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Decisional Capacity of Patients With Schizophrenia to Consent to Research: Taking Stock

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With the growth in recent years of studies of decisional capacity for research among people with schizophrenia, this is an opportune time to ask three questions: What have we learned from these studies? What remains to be learned? And what normative issues still need to be resolved? Among the things learned are that patients with schizophrenia, as a group, have lower scores on measures of decisional capacity than normals, but higher performance than patients with dementia. However, performance is highly variable within the group, correlates most strongly with neuropsychological impairment, and seems susceptible in many patients to successful remediation. The issues that remain in need of exploration include the development of a brief screening instrument for decisional capacity that can be used routinely, and the identification of those patients most likely to benefit from more intensive informational procedures. Finally, among the normative issues still in need of resolution are the degree of capacity needed to consent to research participation, how to deal with fluctuating capacity during research projects, and the legitimate extent of surrogate consent for participation of incompetent patients in research.

Key words: decisional capacity/informed consent/schizophrenia/research

Introduction

Over the last decade, the capacity of patients with schizophrenia to consent to participation in research probably has attracted more attention than any other aspect of the ethics of research with this population. This may be an appropriate point to consider the answers to 3 questions: (1) What have we learned about decisional capacity for research in people with schizophrenia? (2) What do we still need to find out through empirical investigations? and (3) What normative issues remain to be addressed?

It is hardly surprising that the research participation of patients with schizophrenia has become an issue of concern. Given the importance placed on subjects' voluntary informed consent as a prerequisite for the ethical conduct of research, the cognitive and emotional impairments associated with schizophrenia raise obvious questions about patients' capacity to consent. Hence, many of the investigations over roughly the last decade have been aimed at determining the extent to which the presence of schizophrenia precludes patients from competently agreeing to enter research projects.

What Have We Learned About Decisional Capacity for Research in Schizophrenia?

Existing data on decisional capacity for research can best be summarized by saying that, although patients with schizophrenia as a group show greater levels of impairment than non-ill comparison subjects, patients with depression, or patients with general medical illnesses, there is considerable variation, and many patients with schizophrenia score in the same range as comparison subjects. Thus, the presence of a diagnosis of schizophrenia per se is not an indication that a subject is unable to give competent consent to research participation.

The initial study in this area was performed by Carpenter and colleagues,[1] and its findings have since been echoed in other reports. Comparing the performance of 30 patients with schizophrenia or schizoaffective disorder with 24 non-ill comparison subjects on the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR),[2] the investigators found that the group with schizophrenia performed significantly worse on measures of understanding, appreciation, and reasoning. However, standard deviations in the schizophrenic group were large, and there was a good deal of overlap with the non-ill subjects.

Kovnick et al. contrasted the same non-ill comparison group used in the Carpenter et al. study with 27 long-stay inpatients in a state hospital and report very similar findings on the MacCAT-CR.[3] Although Moser et al.,

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comparing 2 groups of 25 subjects each with schizophrenia and HIV infection, found somewhat higher MacCAT-CR scores for their schizophrenic group than the previous studies, these subjects still scored significantly worse on the measures of understanding and appreciation, though not on reasoning or choice, compared with the HIV group.[4] However, using a brief questionnaire that assessed subjects' understanding of several key aspects of the study, Moser and colleagues concluded that 80% of the schizophrenic subjects, compared with 96% of subjects with HIV, had adequate capacity to consent.

If research subjects with schizophrenia generally perform worse than persons with other mental or general medical illnesses, they appear to do better than at least 1 group. Palmer et al. compared 35 outpatients with schizophrenia with 36 patients with diabetes and 30 patients with mild to moderate Alzheimer's disease.[5] The MacCAT-CR scores of the schizophrenic subjects were intermediate between the better-performing diabetic patients and the more impaired Alzheimer's group, although the differences were not consistently statistically significant. And Moser and colleagues have shown, in a small sample of 10 schizophrenic subjects whose antipsychotic medications were stopped for 2 weeks as part of a study protocol, that only MacCAT-CR reasoning scores showed a significant decrease from baseline at the end of that period, suggesting a certain robustness to patients' decisional capacities.[6]

A good deal of effort has been invested in identifying the psychopathologic correlates of impaired decisional capacity. Carpenter et al.'s study was the first to suggest that neuropsychological functioning is the strongest predictor of decisional capacity scores, although they also found significant effects for psychotic symptoms.[1] Since that work, the importance of neuropsychological impairment for decision-making capacity has been confirmed by other groups using a variety of measures.[3–5] In contrast, the relationship between psychiatric symptomatology, including both positive and negative psychotic symptoms, has been markedly inconsistent across studies. Thus, as is true for other areas of functional capacity, the ability of patients with schizophrenia to make competent decisions relates more to their overall cognitive functioning than to the presence or absence of specific symptoms of the disorder.

Finally, the research to date offers some reason for optimism with regard to the possibility of assisting patients with impaired decisional capacity to make their own choices about entering research projects. Carpenter et al. showed that an educational intervention over the course of a week could bring most of their sample who scored poorly on understanding into the range of performance of the comparison group.[1] Other efforts utilizing computerized or videotaped presentations have reported similarly positive results.[7–8] However, our knowledge of how to improve the informed consent process for all patients and subjects is inadequate at best, has been focused on understanding to the neglect of most other decisional capacities, and leaves much to learn with regard to patients with schizophrenia in particular.[9–10] The lessons that can be drawn from the literature on patients with schizophrenia in the research setting are generally seconded by studies not reviewed here that have examined the decisional capacity of schizophrenic patients in treatment contexts.

What Remains to Be Learned?

As knowledge has increased regarding the extent and distribution of decisional impairment among patients with schizophrenia who are asked to make decisions about research, it is hardly surprising that new questions have arisen. Without pretending to present a comprehensive list, it may be possible to point to several useful foci for studies intended to follow up the findings summarized above.

The recent surge in research on decisional capacity—not just in schizophrenia but across medicine—was stimulated to a considerable extent by the availability of conceptually sound instruments allowing the reliable measurement of abilities related to decision making. But instruments that are helpful for the purpose of studying decisional capacity may not always meet the needs of clinicians or researchers looking to screen potential subjects. Thus, the MacCAT-CR, which has been the most widely used instrument for the study of decision-making capacity (along with the MacArthur Competence Assessment Tool for Treatment, its sibling, designed to assess capacity in treatment settings),[11] takes approximately 15–20 minutes to administer, depending on the impairment of the subject. Although that may be perfectly acceptable when the aim is to get a comprehensive view in a study of subjects' capacities, the time investment may be more than would be optimal in a screening setting.

Recognizing this, several research groups have begun to experiment with briefer instruments, especially the Evaluation to Sign Consent (ESC), which presents subjects with 5 questions aimed at assessing their understanding of several important aspects of the study.[12] The ESC has been shown to correlate with MacCAT-CR understanding scores but does not address appreciation, reasoning, or choice.[4] An even shorter, 3-item questionnaire shows strong correlations with the MacCAT-CR understanding measure and moderate, but still significant, correlations with appreciation and reasoning; although the optimal cutoff score offers 100% sensitivity, specificity was only 77%.[5] As the authors of that study suggest, a more comprehensive instrument like the MacCAT-CR may be appropriate for use in studies of populations with high base rates of impaired capacity, whereas a briefer screening instrument might be susceptible to more general use.

What to do with potential subjects who are identified as decisionally impaired is another focus for future work. Findings that it is possible to improve subjects' decisional performance with alternative educational approaches suggest that impaired capacity should be understood as akin to the kind of learning disability that many schoolchildren manifest. The presence of such a disability does not mean that the children cannot learn, just that they may take longer than average to assimilate and process new material. Similarly, many of the research subjects with schizophrenia who show decisional impairment on the MacCAT-CR and other measures can ultimately be brought to the level of understanding, appreciation, and reasoning necessary for a competent decision—at least if the preliminary data we have to date are accurate.

As a consequence, an ability to identify in advance those potential subjects whose decisional capacities are most likely to be assisted by an additional educational intervention would be useful. Studies of this sort have not yet been performed. It may be that the same variables that predict poor initial performance, especially neuropsychological impairment, will also flag those persons least likely to benefit from additional attention, but that remains to be demonstrated. In addition, which interventions are most effective in augmenting subjects' capacities is worth investigation. To date, the few research groups that have explored this area have assumed that multimodal presentations that go beyond the written content of the standard consent form are most likely to be effective. However, from what we know of differences in learning styles in other contexts, not every subject may respond positively to the same kind of intervention. Individual differences in response thus need to be explored as well.

What Normative Issues Remain to Be Addressed?

Empirical studies of the sort described above, and evident elsewhere in this special issue, can provide guidance to policy makers and researchers who are confronting the significant ethical problems that can arise as a result of decisional impairment in persons with schizophrenia. But some problems require more than data for their solution; they call for careful reasoning about normative matters, that is, consideration of moral values and how they should influence policy. Here I offer just 3 examples of the many that could be cited.

First is an example related to the previous discussion: determining the degree of capacity that should be required of a person with schizophrenia prior to allowing him or her to decide about research participation, and whether the requisite level of capacity should be raised or lowered depending on the riskiness of a given research project. This issue has largely been elided to date, with few projects specifying how much capacity their subjects must have, leaving the determination instead to the judgment of the person recruiting the subject. However, it seems likely that Institutional Review Boards (IRBs) will increasingly ask investigators to identify the level of capacity they will require, and some projects—such as the multisite Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study of antipsychotic effectiveness in schizophrenia—have done so already. Even when determinations of this sort have been made, though, lines have tended to be drawn somewhat arbitrarily. Indeed, this has been true as well of many studies of decisional capacity itself, in which varying definitions of impairment have been used to identify those subjects who are considered presumptively incompetent.

What are some options for how this issue might be addressed? From among the large amount of information provided to prospective subjects, we could identify those elements that are so critical to valid consent that subjects will be required to understand, appreciate, or reason about them or will be excluded from participation. This a priori approach might be augmented by data on the performance of non-ill populations, since it seems misguided to require higher levels of capacity on the part of persons with schizophrenia than are manifested by nonaffected groups. The views of potential subjects, members of the general population, and even researchers themselves may constitute additional useful data. Clearly, considerable normative work, informed by these sorts of data, remains to be done on this issue.

A second example of an area where normative work is required derives from the reality that many schizophrenia research projects follow patients over time, either to track the progress of the disorder or to gauge treatment effect. Such longitudinal studies raise questions about whether subjects with schizophrenia, whose symptoms and decisional impairments may fluctuate over time, require special protections in these settings. For example, what should the response be when a subject who offered a competent consent to enter a study becomes notably incompetent at some point in its course? We usually assume that subjects retain the capacity to protect their own interests in a longitudinal study, for example, by withdrawing from participation if they are experiencing unanticipated and intolerable side effects or lack of treatment effectiveness. But incompetent subjects may lack the ability to identify and act on their interests, leaving them vulnerable to harm.

To protect subjects who become incompetent, one could simply withdraw them from the study. Termination of their participation, however, may itself be harmful to them (e.g., if the study intervention has been successful, when others have not) and may contravene their competent wishes. The CATIE study, mentioned earlier, has dealt with this situation by creating the role of a "subject advocate," who is called upon when subjects are thought to have lost decisional capacity. Subject advocates have the power to remove a subject from the study if they

decide that the risk/benefit considerations on which the subject's competent consent was based have changed significantly and adversely.[13]

Whether this is an adequate safeguard may depend, among other factors, on how competently the initial decision to enter the project was made and how well the subject advocate can assess changes in the risk/benefit ratio of continued participation. But the acceptability of this approach also depends on how averse we are to accepting surrogate decisions about continuing research involvement, especially when considerable risk may be present. Should the default rule be to try to follow subjects' previously expressed choices, as best as possible, or to err on the side of protecting incompetent subjects from harm by removing them from studies when the capacity to make decisions is no longer present? This is precisely where the normative analysis must take place.

Finally, there is a related normative issue that involves schizophrenia research but applies more broadly to all subject populations at risk for impaired decisional capacity. There may be studies targeted at persons with severe and intractable schizophrenia that could not be conducted without enrolling subjects who lack the capacity to make decisions for themselves. Surrogate consent for research, including the potential use of advance directives, is even more salient for other research populations—for example, patients with Alzheimer's disease—than for persons with schizophrenia. It is, however, likely to be material to some schizophrenia research projects and is now a gray zone of law and policy that fairly begs for careful attention and reasonable solutions.[14] Some formulations of this problem would largely reject allowing anyone other than the competent subject to make such decisions,[15] while others would allow greater flexibility, especially in light of some preexisting indication of the subject's desires.[16] This might be a circumstance in which data on the views of potential subjects would carry substantial moral weight, and practical clarification is badly needed.

Conclusion

The vulnerability of persons with schizophrenia to impaired decisional capacity has created a substantial body of ethical concerns regarding their involvement in research. Although burgeoning interest in these issues has been evident over the past decade, and a good deal of empirical data has been accumulated, there remain unanswered empirical questions and difficult normative challenges that must still be addressed. Moreover, as is often the case in medicine in general, it has been difficult to translate approaches validated in research studies to the everyday world. For example, a good deal of research has demonstrated that the complexity of consent forms exceeds the abilities of most research subjects to comprehend them. Yet, if anything, forms continue to grow in complexity, driven by both perceived legal imperatives and the culture of IRBs. This example suggests the difficulty of altering real-world behavior, with its many determinants, and the importance of systematic efforts to implement reforms that may flow from current and future empirical ethics work.

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