of the MacCAT-CR, (2) scored significantly higher on the Mini-Mental State Examination (MMSE), (3) scored significantly lower on the total Positive and Negative Syndrome Scale (PANSS) indicating less psychosis, and (4) scored significantly lower on the general scale of the PANSS. The researchers concluded that if better understanding leads to greater willingness to participate, there was support for the informed consent process and the movement toward enhanced informed consent interventions. They noted that when potential participants had vacillating or uncertainty in making a choice, this may raise the researchers' sensitivity to those with thought disorders.

A study by Eyler *et al.*, aimed at evaluating various methods of interactive questioning during presentation of consent information related to clinical research among patients with schizophrenia. Patients were randomized to receive either standard administration (SA) of a consent form or one of two interactive questioning methods: Corrective Feedback (CF), in which the correct answer was given subsequent to the participant's response, or Errorless Learning (EL), in which correct answers were given just before the question. The MacCAT-CR was utilized to determine the DMC abilities, namely, understanding, appreciation, reasoning, and expression of a choice following presentation of the consent form. The study outcomes revealed that potential subjects demonstrated better understanding during the consent process than at the end of the process in both interactive questioning conditions. In both these groups, concurrent and post-consent understanding scores were highly correlated, suggesting that those who understand information well initially are also those who best retain the information presented.

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