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## ORIGINAL ARTICLE

### Brain donation for schizophrenia research: gift, consent, and meaning

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## ABSTRACT

The Neuroscience Institute of Schizophrenia and Allied Disorders's (NISAD) "Gift of Hope" Tissue Donor Program is a volunteer programme for people who wish to donate their brain when they die for neuroscience research into schizophrenia. Organ donation for purposes of research differs from transplant donation in a number of ways, most notably the absence of a single recipient. Within a particular community, however, (people with schizophrenia and their carers) the single recipient is replaced by a sense of shared experience and preventing suffering in others. Donors have an investment in the research.

**Keywords:** brain donation; consent; neuroscience; research schizophrenia

The brain as an organ for donation is seen by some as having special significance, and linked to an emotional depth quite dissimilar to other organs. The meanings attributed to the brain (property, gift, or the source of the troubling thoughts of schizophrenia) are diverse. The trust model for human biological samples is helpful for conceptualising and managing issues of autonomy, societal claim, and fiduciary relationship.

Schizophrenia is a uniquely human disorder. Research in the last two decades has led to a consensus view that it is a brain disease of currently unknown aetiology.<sup>1</sup> The vast majority of neuroscience research in other brain disorders relies on the use of animal models of specific clinical features of such conditions. Important clinical features of schizophrenia, however, such as hallucinations and delusions, cannot be demonstrated using such animal model methodology.

In the past, brain tissue obtained at postmortem examination from people previously diagnosed with schizophrenia has been used to examine a range of hypotheses concerning the neurochemical basis of the disorder. These studies have relied on clinical data obtained from medical records. Recently, it has been recognised that clinical data collected during life from people willing to consent for their brain tissue to be used for research would offer significant advantages over that obtained via posthumous retrospective searches.

A number of ethical questions arise in any donor based research programme: consent; altruism; autonomy; societal claim and family claims, and the commodification of body parts. The distinctiveness of the brain as an organ for research donation takes a sharper focus when many of the donors have an illness that affects their thinking.

## THE NISAD "GIFT OF HOPE" TISSUE DONOR PROGRAM

The Neuroscience Institute of Schizophrenia and Allied Disorders (NISAD) has established a volunteer brain donation programme for people who wish to donate their brain when they die for research into schizophrenia. The "Gift of Hope" Tissue Donor Program (TDP) is a database of people willing to undergo a research programme during life, including comprehensive psychiatric history, magnetic resonance imaging, and longitudinal medical and psychiatric histories with annual follow up. The aim is to provide the highest standard of clinical information to researchers who will subsequently utilise the brain tissue samples. The "Gift of Hope" TDP works closely with a linked TDP based at the University of Sydney (the "Using Our Brains" TDP: [www.braindonors.org](http://www.braindonors.org)), which focuses on brain donors from the general public for research into all brain diseases. (This is an attempt to meet the widely recognised need within neuroscience research for control material to

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complement the availability of the available donor tissue).

"Gift of Hope" TDP donors are 18 years of age or over. Some have schizophrenia and some are people with no history of mental illness. The consent of the next of kin is required. Thus far over 100 donors have enrolled, not all of whom have yet completed the consent process. Approximately one third of donors have schizophrenia and a further one quarter have a first degree relative with the disease. After the initial research programme has been conducted, annual contact is maintained with donors to update clinical and demographic data, and to reaffirm the decision to donate. One donor has died since the programme began. Protocols are in place for data and tissue procurement, management, and distribution. Ethics approval has been granted by area health services and the University of Sydney. The Neuroscience Institute of Schizophrenia and Allied Disorders and the TDP have the strong support of mental health consumer and carer organisations. The patron of the TDP is a consumer educator who herself has schizophrenia and is enrolled as a donor.

Arrangements are in place so that when a prospective donor dies, rapid notification procedures ensure that the donor's brain tissue can be removed and the donor's body returned to the funeral director of the family's choice. At the time of enrolment, donors are told that the removal of the brain leaves no visible marks or changes, should viewing at the funeral be contemplated, and that removal of the brain will not interfere with the funeral plans.

The "Gift of Hope" TDP is donor focused. Valuable tissue collections for research and teaching purposes exist in institutions internationally, acquired from anonymous sources, and developed during a period when medical paternalism sidestepped questions of significance to the donor. The latter part of the 20th century has seen people with schizophrenia adopt an interest in the research from a consumer perspective, becoming active participants in driving the agenda. The neuroscience research culture is increasingly collaborating with consumer groups and typically a brain tissue collection is regarded as "essentially a prospective project for the collection of human CNS material with the underlying support of donor programs".<sup>2</sup>

Because the "Gift of Hope" TDP also asks donors to take part in research during life, the moral status of the brain as an organ for donation is, for some donors at least, an issue of interest. Consumer involvement thus compounds the complexity of consent, requiring the donor to be informed on such issues as archiving of DNA (and others) without the consent becoming itself an onerous process.

## CONSENT

The enrolment process fosters a situation in which information that is designed to cultivate an interest in the TDP is made easily available through the consumer and carer network, so that the donor makes the initial contact with NISAD. This step is regarded as a strong indicator of voluntariness. Consent is regarded as a continuous process, given after deliberation, continuing throughout life, and revocable at any time.

It is well known that some people with schizophrenia may at some time have difficulty in understanding and reasoning, or lack insight into the presence of their illness and the need for treatment. This, on occasion, can make it difficult for them to anticipate the consequences of their decisions. Recent data suggest, however, that people with schizophrenia are, in fact likely to have capacity to consent to research, and where this capacity is impaired, cognition appears more relevant than psychosis.<sup>3</sup> Further, after educational intervention subjects with schizophrenia perform as well as subjects without psychiatric disease.

Potential donors are encouraged to take time to make the decision, in part to be sure that people with fluctuating decision making capacity will not be acting on impulse. The criteria for determining competence include the person's ability to appreciate the nature of the situation, to understand the information and believe it, and to understand decisions and make choices. Of donors who have a mental illness, only one has demonstrated a period of ambivalence, which subsequently resolved into a decision to continue.

The Neuroscience Institute of Schizophrenia and Allied Disorders does not encourage case managers and clinicians to recruit their clients and patients. This is in order to avoid both the potential for conflict of interest<sup>4</sup> and the creation of an environment of perceived coercion within the therapeutic relationship.

The consent of the next of kin is not legally necessary in Australia, but is sought to ensure that the issue has been discussed and that there is agreement with significant others. There is provision for the next of kin to withdraw consent, and consent is confirmed at the time of the donor's death. If it is withdrawn at this time the donation will not proceed.

## "THE GIFT" AND ALTRUISM

Organ donation continues to be one of the most sociologically intricate and powerfully symbolic events in modern medicine.<sup>5</sup> Fox and Swazey's thick description of the "gift giving" framework for organ donation for transplant describes its persistence in the face of market oriented economists' and policy makers' attempts in the 1980s to deal with the increased need for organs. In the early days of transplant, the psychological, social, and cultural meaning of the gift/exchange aspect of transplant organ donation only became evident after transplant teams were initially startled by observing the animistic experiences of donors, recipients, and their families. Donors and recipients implored and cajoled transplant teams to reveal the identity of the other party. "Their conceptions of the modern and the scientific did not prepare them for such 'magical' reactions to this 'gift of life'".<sup>6</sup>

Using Mauss's sociological depiction of symmetrical and reciprocal gift giving obligations, which create a "sort of spiritual bond" between donor and recipient, Fox and Swazey say that these "anthropomorphic connotations of the gift have proved to be as characteristic of the modern medical scientific and technological milieu in which the giving and receiving of organs through

transplantation takes place as the settings in 'primitive' and 'archaic' societies that were the context of Mauss's study".<sup>7</sup>

Research organ donors are not subject in this way to the immediacy of a recipient. The theme of "gift" has, however, captured the imagination of donors in this programme and in similar programmes internationally. The gift/exchange paradigm of Mauss's work brings into stark relief the personalised nature of the transplant donor's inner and outer pressures, when compared to the diffuse beneficiary of the research donor's gift. The altruism of research donation is not subject to the potentially onerous creditor/debtor vice which can weigh heavily on the recipient of a transplanted organ.

The motives for people wanting to be brain donors with the "Gift of Hope" TDP appear (anecdotally) to be largely their interest in the research. A small proportion of donors are people who have no contact with people with mental illness, have heard about the programme in the media and inquired because it sounds "like a good thing to do". The majority, however, are people with schizophrenia and their carers. They hear about the TDP through the network at conferences and via promotional talks. Like most networks of people with chronic illness and their carers, they regard research as a source of hope for amelioration of the distress caused by this terrible illness.

Many are well versed in research and seek to participate when they are able. When an obstacle presents itself, a potential research subject may seek to resolve the problem in order to be able to participate, such is their investment in the research. Occasionally a consumer will comment that the illness has drained them of resources and made them dependent on their community. Becoming a brain donor gives them a sense of being able to contribute.

## AUTONOMY, SOCIETAL CLAIM, AND NEXT OF KIN

Donating one's brain for research was referred to as a "gift of hope" by W W Tourtellotte, who initiated the collection and cryopreservation of brain tissue in 1961.<sup>8</sup> Properly organised brain banks have a relatively recent history with an increase in activity during the World Health Organisation's decade of the brain, the 1990s. The international brain banking network is aware of the importance of the social structure and the anthropological and cultural background of the communities in which they are based.<sup>9</sup> In Korea—for example, the Christian minority contributes to research as donors while the Confucian majority observes cultural prohibitions about the dead body that result in low participation rates.

A tension also exists between organ donation as a gift and the societal claim to cadaveric tissue, in which the community may be said to have sufficient right to dead bodies because of the public benefit that results from their value to research. A pendulum swing has taken place over recent decades. In Australia this has culminated in the distressing discovery by some family members that their loved ones had been buried after organs had been retained for research purposes. An inquiry into the practice at the Institute of Forensic Medicine in Sydney (IOFM) found that there was no legal or ethical problem with the handling of brains in and following postmortem examinations.<sup>10</sup> It found that some areas of administration were poor and the IOFM was dissolved and continued under the local area health service with a new administrative head. The practice of retaining brains "ceased to raise questions of lawfulness, receded as to matters of ethics, and resolved into a tension between some community attitudes and a difference in professional preferences".<sup>11</sup> The retention of brains ("within the traditional and orthodox procedure of a three-cavity postmortem examination")<sup>12</sup> was, however, noted by Walker, Senior Counsel, as "possibly one of the most resented aspects", perhaps because "profound feelings are engaged for many people in our society with the brain, and to a lesser extent the heart".<sup>13</sup>

In the same year an inquiry into the events at Alder Hey Hospital in the UK brought down findings of what was widely regarded as a scandal, warranting disciplinary procedures and urgent amendment of the Human Tissue Act.<sup>14</sup> Over a number of years at Alder Hey, organs had been removed at autopsy from children without the knowledge or consent of their parents. No significant research was ever conducted on these organs, so that there was no possible benefit to patient care. In both the IOFM and Alder Hey, many of the reforms recommended were directed at ameliorating the distress of the next of kin and significant others, and at ensuring that the central principle of properly informed consent should be enshrined in law. These reforms reflected the pendulum swing in favour of the individual.

As recently as the 1970s the Australian Law Reform Commission (ALRC) and some state parliaments chose to tilt the balance in favour of the public good. The ALRC has, however, recently responded to the shift in public opinion by opening discussion about the wishes of the deceased and those of the next of kin regarding the uses of tissue taken at autopsy. Whether Australian legislation would then allow next of kin to override the decision of the deceased regarding organ donation thus became one instrument for assessing the standard against which autonomy may be judged. Autonomy is associated with the status ascribed to rational beings as persons in the morally relevant sense, uniquely qualified to decide what is in their best interest. Where a person has expressed a wish during life for their brain to be donated for research, that autonomous decision remains after their death.

This must be weighed against the impact on a family member who revokes the consent at the time of death, perhaps due to unexpected strong feelings about intact burial. The argument that the family's psychological wellbeing is a "weak claim"<sup>15</sup> is not well founded, especially where it rests on the primacy of rationality. If we dismiss the feelings shaped by a strong commitment to intact burial, we do so at our ethical peril.<sup>16,17</sup>

It is for this reason that discussion takes place at the time of enrolment in the "Gift of Hope" TDP about the requirement for the next of kin's consent, and is centred around encouraging next of kin and significant others to be included in the donor's decision. Because the next of kin's consent is not legally necessary, there is a range of views among donors about the requirement: some people have elected not to proceed in the light of objection from another family member. At the other end of the spectrum, some donors object to the requirement because "it's my body". Those in

the latter category tend to engage in discussion about the possible consequences, after their deaths, of failure to seek consent of their next of kin.

The enrolment process openly invites questions from the donor and from significant others about other sensitive issues. For example, family members might ask whether the results of an examination of the brain will be made available to them. A subtext percolates through this discussion: "Finally, if the scientist looks, she will see the distress this illness has caused him!", or "Will you be able to tell me why?"

Circumstances at the time of the donor's death mean it is probable that the next of kin will be active in notifying the TDP. In contrast to the transplant donor, they will thus have more control over the situation than the next of kin who is approached during a crisis by an authority figure with a request for organs for transplant. Resolution may come more easily, and where there are fewer confounding problems in the emotional landscape it becomes possible to contemplate meaning.

## "THE GIFT" AND COMMODIFICATION OF BODY PARTS: THE BRAIN

There are moral and emotional objections to commodification of the body. There are also arguments in favour of according property rights to human tissue<sup>4</sup> although these may be hardest to sustain when they are applied to the brain. Where the meaning ascribed to donating one's brain for research is conceptualised as a gift, it permits both the monist view of the human body as integrally bound up with the self,<sup>18</sup> as well as our notions of personhood being defined more by our ability to think, our sentience and cognitive abilities, and our thoughts and feelings.<sup>19</sup> The Aristotelian idea that the essence of being is located in the brain is profoundly meaningful, and itself creates distance from the body as object or property.

Human tissue is not regarded as property under Australian legislation, but there are the means for it to be the subject of what may be construed as a gift or bailment.<sup>20</sup> Gottlieb<sup>21</sup> proposes the trust as the ideal model for property transfer of human biological samples to a repository. By this analysis, most transfers can be characterised as abandonment, bailment, or gifting. Abandonment includes the idea that it may be appropriated by the next comer or finder. Bailment is the delivery of personal property by one person (the bailor) to another (the bailee), either for some particular use or merely for deposit; after the purpose has been fulfilled the property is redelivered to the bailor. Bailment is a good model for transfer of tissues such as sperm, pre-embryos, or blood that are meant to be used in future by the bailee. As Gottlieb points out, however, the fit is not perfect.<sup>21</sup>

A gift is the voluntary transfer of property to another, made freely and without receiving anything in return. Some transfers of biological samples to repositories can be considered gifts, such as the banking of blood and bone marrow, or of tissue for research. A trust is a fiduciary relationship in which one person, (the trustee) holds title to the property and has an obligation to keep or use the property for the benefit of another (the beneficiary). It is distinguished from a gift in that it requires a settlor (the donor), a beneficiary (future patients), a trustee (the tissue bank), a corpus (the brain tissue), and intent to create a trust (expressed in the consent agreement).

Gottlieb further notes that the core of the trust is the fiduciary relationship between the trustee and the beneficiary.<sup>21</sup> In the case of the "Gift of Hope" TDP, the beneficiary is the community (present and future) affected by the research. The trustee also has a continuing responsibility to the donor after death. This includes ensuring that respect is accorded to the dead body, encompassing the deontological notion that it is possible to be wronged without being harmed, as occurred (to the deceased) at Alder Hey.

Australian research culture works on a form of honour system, with samples shared between researchers, overseen by research ethics regulatory bodies. Where human tissue has monetary value, this is usually in the context of the development of commercially valuable products such as pharmaceuticals. "Gift of Hope" TDP donors are required to waive rights to any royalties on their DNA material that may arise from the research, and are also informed that NISAD will not benefit from royalties from their DNA material. Although a lively discussion exists about commercial transaction of organs for transplant,<sup>22</sup> the prevailing view in both the Asian<sup>2</sup> and European<sup>9</sup> networks of brain tissue banking for research remains one of custodianship or stewardship of the tissue.

The prohibition of financial gain by research subjects of tissue donor programmes (including NISAD's "Gift of Hope" TDP) is also in line with the research practice of prohibiting inducement. The patron of the "Gift of Hope" TDP, Marilyn Mitchell, has argued,<sup>23</sup> however, that donors who have a mental illness should be paid a one off sum during life for enrolling in the programme. The grounds for her argument are those of social and economic inequity between consumers and the general public; the potential for pharmaceutical companies and research to earn major profits from others' altruism, and compensation for any stress or inconvenience caused. As an invited speaker at a conference in Kyoto, Japan in 2002, she described her experience with schizophrenia and her motives for being a brain donor, evoking an enthusiastic response. A number of people in the large audience declared their intention to become donors, indicating a shift away from the stigmatisation of both mental illness and organ donation.

People familiar with schizophrenia sometimes speak of donating their brain as giving something of value that could help to save their children or grandchildren from the disease. Mauss's sociological depiction of gift giving obligations are borne out in the donation of the brain. Research currently being undertaken by the University of Sydney and NISAD is looking at donors' initial motives, in particular those donors who do not suffer mental illness. For those who do suffer schizophrenia, the motives are inextricably linked with the conundrum that the illness presents. The same organ that constructs the activity we call the mind, much of which has yet defied either anatomical or functional localisation,<sup>24</sup> is also the vehicle of the tormenting thoughts of schizophrenia. Whether donors with schizophrenia accord different values, meaning, and significance to their brains as distinct from their other organs, is a question requiring robust and qualitative analysis of motives. Such analysis will need to address both rational reasons and those that are not in the realm of the

rational: "the yuk factor" discussed by Midgley,<sup>16</sup> and the feelings shaped by a strong commitment to intact burial.

The motives of those who do *not* want to donate should not be ignored or dismissed. The protection from coercion of those who do not wish to become donors is also within the fiduciary responsibility to ensure voluntarism.

## CONCLUSION

Brain donation for research by people suffering from schizophrenia raises important ethical issues. The ability of the "Gift of Hope" TDP to address these issues is attested to by the acceptance of the protocols by various ethics review bodies. Perhaps more compelling evidence is provided by its acceptance within the community of volunteers who have enrolled, patients, their families, and the general public.

Voluntarism is embedded in the "Gift of Hope" TDP, giving donation a particular meaning as gift. The programme's incorporation of the trust model emphasises the fiduciary relationship with donors, and helps to prevent undue pressure to participate. Research aims to cure or prevent schizophrenia, and is only beginning to ask many of the questions whose answers might lie in banked brain tissue.

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## FOOTNOTES

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