

A follow-up neurobiological study: why volunteer?

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There is usually great concern over the use of psychiatric patients for clinical research, as it raises the ethical and legal issues of human dignity and autonomy. In this paper the authors describe and evaluate a follow-up neurobiological study of patients who had been discharged from a psychiatric research ward at least ten months earlier. It is pointed out that such studies are rare and that the writers were provided with the unique opportunity to examine attitudinal and motivational dimensions involved in the patients' agreement to participate in the study.

Introduction

Participation of psychiatric patients in clinical research studies has raised legal and ethical issues regarding human autonomy and dignity as well as concern about the conduct of the research itself.^{1,2} Attesting to these concerns is the relatively recent development of institutional human investigation committees which perform independent evaluations of proposed clinical studies for their conformity to accepted ethical procedures. Balanced against the risk of unethical experimentation on some human subjects is the potential benefit to be derived from ethically conducted studies. Indeed, some have suggested that there is a scientific and moral obligation to carry out clinical research.^{3,4}

To achieve the goal of obtaining new knowledge about psychiatric illness while eliminating unethical research, formal institutional review systems need to be augmented by research on the research process itself. This effort, to date, has been relatively meagre and has consisted primarily of sociopsychological analyses of clinical research wards and attitudinal studies of research staff members and research patients. Conflicts between research and treatment priorities have been examined and found to affect both patient care and conduct of research.^{5,6} Patients' ethnic or social background has been reported to have a significant influence on attitudes toward research of both patients and research staff.⁷ Other studies have focused on patients' attitudes and fantasies regarding research and their influence on continued participation as research subjects.^{8,9}

Among the most important current strategies of clinical psychiatric research is the longitudinal

design in which variables of interest are measured repeatedly in the same patients over a period of time. Although such studies may intensify ethical problems in some aspects,¹⁰ they are critical for the further understanding of 'state-trait' relationships as well as for further specification of the course of psychiatric illness and its modification by various treatment modalities. The major difficulty in successfully carrying out longitudinal studies is inability to contact or to enlist the further cooperation of individuals who were previously studied. This difficulty may be magnified by the degree of inconvenience or discomfort involved in the research design. For example, being interviewed or completing 'paper-and-pencil' questionnaires may be a good deal less threatening than neurobiological studies focusing on collection of specimens of body fluid such as blood or urine.

We have recently carried out a neurobiological follow-up study of depressed patients in which patients were restudied at least ten months after being discharged from a psychiatric research ward.¹¹ Such studies have been very rare, and we were provided with the unique opportunity to examine the attitudinal and motivational dimensions involved in the patients' agreement to participate in the study.

Background to the study

The neurobiological study involved female subjects who had been diagnosed as having a primary affective disorder by the Washington University Criteria¹² and who had been treated and studied previously on the research ward. At least ten months after discharge they were asked to participate in a follow-up study which involved a 3-day period of 24-hour urine collections, self-rating scales, blood collection, and several interviews with a psychiatrist. They were also placed on a special diet throughout the period of the follow-up study. Subjects taking psychotropic medications were studied for the 3-day period, withdrawn from the medications and restudied after at least 21 days. Subjects were paid a modest fee for each of the 3-day periods in which they participated. Twelve females were invited to participate in the study. Eight accepted while four declined.

Interviews were conducted with the subjects within forty-eight hours after they had given voluntary informed written consent for their participation in the study. These interviews,

modelled on Gray's interviews with subjects in medical research,¹² were carried out by the senior author, who had known and participated in the treatment of the subjects during the time of their previous hospitalisation. The first part of the interview was semi-structured with open-ended questions concerning:

- 1) The patients' reactions to the decision to participate
- 2) Their understanding of the research
- 3) The process of their decision to participate.

The second part of the interview was based on Gray's structured questionnaire designed to evaluate the relative importance of factors in subjects' decisions to participate in research. This included:

- 1) A checklist of factors related to decision to participate, to be answered yes or no, then ranked in order of importance
- 2) A second checklist of factors to be answered in terms of whether each factor was given much thought, some thought, or no thought at all.

The checklists were read to the participants and the information was recorded by the interviewer at the time it was given. A second interview was conducted with participating subjects within a week of the patient's completion of participation in the study. Briefer structured interviews were administered to the four individuals who declined to participate in the follow-up study.

Results

The following information was obtained from the semi-structured part of the initial interview with the participants. In answer to the question: 'How do you feel about your decision to participate?' six of the eight participants expressed ambivalence, including fear and anxiety. One of the six, whose participation involved being taken off medications, expressed directly the fear of becoming ill again. Five of the six expressed anxiety over the possibility of 'reliving' the experience of their previous hospitalisation on the research ward for acute depression. In answer to the question, 'Who was involved in your decision to participate?' seven of the eight participants had discussed the invitation to participate with family members before making the decision. In several cases advice had been sought from extended family and friends as well. In answer to the question, 'What is your understanding of what will be done in the study?' all eight of the participants could explain the procedures, and when asked, all expressed satisfaction with the amount of information they had been given.

Responses of participants to the structured questionnaire are shown in Tables I and II. On the first checklist (Table I) all eight of the participating subjects reported that one of their reasons for

volunteering was the belief that their participation would result in direct benefit to others. Six of the eight gave this as a primary reason for taking part, i.e. ranked it first or second. Six of the eight subjects also believed that the study would result in direct benefit to themselves, other than financial. In four cases this belief was related to the opportunity to have a trial off medications while being carefully observed. However, only three of the six subjects expecting direct benefit gave this as a primary reason for participating. Five subjects gave financial benefits as a motivating factor, but only three saw this as among primary reasons for participating. Six subjects felt some obligation to the research unit which had provided their treatment in the past. Interestingly, although subjects' current therapists were contacted prior to contacting subjects themselves, none of the six subjects in therapy at the time felt that the current therapist had any influence on the decision to participate.

Table I *Factors considered important by eight subjects who decided to participate in the follow-up study*

| Factor | Considered Important | | Rank of Importance | |
|--|----------------------|---------|--------------------|-------------|
| | Yes N | No N | First N | Second N |
| Influence of current therapist | 0 | 8 | 0 | 0 |
| Expectation of financial benefits | 5 | 3 | 1 | 2 |
| Belief in direct benefit to others or to medical science | 8 | 0 | 3 | 3 |
| Influence of family | 3 | 5 | 1 | 0 |
| Belief in direct benefit to self | 6 | 2 | 1 | 2 |
| Feeling of obligation to research unit | 6 | 2 | 2 | 1 |

On the second checklist (Table II) six of the eight participants gave 'much thought' to belief in direct benefit to self. Seven of the eight participants gave 'much thought' to belief in benefit to others and to belief their participation might help advance medical science. Again, none of the eight participants felt she was influenced by the current therapist's reaction.

In follow-up interviews all eight participants expressed positive feelings towards having participated in the study. Feelings of accomplishment were related either to perceiving they had helped others or to having successfully completed a difficult task.

Responses of the four persons who declined to participate are shown in Tables III and IV. For these four patients the major factors given were inconvenience and perceived lack of benefit to self. Three of the four showed no signs of ambivalence.

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Table II *Relative amount of thought given to decision-related factors by eight subjects who participated in the study*

| Factor | Thought Given | | |
|--|---------------|-----------|-----------|
| | Much N | Some N | None N |
| Belief in direct benefit to self | 6 | 0 | 2 |
| Belief research might produce knowledge to help self or loved ones in future | 3 | 3 | 2 |
| Family reaction—strong for or against | 2 | 1 | 5 |
| Current therapist's reaction | 0 | 0 | 8 |
| Belief in benefit to others | 7 | 1 | 0 |
| Financial benefits | 4 | 2 | 2 |
| Belief in risk of complications | 3 | 2 | 3 |
| Belief inconvenience would result | 1 | 4 | 3 |
| Expectation of physical pain or discomfort | 0 | 1 | 7 |
| Fearful—not knowing what to expect | 3 | 1 | 4 |
| Belief might affect future psychiatric treatment | 1 | 4 | 3 |
| Belief might be interesting experience—curiosity | 2 | 5 | 1 |
| Belief researcher felt she should participate | 2 | 1 | 5 |
| Belief would help researcher | 1 | 1 | 6 |
| Might help advance medical science | 7 | 0 | 1 |
| Positive or negative feelings about research unit | 5 | 2 | 1 |

Table IV *Relative amount of thought given to decision-related factors by four individuals who declined to participate in the study*

| Factor | Thought Given | | |
|--|---------------|-----------|-----------|
| | Much N | Some N | None N |
| Belief in direct benefit to self | 0 | 1 | 3 |
| Belief research might produce knowledge to help self or loved ones in future | 0 | 1 | 3 |
| Family reaction—strong for or against | 0 | 1 | 3 |
| Current therapist's reaction | 1 | 0 | 3 |
| Belief in benefit to others | 1 | 1 | 2 |
| Financial benefits | 0 | 2 | 2 |
| Belief in risk of complications | 2 | 0 | 2 |
| Belief inconvenience would result | 2 | 2 | 0 |
| Expectation of physical pain or discomfort | 0 | 0 | 4 |
| Fearful—not knowing what to expect | 0 | 1 | 3 |
| Belief might affect future psychiatric treatment | 0 | 1 | 3 |
| Belief might be interesting experience—curiosity | 1 | 2 | 1 |
| Belief researcher felt she should participate | 0 | 0 | 4 |
| Belief would help researcher | 1 | 1 | 2 |
| Might help advance medical science | 1 | 1 | 2 |
| Positive or negative feelings about research unit | 0 | 3 | 1 |

about their decision to decline. One of the four said she would like to have participated but was reluctant to go off medications because of unusual stress in her family at the time.

Table III *Factors considered important by four individuals who declined to participate in the follow-up study*

| Factor | Considered Important | | Rank of Importance | |
|---|----------------------|---------|--------------------|-------------|
| | Yes N | No N | First N | Second N |
| Risk of complications | 2 | 2 | 2 | 0 |
| Lack of benefit to self | 3 | 1 | 1 | 2 |
| Pain or discomfort | 2 | 2 | 0 | 0 |
| Inconvenience | 4 | 0 | 1 | 1 |
| Fear—not knowing what to expect | 1 | 3 | 0 | 0 |
| Attitude toward unit from previous experience | 2 | 2 | 0 | 0 |
| Belief participation might affect current or future therapy | 0 | 4 | 0 | 0 |
| Family attitude | 1 | 3 | 0 | 0 |
| Influence of current therapist | 1 | 3 | 0 | 1 |

Discussion

Human subjects who agree or decline to participate in research are influenced by a variety of complex risk-benefit factors, some of which are conscious and expressed, and some of which may be unconscious. In this study a primary reason given for participation was for the benefit of others. How much this response may have been influenced by social desirability and how much by a commitment to research¹³ carried over by subjects from their previous collaboration with research on the ward is unclear. The majority of subjects also expressed belief in benefits for themselves. For four subjects the benefits perceived were related to the desire to go off medication, the need for which was seen by them as a sign of weakness. The risk of a trial off medication was viewed as worth taking in the hope of proving that they were no longer ill. Interestingly, subjects on medication saw it as less of a risk to be taken off medication under the controlled conditions of the study, however inconvenient or frightening, than to do so under the supervision of their therapists alone.

None of the subjects felt influenced by the therapists in the decision to participate; on the other hand, none of the therapists approached the

research staff with objections to the participation of their patients. Contrary to what might be expected, neither subjects nor therapists showed concern that participation in the study might prove to be a risk to the efficacy of the therapeutic alliance between therapist and patient.

The psychological benefits described by subjects in our study included not only general positive feelings from the sense of helping others but more specific feelings of importance and self-worth related to being invited to participate, comparing themselves in their recovery phase with themselves in their acute illness state, receiving attention from the staff of the research ward, and proving they could overcome initial anxiety and complete the task without becoming acutely depressed again. Though one 57-year-old subject expressed great pride in earning money for the first time in her life, for most other subjects primary motivating and gratifying factors were not related to financial remuneration. In any event, successful participation of subjects required the psychological support of investigators and ward staff, which involved a large investment in time and effort.

For the four individuals who declined to participate the primary reasons given were inconvenience and lack of benefit to self, though three of the four showed curiosity as to whether participation might be an interesting experience. Gray has speculated that inconvenience and curiosity factors are of greatest power for subjects by whom both risks and benefits are conceived to be at a minimum.¹⁴

Conclusion

Our findings differ from Gray's in that, in his study, a substantial number of human subjects in medical experimentation participated out of ignorance of the research or feelings of constraint which prevented their refusal. Our findings concur with Gray's in concluding that some subjects are able to use research for their own needs, while being used by the research, and that some subjects derive feelings of satisfaction and accomplishment from doing something of benefit to others.¹⁴

Though the size of the sample may limit generalisation of our findings, these data are the first to be reported on responses of psychiatric patients

to participation in longitudinal studies. In the neurobiological study two-thirds of the individuals who were invited volunteered to participate and all completed the study to their satisfaction, providing provocative data reported in another paper.¹⁵ The success of future longitudinal studies will depend in part on further research on the research process itself.

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