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A PARADOX OF PSYCHOSURGICAL EVALUATION

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PREAMBLE

Many branches of medicine and surgery are going through difficulties, if not actual crises, in relation to the evaluation of therapy. A new generation trained in the principles of clinical science is refusing to accept the "bedside" evidence which is given to justify many of our established treatments; they have been taught in medical school of the biases which can distort the results of uncontrolled trials; they are demanding, as they have been taught to demand, evidence from one or preferably several randomised prospective controlled trials before they make up their minds about the effectiveness of a new (or even an old) treatment. Those in senior positions in our professional organisations are sympathetic to this demand for well-controlled evaluation; indeed, they themselves have largely stimulated it. In actual practice, however, it is proving unexpectedly difficult to carry out these trials. There is no shortage of research units or personnel with the necessary skills or of motivation; but for some reason the trials just do not get done. The reason for this difficulty in responding to a logical, widespread and persistent demand is obscure.

The problem as it affects surgery in general has been stated very lucidly by David H. Spodick of the University of Massachusetts Medical School and twelve colleagues from all over the U.S.A.[1] On the day that Dr. Spodick's letter appeared in the Lancet, there was editorial comment in the British Medical Journal[2] regretting the lack of controlled trials of palliative surgery. In psychiatry, we have had extensive recent agonising over the evaluation of ECT, and an extremely well-mounted trial of psychotherapy[3] ended in dismal failure with the general conclusion that psychotherapy is barely amenable to evaluation. In general it appears to be the "important" treatments which are difficult to evaluate - important in terms of time, money, skill of the therapist and significance to the patient. Less "important" treatments such as drug therapy have had their problems of evaluation[4] but in more recent years very large numbers of well-controlled studies have been carried out; for example, the long term trials of maintenance therapy in schizophrenia and affective disorders reviewed by John M. Davis.[5]

The important question arises, is the evaluation of "important" therapies just running a bit behind the evaluation of drugs, or is there some fundamental impediment about the "important" therapies which makes them in some way not susceptible to the techniques of clinical science?

I hope that a discussion of the particular case of the psychiatric surgeon may throw some light on this difficult problem. I make no excuse for offering the contribution of a general psychiatrist with no special knowledge or experience of psychiatric surgery; from a distance one may see the wood rather than the trees; and from this vantage point it does appear, as I hope I shall be able to demonstrate, that one possible difficulty in our attempts at evaluation is the relative contribution we expect of the generalist and the specialist in the common task. I do ask pardon, however, for stating my case rather baldly and brashly, for overstating it in places, and for contradicting myself at one stage in the main thesis of the argument.

THE PARADOX

Brain operations for mental disease are too important to evaluate, too important not to evaluate.

INTRODUCTION

Of all the therapies available to the psychiatrist, brain surgery deserves the most rigorous evaluation. The most rigorous method we have of evaluating a new treatment is to compare it is a randomised trial with the best available conventional treatment. After 43 years of psychosurgical practice, there is no reported instance in the literature of a patient being randomised between psychiatric surgery and non-surgical treatment.

The three preceding statements underlie the paradox of psychosurgical evaluation.

I will not argue the case for the first statement; suffice it to say that the decision to advise referral for evaluation by a psychosurgical team is one of the most important a psychiatrist is likely to make. There are not only the usual hopes and anxieties about a grave procedure; there are also specific anxieties about the effect of damage to that part of the brain which deals with feeling and higher mental function; and there is the ever-present awareness of hostility to psychosurgery both within the profession and outside it. In these circumstances the psychiatrist should have exceptionally fool-proof evidence on which to base his decision and by which he can justify it to the patient, the relatives, the general practitioner, his junior medical staff

and the other members of his multi-disciplinary team - all of whom are likely to have strong and usually negative feelings about psychosurgery.

Nor will I argue the case for the randomised trial; this has been given a recent exposition[6] and those who do not accept it now are not likely to be influenced by anything that can be said here.

Rather I will devote this paper to an exploration for the reasons for the third statement. The lack of randomised trials has been documented and deplored in the literature with reference-clogging regularity[7], and strong pleas for such trials have been made in the editorial columns of medical journals at least since 1962[8,9,10]. It has been assumed that the situation they deplore is due to inertia. This may not be true, and we should consider the possibility that there is some real impediment to a randomised trial of psychosurgery, which if discovered might be overcome; but if left covert might block our research for many years. Anticipating the results of my own thinking, it seems likely that there is a serious impediment which derives from that very importance of psychosurgery which makes evaluation so necessary. But first I will consider some other possible impediments which may seem fanciful or even cynical.

POSSIBLE IMPEDIMENTS

Resources. The pharmaceutical companies dispense large sums for the evaluation of drugs, but they are not interested in surgical treatment. This might account for some of the hundreds of controlled trials of psychotropic drugs, but it cannot account for the complete absence of trials of surgery because other sources of funds are available. Moreover, the element of randomisation in drug trials has been introduced not so much on the initiative of the drug companies but because of adverse editorial and other commentary on uncontrolled trials. Considerable resources of time and money have been devoted to uncontrolled evaluation of psychosurgery. Randomisation is cheap; it is the pre- and post- operative evaluation that is expensive.

Administration. The very small proportion of patients who might be suitable for surgery raises a problem. However, now that psychosurgery is largely confined to specialist units which carry out something in the region of 50 to 100 operations a year, this should no longer apply. Patients are considered carefully for surgery by a multi-disciplinary panel consisting of at least a surgeon and a psychiatrist. There is no administrative reason why a randomisation element should not be introduced at this stage.

In the proceedings of the Fourth World Congress, the research committee of the Royal College of Psychiatrists presented a protocol of a trial[10] in which it

was planned that the college would co-operate with two well known psychosurgical teams. This trial has unfortunately been abandoned, but not for lack of potentially competent administration.

Politics. There is a certain amount of public feeling hostile to psychosurgery, and it may be that grant-giving bodies close to the government do not wish to appear to be supporting "experiments" on the human brain. Such considerations do not appear to have influenced the fate of the Royal College trial. Our Department of Health is already perceived to be supporting psychosurgery, and a controlled trial would give it evidence on the basis of which it could either justify its support or withdraw it.

In recent years the West has been rightly critical of the abuse of psychiatry for political purposes in the Soviet Union. There are several aspects of our own psychiatry which could be critisised in return, and psychosurgery is one of them. Stalin banned psychosurgery in the Soviet Union in 1944; his successors could claim that we are using it to silence those members of our society whose depression, anxiety or aggression is a manifestation of their inability to cope with our competitive capitalist culture. In the face of such potential critisism it would be useful to have the most rigorous evidence that operated patients, when compared to non-operated controls, showed not only a reduction of complaints but an actual improvement in the quality of their lives.

Unethical to do dummy operations. Some dummy operations have been performed, but unfortunately the results have only been reported anecdotally.[11] There are arguments for and against such procedures, and my own personal preference,[12] in the unfortunate event of being a patient in a randomised trial of psychosurgery, would be to have a dummy operation and not to know I was in a trial. However, the weight of opinion is against dummy operations,[13] and it is unlikely that a protocol which included them would be accepted by ethical committees or funding organisations.

The lack of dummy operations in the control group creates two difficulties; a placebo effect cannot be ruled out, and the rating of outcome cannot be completely double-blind. Although a placebo effect may seem unlikely with follow-up at one or two years, it cannot be ruled out. The lack of double-blind ratings should not be so much of a problem with relatively objective measures applied by independent and impartial raters. However, scientists tend to be pernickety people and it may be that, to some extent, the evaluation of psychosurgery has been impeded by the feeling that "if a thing can't be done properly, it is not worth doing at all".

Of course, from the point of view of the patient, it does not really matter whether the improvement is due to operation or placebo and what the referring psychiatrist wants to know is whether his referral will increase his patient's chance of recovery; it would be interesting, to it clinically irrelevant, to know which component of the treatment programme was effective. If a placebo effect cannot be obtained in any other way, then let it be obtained by operation.

Possibly the introduction of a new technique might help to overcome this problem? Lesions have been successfully induced on both simian and human brain by induction heating.[14] In this technique a piece of electro-magnetically sensitive metal is placed at the target site in the brain, and at a later date the lesion is created by placing the patient's head in an electro-megnetic field - the metal becomes hot and destroys the surrounding tissue. A very felicitous property of some metals is that they have specific temperatures above which they cease to take up electro-magnetic energy, so that by varying the components of an alloy it is possible to create an implant which on induction reaches a constant temperature just above that required to destroy brain tissue - the size of the lesion can then be carefully controlled by varying the duration of the inducing current. The efficacy of the treatment could be estimated by comparing the effects of randomly allocated lesion sizes, or possibly it might be considered ethical to permit, in the control group, a delay of several months between insertion of the implant and the application of the inducing current.

Reluctance to submit skill to evaluation. Not only psychosurgery but also psychotherapy has been found very difficult to evaluate, and one thing that psychotherapy and psychosurgery have in common is the need for considerable skill, acquired over a long period of training, on the part of the practitioner. To administer a relatively new psychotropic drug, on the other hand, requires relatively little skill specific to that drug. It is one thing to carry out a trial which may show that a drug is without therapeutic value - it is quite another thing to take part in a trial which may show that one's surgical technique is ineffective. Nevertheless, this was not a problem in the case of the Royal College trial, where the co-operation of two surgical teams was freely offered.

The problems of evaluating psychosurgery and psychotherapy are different, and this suggests that their common element of skill may not be relevant. The main problem encountered in a psychotherapy trial[3] was an insistence on the part of the therapists to include only "eminently suitable" cases in the trial, making it virtually impossible to achieve the requisite numbers. One objection to the Royal College psychosurgery trial was the insistance of the psychosurgical teams

on excluding very suitable cases so that they could receive surgery without risk of allocation to the control group; they were confident that their skill could be amply demonstrated on less than "ideal" patients. It is this firm belief of psychosurgical teams in the effectiveness of their treatment which gives rise to the next impediment, which I suspect is the most important of all.

Ethical Conflict between present and future patients. The profession as a whole has a general ethical duty to evaluate new treatments so that the advantages and disadvantages may be known for the benefit of future patients. This general ethical duty leads to the carrying out of randomised controlled trials. It conflicts with the individual ethical duty to the patient who presents for treatment, to whom one's duty is to advise on the best treatment available. Most doctors would interpret this rather ambiguous word "best" to mean, not what appears best from a statistical review of the literature, but what the doctor concerned really believes is best for the patient, after taking the statistical review of the literature into consideration along with a lot of other factors.

If a treatment is perceived as very important it is likely to be invested with strong belief either for or against, even in the absence of evidence on which to base the belief - this is a property of belief which is not only evident from everyday experience but is predicted from cognitive dissonance theory.[15] In the case of an important treatment, it is therefore difficult to maintain that attitude of doubt which is necessary for a randomised trial. Furthermore, the more important the treatment, the more exactly must be balanced the possible advantages and disadvantages for randomisation to be acceptable. Finally, the more concerned a person is with the treatment the more likely he is to have strong beliefs about it.

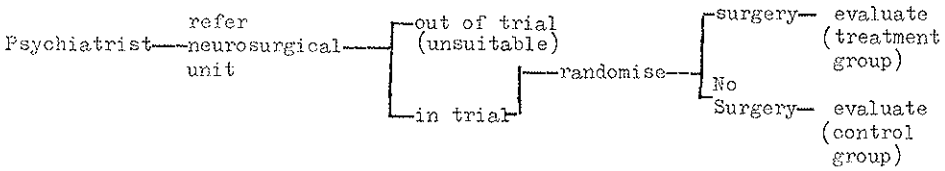
In view of these considerations, it would be unrealistic to expect the members of a psychosurgical team not to believe in the effectiveness of their treatment. And if they have such a belief, how can they participate in a decision to randomise a patient in such a way that he has to accept a 50-50 chance (or any chance, for that matter) of being denied the only treatment which can help him?

According to this view of ethics, psychosurgical teams cannot take part in randomised trials, and randomised trials of psychosurgery cannot be done without psychosurgical teams. If our profession is ethical, randomised trials of psychosurgery are impossible. Therefore, the absence of reports of randomised trials in the literature is not so much a disgrace to our general ethics as a tribute to the individual professional ethics of those who have practised psychosurgery

in the past - a considerable tribute, in view of the pressures to which they have been subjected.

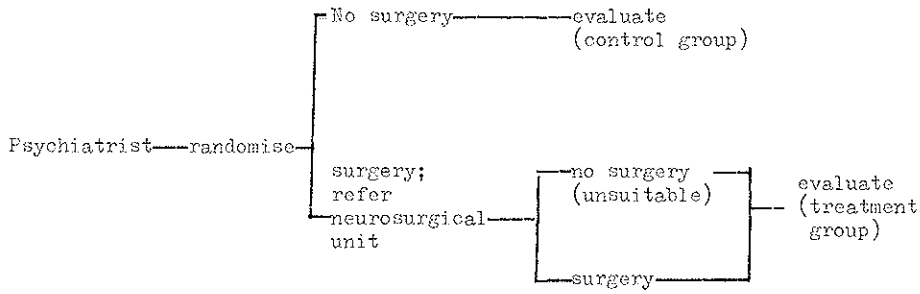
IMPORTANCE OF THE FLOW DIAGRAM

Who, if anyone, is in a position to advise a patient to enter a randomised trial of psychosurgery, knowing that he would give the same advice to his sister or his mother-in-law, and feel confident afterwards that he had done the very best for his patient? Certainly, as I have argued above, no member of a psychosurgical team - even if any were undecided at the beginning of the trial it is almost certain that they would have formed a view either for or against before the trial was far advanced. Randomisation therefore cannot take place after referral to the psychosurgical unit, at which time the members of that unit take over clinical charge of the patient. The Royal College trial was doomed either to stagnate or to place intolerable ethical strains on the staff because it had the following flow diagram:



For some reason we have become obsessed in the design of our trials with the idea that the specialist should be closely concerned with the randomisation procedure, in spite of the impossible situation to which this method of organisation gives rise. Let us consider the experience of an attempt to evaluate psychotherapy[3], which might well have appeared in the final report of the Royal College trial of psychosurgery if that had ever been mounted:

"The investigating team itself must, of necessity, contain members who are experienced in the therapy under examination; they are much more troubled by ethical problems than other members of the team, who see the study simply as an attempt to evaluate a treatment the effectiveness of which has not yet been established". One hundred and thirteen patient were referred to this trial, of whom 8 were accepted by the evaluating panel. What we must question is the necessity for the investigating team to contain members who are experienced in the therapy under examination, for this clearly does not work either in theory or in practice. For a trial of psychosurgery we might propose the following flow diagram:



There are disadvantages in this flow diagram, but they are not insuperable. A proportion of the treatment group would be found unsuitable by the psychosurgical team and would not have the treatment. This does not matter provided it is a relatively small proportion. In any trial some of the treatment group do not get treatment. In a drug trial they may fail to take their drugs, or they may be fast metabolisers of drugs and not achieve a therapeutic blood level on the schedule permitted in the trial. Even when surgery is given, there may be a proportion of patients in whom the lesion is not made in the right place. Such untreated patients in the treatment group merely reduce the mean treatment effect; they do not negate the trial, they just increase the sample size required to detect a treatment effect of any given size.

Pre-trial ratings could not be made under controlled conditions in the psychosurgical unit. Even if pre-trial ratings were considered necessary, and many would argue that they are not, all patients could be visited at home or in hospital after randomisation and before referral of the treatment group.

The most serious objection is that even general psychiatrists with no particular experience of psychosurgery are likely to have beliefs about its efficacy, even though they may be irrational. And certainly after one referral belief is likely to develop depending on the outcome of that one case. Therefore if a small group of referring psychiatrists is selected and trained in the indications for surgery, the supply of patients to the trial is likely to dry up. It would be realistic to expect one referral from each psychiatrist; in fact there are good reasons for asking each psychiatrist to refer 2 well-matched patients at the same time, one of whom would be allocated to the treatment group and one to the control group. It is possible that there are enough psychiatrists with an interest in psychosurgery and a very genuine doubt about its efficacy to make a randomised trial possible without any compromising of ethical standards.

THE ETHICS OF DOUBT OR DOUBTFUL ETHICS

Let us imagine, in the distant past, two general practitioners meeting in their club and discussing the claim of Arbuthnot Lane that neurasthenia is due to toxins entering the system from the large bowel and that he can cure it by means of total colectomy. We can sympathise with their interest, as they each have a patient with a long-standing neurasthenia which has proved unresponsive to all known remedies. We can also sympathise if they show scepticism and are worried about the possible adverse effects of total colectomy. Each might be in a state of genuine doubt about whether to refer his patient. It would be quite reasonable for them to decide to refer one patient and see what happened to him or her before sending the second. But which patient to refer? Which of the two should make the referral? In this situation I do not think it would be unethical for them to toss a coin to make the decision for them. And thus an element of randomisation can be introduced into a grave treatment decision without the ethical standards of either being brought into doubt.

Let us now turn our imagination to the consulting room of Arbuthnot Lane, who has spent several years perfecting the technique of total colectomy and advising patients to undergo the procedure. How will he feel if he has finally been persuaded by professional opinion to subject his operation to controlled evaluation? Can we envisage the mental process by which he advises a patient that it is in her best interest if he tosses a coin to decide whether to operate on her or not? Can we imagine the great surgeon telling his patient that his operation is of such doubtful value that she would be just as well off without it? And, if she is allocated to the control group, what will she say to her general practitioner who has spent several months persuading her to accept referral to the surgeon and representing colectomy as her only remaining chance of leading a normal life? This hypothetical situation jars on my sense of ethics and also on my sense of what is correct professional behaviour between the general practitioner and the specialist.

Before the days of clinical trials evaluation (such as it was) took the form of evaluation of the claims of the specialist by the generalist who referred him patients. Only the generalist could afford to have doubt, and to express his doubt to the patient. For some reason, with the introduction of modern clinical science, we have abandoned this form of procedure and have had the expectation that the specialist should evaluate his own treatment, or at least be clinically involved with its evaluation. This only works with relatively unimportant treatments in which it is possible to fudge the ethical issue, and in which the thought of benefit to patients in the future can distract

the mind from the fact that the advice being given to the patient on the other side of the table is not the very best that one could give. I have had this experience personally and I imagine it must be not uncommon in specialist centres.

Every level of specialisation should be evaluated by the level below. In the case of psychosurgery, psychosurgical teams should be evaluated by general psychiatrists, who should be evaluated by general practitioners, who should be evaluated by non-medical representatives of the general public. This is the only ethical flow-diagram of evaluation, and even then it may be impossible to find sufficient genuine doubt on the part of the referring doctors to justify randomisation unless the doubt is augmented by shortage of the treatment concerned.

SHORTAGE OF CLINICAL FACILITY

If a treatment is not only of doubtful efficacy but is also in short supply, its evaluation becomes very much easier. Thus because of shortage of drug supplies the Medical Research Council was able to mount an excellent randomised trial of streptomycine in the treatment of pulmonary tuberculosis in 1947. If the demand for psychosurgery in an area was more than twice the capacity of the local psychosurgical unit, that unit could quite ethically accept patients only from the randomising agency of the trial. In fact it would be more ethical to do this than to favour any other method of selection, since each patient who required surgery would have an equal chance of getting it. Such a method of selection might be more humane than attrition on a long waiting list, and since all patients would be severely ill a selection procedure according to severity would not be appropriate.

If all referrals forpsychosurgery went through a randomisation procedure, the ethical problem for the referring psychiatrist would disappear. He could refer all patients whom he felt might benefit from surgery, knowing that half of them would be evaluated by the psychosurgical team and knowing that the other half could not have surgery anyway. He could advise his patients to their best advantage without any shadow of an ethical doubt - in fact, with an assurance which I personally do not believe it would be possible to obtain in any other way.

Naturally, one deplores shortage of opportunities for treatment. But they do occur, and I cannot see any ethical or other reason why they should not be exploited in the interest of controlled evaluation. Psychosurgery is now very unpopular in many areas; due to many factors not the least of which is the

influence of the delegates to this conference, it is likely to become much more popular in the future. No doubt the setting up of new psychosurgical teams is likely to lag behind the increasing demand for treatment. One hopes that these new teams would take advantage of their inability to supply demand and begin their practice on a randomised sample of their potential patients, for the imbalance between supply and demand might not last for long.

SUMMARY

There is an ethical conflict between the need to evaluate treatment with randomised trials and the process of advising an individual patient to accept randomisation. The latter requires a genuine doubt about the efficacy of the treatment. Doubt is less likely in the case of important treatments such as psychosurgical operations; it is also less likely in those who are closely concerned in the administration of the treatment. Randomised evaluation is therefore not likely to be successful unless the randomisation occurs before referral to the specialist team; and it will be easier if the specialist team has facilities to treat only a proportion of the potential referrals. The best opportunity for effective evaluation would be the establishment of a psychosurgical team in a country which had previously been unfavourable to psychosurgery, where the local psychiatrists were interested in but doubtful about psychosurgery and possessed the organisation to randomise potential referrals, and where the new psychosurgical team agreed to accept referrals only from the randomising organisation.

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AFTERTHOUGHT

If it had been possible for me to give this paper in Boston as I would dearly have liked, I would have spoken about Henry Cabot Lodge and the Cambridge-Somerville youth study. It is tantalising to think that such an excellent randomised trial could have been designed and implemented in the nineteen thirties, before the introduction of psychiatric surgery to Massachusetts. Even in psychiatric surgery the Bostonians were ahead of their time and produced the only randomised trial of different psychosurgical operations ever to be reported[16] if the influence of Lodge had been greater the Boston Psychopathic Hospital trial might have had larger numbers, independent evaluation and a non-operated control group. In that case, I suspect that either we would now be attending the Twentieth International Congress of Psychiatric Surgery, or we would not be here at all.

ACKNOWLEDGEMENT

I should like to thank my fellow members of the erstwhile Psychosurgery Subcommittee of the Research Committee of the Royal College of Psychiatrists, and particularly its chairman Dr. Brian Barraclough, who stimulated my interest in the field of psychiatric surgery and who taught me most of what little I know of it.