Ethical Aspects of Neural Tissue Transplantation
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The method of neural grafting is considered to be a very promising therapeutic strategy for the treatment of certain neurodegenerative disorders such as Parkinson's disease or Huntington's disease. During the last 15 years, clinical transplantation studies have been carried out worldwide in several hundreds of patients with Parkinson's disease. In these studies, primarily fetal mesencephalic tissue derived from aborted human fetuses has been used for implantation. Neural tissue transplantation gives rise to ethical issues in two different areas that need careful examination: the first, ethical problems linked to the use of tissue from aborted human fetuses; and the second, ethical issues concerning the graft recipients in clinical trials, i.e., his or her well-being, personality, and personal identity.

Key words: clinical ethics; ethics, medical; deontological ethics; fetal tissue transplantation; Parkinson's disease; Huntington's disease; neurodegenerative diseases; neurotransmitters; personality; transplantation, brain tissue

The method of neural tissue transplantation is considered a very promising therapeutic strategy for the treatment of certain neurodegenerative disorders such as Parkinson's disease or Huntington's disease. The aim of neural grafting is to substitute the neurons that have been lost due to degeneration by other material that is expected to assume functions of the formerly intact neurons (1-7).

The field of neural tissue transplantation is not a wholly new research area. Towards the end of the 19th century, early neural grafting studies had already been carried out (8,9). Current interest and hope placed in the method of neural tissue transplantation stems from animal experiments performed in the 1970s. These experiments showed that tissue, especially fetal tissue, implanted into the brain of rodents is able to survive, grow axons, and have a functional effect in the host brain (10,11). Up to now, clinical neural tissue transplantsations have almost exclusively been carried out on patients with Parkinson's disease. In parkinsonian patients there is a selective degeneration of the neurons located in the mesencephalon that normally produce the neurotransmitter dopamine. It is this degeneration-induced loss of the neurotransmitter dopamine, especially in the basal ganglia, which leads to the typical symptoms of Parkinson's disease. These symptoms are mainly on the motor level, and they include tremors, muscular rigidity, hypokinesia, and postural instability. In addition to these motor symptoms, it is characteristic for parkinsonian patients to have certain, albeit in most cases minor, cognitive abnormalities (12,13). The aim of the neural tissue transplantation in these patients is to implant grafts that might replace the former activity of the cells and restore their function (14). Apart from the fact that an adequate long-term therapy for Parkinson's disease is still wanting, there are several neuroanatomical aspects that seem to make Parkinson's disease a good candidate for establishing the new therapy of neural tissue transplantation: in Parkinson's disease a clearly defined group of neurons with quite a confined target area is lost due to neurodegeneration. These dopaminergic neurons exert mainly modulatory functions (4,15).

In the literature on neural tissue transplantation for Parkinson's disease, the dominant working hypothesis assumes that the grafted material exerts its function mainly by secreting the neurotransmitter dopamine. In particular, the formation of synaptic contacts with the host brain seems to be highly advantageous. Only fetal neurons are able to partially integrate themselves into the host brain by forming synaptic contacts with it. However, the exact way in which the grafts exert their function is still unknown. There is also a great number of other mechanisms under discussion, such as lesion-induced unspecific effects or the secretion of growth factors (5,15,16).

During the last 15 years, clinical transplantation studies have been carried out worldwide on several hundred patients with Parkinson's disease suffering from incapacitating motor symptoms. In the first years of clinical trials, autologous adrenal medullary tissue was used for neural tissue transplantation where their own adenal medullary tissue was implanted into the brain of parkinsonian patients (4,6). Although the first neural tissue transplantation using adrenal medullary tissue had been carried out in
1982 in Sweden (17), it was not until 1987 that neural grafting entered a phase which attracted intense worldwide interest. In 1987, a group of Mexican researchers reported on startling amelioration of the motor performance of parkinsonian patients after neural tissue transplantation using adrenal medullary tissue (18). Although the data presented were very fragmentary, researchers began carrying out clinical grafting studies all around the world in the hope of attaining therapeutic results and scientific success. However, in spite of the fact that several hundred patients with Parkinson's disease worldwide underwent an operation in which adrenal medullary tissue was transplanted, never again were researchers able to obtain such excellent results (19-21). In most of these transplantation studies, at best only minor improvements in motor functions were observed after the operation. Apart from partial – albeit most often only temporary – improvements of the motor symptoms, severe side effects were recorded in a large number of the autologous adrenal medullary tissue transplantations. Besides neurosurgical, cardiovascular, and other complications, these side effects included psychiatric dysfunction such as delusions, confusion, hallucinations, depression, insomnia, and hypersomnia. Some of these psychiatric abnormalities persisted at least one year after the operation. A high number of deaths occurred after neural grafting, some of which were clearly related to the operation (19,20).

These studies showed that there is no long-term survival of the dopamine-synthesizing cells derived from the adrenal medulla in the host brain and that there is only minor improvement in the patients' motor performance and an enormous range of complications. In view of the slight therapeutic success and the large number of negative side effects, in recent years clinical neural tissue transplantations with grafts derived from adrenal medullary tissue have not been carried out in most research centers.

In the last few years, fetal mesencephalic tissue has been favored for the implantation in clinical grafting studies. The fetal tissue has been derived from human fetuses aborted in the first trimester of pregnancy. Most often, human fetuses at a gestational age between 8 and 10 weeks have been used. Up to now, between 100 and 200 patients with Parkinson's disease have undergone neural tissue transplantation in which dissociated fetal mesencephalic tissue has been stereotaxically implanted into the host brain (1,2,6,7,22).

It is very difficult, if not impossible, to compare the various studies carried out by different research teams since the operation procedures and the methods of patient evaluation differ significantly, especially the age of the embryos and the amount of fetal tissue used for implantation. In addition, there is no uniform implantation site – fetal grafts have been implanted in various regions of the basal ganglia and between 2 and 14 injection sites have been used (3,4,6,7,23,24). It seems that, in principle, dopaminergic cells derived from fetal mesencephalic tissue are able to survive in the human brain, to grow axons, and to exert certain functional effects. In spite of the enormous procedural differences in the design of the studies, the results obtained are very similar. Many of the studies showed that there was a partial improvement of the motor functions in a large number of the patients. Nevertheless, symptoms clearly persisted after the operation (3,6,23,24). Most often the transplantation had only comparatively slight negative side effects (15,24). However, there are also reports of deterioration in the psychiatric status of the transplanted patients, as manifested primarily in depressive and non-specific emotional and behavioral symptoms (25).

Although the results obtained are quite encouraging, neural grafting is far from having an unequivocally proven therapeutic effect: neural tissue transplantations still have to be considered highly experimental.

In this article we will examine two ethical issues related to neural grafting: problems linked to the use of tissue from aborted human fetuses, and issues related to the graft recipients.

Use of Tissue from Aborted Human Fetuses

The use of human fetal tissue for medical purposes is a highly controversial issue (26-28). While some authors tend to generally reject the use of material derived from aborted human fetuses (29), others consider it ethically acceptable. Among this latter group of authors, some aspects concerning the retrieval and use of human embryonic or fetal donor tissue for neural tissue transplantation seem to be almost uncontroversial (30,31): (a) it is only permissible to retrieve tissue from dead embryos or fetuses; (b) it is not allowed to keep intact embryos or fetuses alive artificially; (c) the decision to terminate pregnancy must precede any mention of the possibility of embryo donation and there must be no link between the donor and the graft recipient; (d) it is necessary that the woman involved gives informed consent; (e) no profit or remuneration may be involved in embryo or fetus donation; and (f) approval of the local ethical committee is necessary.

However, there are some problematic issues which are worth discussing here. One of these deals with the question of whether there is a relation between a woman's decision to terminate pregnancy and her decision to donate the embryo or fetus (26-28). In the "Ethical guidelines for the retrieval and use of human embryonic or fetal donor tissue for experimental and clinical neurotransplantation and
research" adopted by NECTAR, the Network of European CNS Transplantation and Restoration, item 3 reads: "The decision to terminate pregnancy must under no circumstances be influenced by the possible or desired subsequent use of the embryo or fetus" (32). While such dissociation may be possible in the experimental stage of neural tissue transplantation, it seems almost impossible if neural tissue transplantation should ever become a broadly used therapy. If neural grafting were established as a routine treatment, the demand for human embryos would dramatically increase, so that, statistically speaking, a very great number of the women undergoing an abortion would have to donate their embryo in order to satisfy the demand. If in some years' time neural tissue transplantsations with grafts derived from aborted human embryos were to be carried out widely, it would seem almost impossible for women seeking abortion to ignore the fact that other persons might profit from the aborted fetus. This possibility of helping other people by donating her embryo will have enormous consequences on a woman's attitude towards abortion.

Another aspect I consider problematic is the item 4 of the NECTAR guidelines (32): "The procedure of abortion, or the timing, must not be influenced by the requirements of the transplantation activity when this would be in conflict with the woman's interests or would increase embryonic or fetal distress." This differs considerably from the corresponding guidelines of the British Medical Association (31): "Transplantation activity must not interfere with the method of performing abortions, nor the timing of abortions, nor influence the routine abortion procedure of the hospital in any way."

The very liberal formulation in the NECTAR guidelines reflects not only the expected enormous demand for human fetuses, but also the fact that embryos resulting from routine abortion often are so destroyed that they can no longer be used for grafting. From this point of view, it seems clear that the abortion procedure and its timing will have to be adjusted in order to satisfy the expected needs of transplantation medicine. However, the NECTAR guidelines support a strategy in which the woman's and the embryo's interests and anticipated suffering are being weighed against the anticipated future benefit for the graft recipient. A balancing strategy like this which includes the killing of fetal tissue donors has no analogy to "normal" organ transplantation in which organs from already dead donors are used. In a strategy like this, women and embryos are being inadmissibly instrumentalized in order to satisfy the needs of neural tissue transplantation.

In view of such enormous ethical problems linked with the use of tissue from aborted human fetuses, researchers are intensively looking for other dopaminergic material that might be used instead of fetal tissue as a graft in parkinsonian patients. In particular, experiments with genetically engineered cell lines or cells, with encapsulated cells, or with dopamine-releasing polymers proved to be very promising (4,6,33-35).

Graft Recipient

It seems clear that in a therapy like neural grafting, in which there is an operative intervention in a person's brain, the possibility of changes in character traits occurring in the graft recipient cannot be totally ruled out. However, in most of the neural tissue transplantation studies on patients with Parkinson's disease, evaluations have been almost exclusively concerned with the patient's motor symptoms. Detailed neuropsychological tests on patients with Parkinson's disease which take into account influences on mental characteristics that might arise after dopaminergic material has been implanted in the basal ganglia, have hardly got off the ground (4,24,25). In most studies, especially the older ones, considerations of the influence a neural tissue transplantation might have on the graft recipient's personality and personal identity have been neglected. Thus, in neural tissue transplantation research it is absolutely necessary to pay more attention to the patient's mental characteristics, especially to questions concerning the personality and personal identity of the graft recipient (36-40).

Personal Identity

With regard to personality and personal identity, one of the main questions is: what kinds of characteristics are relevant for the identity of a person, i.e., for the fact that a person remains essentially the same? A number of different answers have been given to that question. In principle, there are two different views: those who think that bodily characteristics are of utmost importance, and those who think the same with regard to mental characteristics (41-43).

In what follows I would like to present some of these positions on personal identity and describe some implications that may arise in the context of neural tissue transplantsations.

Bodily Characteristics

For physical objects, the criterion of identity is spatio-temporal continuity. A certain object, observed in a certain condition, is considered to be identical with an object in another condition if there is spatio-temporal continuity, i.e., if a connection exists between them in time and space (42). The same is true for a human body. In spite of permanent molecular turnover and other continuous modifications, but also in spite of discontinuities in a human body caused by organ transplantation or other kinds of
Normally, a person's character arises after neural tissue transplantation (4). Normally, transplantation is carried out in a clearly defined and comparatively small region of a human body so that, owing to the spatio-temporal continuity of the rest of the body, the identity of that body, on a whole, is not at risk. Influences of these organ transplantations on a person's character traits are, if they exist at all, indirect in nature and most often comparatively small.

If only this quantitative aspect is taken into account, bodily identity does not seem to be at risk in the case of a brain transplantation. However, the assumption is very plausible that, after a transplantation of the entire brain, the body, which is left behind but endowed with a new brain, would suffer from the loss of personal identity (45). This example clearly indicates the unique function of the human brain, being the organ crucial for personality and the identity of a person. In order to underline the special role of the brain in questions concerning personal identity, some authors (42, 45, 46) no longer consider spatio-temporal continuity of the whole human body to be the decisive criterion of personal identity, but restrict it instead to spatio-temporal continuity of the human brain.

In the transplantation of the whole human brain, this direct inference from continuity of a brain to the identity of a person, assuming that personal identity goes with the brain, may be of some use. However, all other parts of the body also are of great importance to the identity of a person (47). In neural tissue transplantation, however, such a direct conclusion is inappropriate. The reason is that, after an abrupt change in the brain structure caused by some operation or neural tissue transplantation, it may well happen that, due to the brain's plasticity and enormous complexity, there are no changes in the personality traits at all. Since changes in the brain structure are not necessarily accompanied by changes in character traits, what is of utmost importance in this context are not structural but functional changes affecting individual behavior and personality.

All those criteria using spatio-temporal continuity of the entire brain or of parts of it, ignore the fact that in real situations it would be pointless to use brain identity as a criterion of personal identity, since, apart from computerized visualization techniques, a person's brain structure is not directly accessible at all. Strictly speaking, of course, there is no such thing as brain identity, but only its continuity. Normally, brain continuity can only be deduced indirectly by means of brain functioning, the behavior of a person, or his personality traits. Thus, what primarily serves as a criterion for the identity of a person, is not spatio-temporal continuity of the brain, but these latter parameters directly accessible in everyday life. A similar kind of argumentation is used by Sydney Shoemaker in his famous case of Mr Brownson (48).

I think that a similar argument should also be used in the context of neural tissue transplantations for, in spite of spatio-temporal discontinuity of parts of the brain brought about by the operation, changes in the personality traits need not necessarily arise. In contrast, if in this kind of therapy for neurodegenerative disorders, the implant were able to perform more or less the same function as the formerly intact, now degenerated neurons, pathological changes in character traits and loss of personal identity might even be prevented despite there being no spatio-temporal continuity of the entire brain. Thus, the decisive criterion in neural tissue transplantation is not spatio-temporal continuity, but functionality.

With an implant that functions in the same way as the formerly intact, now degenerated brain structure, there is no influence on the graft recipient's mental or physical characteristics, and therefore no influence on his or her identity. Ethical reflection focuses on those cases in which the implant is not able to perform all functions in an equivalent way and in which modifications in the graft recipient's character arise after neural tissue transplantation (4).

In such an evaluation, mental as well as physical aspects play an important role. Since a person is entirely dependent on his physical condition, which is a presupposition for any kind of action, communication, or social contact, the body of a human being has to be considered an important component of individual personality. Modifications in a person's physical condition, especially any kind of restrictions in everyday life, may influence the person affected in many respects.

In Parkinson's disease, the motor symptoms often enormously influence not only the way of life, but also the patient's individual character (49). Incapacitating motor symptoms such as hypokinesia, muscular rigidity, tremors, postural instability, or dyskinesia often induce affected persons to avoid social contact and to retire from public life. In addition, the patients tend to develop a kind of inferiority complex, since, owing to the motor symptoms, they need much more time than other people to perform certain activities, and their actions are often clumsy. In parkinsonian patients, there are quite significant effects on the personality brought about indirectly by the disease-induced motor symptoms. Thus, modifications in bodily characteristics may have quite conspicuous effects on a person's character traits.

Mental Characteristics
Normally, a person's character is quite stable, and undergoes only comparatively small modifications
over time. In everyday life, such quasi-stability in the character traits is very important since it allows a person to identify with his or her past and to adequately plan the future course of life. Adequate plans for the future are only possible if relevant interests, preferences, and character traits can be considered to persist over time. In addition, people only change gradually in the course of time. Only after certain drastic experiences or accidents or as a result of serious diseases, brain injuries, or after brain operations, do abrupt changes occur in a person's character traits, beliefs, interests, desires, and preferences. This may lead to pivotal changes in the person's way of life and involves the danger of alienation from the person's own past, as well as difficulties in continuing plans and projects initiated at an earlier date.

In order to describe these aspects, philosophical discussions often use the term "connectedness". Derek Parfit defines psychological connectedness as "the holding of particular direct psychological connections" (43). He describes several kinds of direct psychological connections, such as those relations which hold between a memory and the experience remembered, or between an intention and the later act in which this intention is carried out, or between different expressions of some lasting characteristics, such as desires or hopes. Psychological connectedness is of great importance in social life, not least because it is a prerequisite for a person's ability to take responsibility for something done in the past. Also, a person's fellow beings, his relatives, colleagues, and friends, expect there to be a certain stability in his or her character traits. Significant changes in the personality traits, especially if they occur abruptly, often lead to serious consequences in social contexts and also tend to make it difficult for a person's long-term interests, plans, and desires to materialize.

Most people possess a relatively high degree of connectedness insofar as their memory is intact and, on the whole, they stay almost the same over a certain period of time. However, a person's character traits normally change gradually in the course of time and sometimes do so to a considerable degree. In cases of reduced connectedness, whether a person is still able to continue his or her long-term projects and to attain his or her long-term goals is of great importance. Changes or diseases which interfere with a person's long-term interests are mostly considered especially serious. Therefore, serious changes in mental characteristics, such as depression, disturbed memory, senility, or some kinds of psychiatric dysfunction, not only reduce psychological connectedness directly but also have disastrous consequences on a person's long-term life-plans. Thus, in order to evaluate the implications of reduced connectedness adequately, not only the number of lost direct psychological connections but also the quality and the importance the affected person attaches to them has to be taken into account. Changes in character which are caused by certain disorders are often considered especially grave for, apart from the aspect of connectedness, they lead to unwanted and troublesome alterations. On the other hand, if, in a person suffering from a chronic illness that has a great influence on the personality traits, there is an amelioration of symptoms leading to a "normalized" personality, this reduction in connectedness is generally very welcome. One reason surely is that in these cases, a person's original mental characteristics are restored, i.e., the characteristics a person considers as his or her genuine ones and not influenced by the disease. In addition, it is also very important that a better state of health is attained that allows for increased autonomy. As long as the changes in personality traits have the desired effect and lead to improving a person's well-being and state of health, these changes are often evaluated differently from cases in which unexpected and undesired changes in the character traits occur.

Graft Recipient in Clinical Trials

In the context of neural tissue transplantations, the possibility of reduced connectedness cannot be ruled out. These reductions may be unforeseen and undesired. They depend on the exact operation procedure, the implantation site, and the implanted material. Most of the neural tissue transplantation studies on patients with Parkinson's disease have been evaluations of the patients' motor symptoms. Detailed neuropsychological tests on parkinsonian patients which take into account influences on mental characteristics that might arise after implanting dopaminergic material in the basal ganglia, have hardly ever been carried out. In those transplantation studies in which certain neuropsychological data were presented, relatively mild effects on the mental characteristics of the parkinsonian patients who underwent transplantation were reported; these include improvements in visuospatial deficits, amelioration of frontal lobe-type symptoms, improvements in visual and verbal memory, increases in IQ, as well as panic attacks and depression (4,24,25). Since these effects were due to implants that were not very effective at the motor level, it may be speculated that implants that have more effect on motor symptoms might also have greater influences on mental characteristics.

To what extent is it possible that neural tissue transplantations induce changes in the character traits? On the one hand, neural tissue transplantations may have similar effects as pharmacological therapies. This is so because, as it is currently assumed, a great part of the therapeutic effect of
neural tissue transplantations is based on the fact that the neurotransmitter reaches per diffusionem the surrounding host brain. However, it has to be mentioned that there are enormous uncertainties with regard to the exact mechanism that underlies the therapeutic effect of neural tissue transplantation in Parkinson's disease, and that there is a great number of other mechanisms under discussion. In particular, the extent to which the fetal implant is able to form synaptic contacts with the surrounding host brain plays an important role (5,15,16,33). Changes in the personality traits may occur both with pharmacological therapies and with neural tissue transplantations when the therapeutic material invokes changes in the brain which lead to modifications in behavior. However, there are also important differences between neural tissue transplantations and drug-based therapies. In pharmacological therapies the drug is applied systemically and reaches most parts of a person's body, whereas in neural tissue transplantations the therapeutic substance directly reaches a specified region of the host brain. In addition, during pharmacological therapies the drug has to be administered in a regular manner, in Parkinson's disease often several times a day, in order to have an ongoing therapeutic effect and to avoid fluctuations. This permits adjusting medication to the patient's individual requirements and to optimize therapeutic effect. It also permits adapting the treatment to the course of the illness. Negative side effects can — to a certain extent — be met by a change in medication.

In contrast to this, neural tissue transplantation is an operative procedure with irreversible consequences. Once the graft has been implanted in the host brain, it is no longer possible to directly control the influences exerted by the implant on the graft recipient. There is no fine tuning possible with regard to the amount of neurotransmitter that is being secreted by the implant, and no accommodation to the course of the illness is possible. Thus, there is no way to influence the amount of therapeutically active neurotransmitter that is being secreted into the surrounding host brain, nor is there any influence on the way in which other substances, like growth factors, are secreted into the surrounding brain. The patient is at the mercy of long-term effects the neural tissue transplantation might have. These long-term effects may include enormous modifications in the secretion of the neurotransmitter, immunoreactions, and the destruction of the implant (6,24,50).

In conclusion, the lack of detailed neuropsychological studies has to be considered highly problematic. After an implantation of dopaminergic material into the basal ganglia, changes in the personality traits cannot be totally ruled out since the neurotransmitter dopamine exerts various influences on human behavior (51,52). Together with other neurotransmitters in the basal ganglia, dopamine is necessary to establish a balance between spontaneous switching and continuation of ongoing behavior, and between the use of endogenous and exogenous information (53). Due to dopamine deficiency, parkinsonian patients exhibit an increased dependency on external stimuli, and spontaneous switching between different behavioral patterns is reduced. In addition, an increased incidence of certain character traits which have been interpreted to reflect the loss in the neurotransmitter dopamine has been observed in these patients. Patients with Parkinson's disease have often been characterized as being conscientious, introverted, stoic, and emotionally under control. This characterization matches quite nicely with a scale developed by C.R. Cloninger, in which a person's character traits are shown to be in certain aspects dependent on the dopamine activity in the brain (51,52). According to this, there is a positive correlation between high dopaminergic activity in the brain and a tendency to explorative behavior, which may be expressed in excitable, impulsive, extroverted, and capricious behavioral tendencies. According to Cloninger's scale, these tendencies diminish parallel to the reduction in dopaminergic activities. At the lower end of the scale, there are persons with very low dopaminergic activity and very low explorative behavior who can be characterized as being pensive, rigid, stoic, loyal, and modest. These character traits are important aspects of the individual personality of patients with Parkinson's disease. Significant modifications in a person's mental characteristics may occur after neural tissue transplantation, when there is a drastic increase in dopamine concentration in certain regions of the basal ganglia, i.e., in ventral parts of the caudate nucleus. Thus, modifications in dopamine concentration may not only lead to an amelioration of motor symptoms in parkinsonian patients, but may also influence the patient's personality and lead to significant modifications in his or her way of life. However, up to now effects like these have not been observed in the context of neural tissue transplantations, not only due to the very low effectiveness of the implants that have only had a small influence on the motor level. In parkinsonian patients, the dopaminergic graft is implanted in the striatum (caudate nucleus or putamen). This implantation site is a part of the so-called basal ganglia circuits that connect the basal ganglia with the thalamus and several cortical areas (54). In particular, the caudate nucleus, the implantation site most often used, is a component of the so-called "complex pathway", which involves regions of the frontal and prefrontal cortex. Thus, influences on cognitive functions commonly attributed to the frontal and prefrontal cortex cannot be excluded.
In the clinical transplantation studies carried out so far, after human fetal mesencephalic tissue had been implanted in the brain of parkinsonian patients suffering from incapacitating motor symptoms, there was a partial improvement of motor symptoms in many cases. Unfortunately, neuropsychological tests for possible influences the operation might have on mental characteristics have been greatly neglected. It is absolutely necessary that a more detailed neuropsychological testing be carried out in clinical trials in order to more clearly specify the consequences of the transplantation procedure not only on the level of motor symptoms but also on the level of mental characteristics. In particular, it is necessary that all researchers doing clinical trials evaluate their patients according to the same, commonly designed schedule specific to the neurodegenerative disorder in question. This would allow the comparison of the various studies carried out in different research centers. The impossibility of comparing the results of the different clinical studies is one of the major problems in assessing the outcome of neural grafting on patients with Parkinson's disease.

The question of the extent to which changes in character traits, personality or personal identity could be tolerated seems to be a question of adequate balancing. In any case, it is a field with high ethical relevance that needs intense interdisciplinary discussion, especially in view of the great importance the issues concerning a human being's personality and personal identity have in moral and social contexts.

Patients with Parkinson's disease suffer almost exclusively from motor disturbances and most often have only minor cognitive abnormalities. In neural tissue transplantations, the risk that modifications in a person's mental characteristics might arise has to be carefully balanced against the problems linked to the disturbances in motor functioning. In view of the great importance of mental characteristics for personality and personal identity it cannot be dismissed that the negative mental side effects of a neural tissue transplantation might be more serious than the pretransplantation motor symptoms. Thus, for patients with Parkinson's disease, in this early stage of neural grafting studies it does not seem appropriate to take this great risk, especially in view of the fact that relevant data on mental aspects of neural grafting are almost non-existent.

It is well known that one of the reasons why the method of neural grafting has been introduced on patients with Parkinson's disease is the apparently optimal anatomical and neuropathological situation in Parkinson's disease. However, from an ethical point of view it seems much more appropriate to introduce neural grafting in patients for whom the risk-benefit-ratio would be much better: those patients who are at a high risk of losing personality or personal identity, or who already have undergone serious modifications in important mental characteristics or who suffer from mental disturbances. In these cases, neural tissue transplantation would aim at preserving the patient's mental characteristics. This aim might be worth the risks involved, since not only the risks but also the benefits of the operation would be in the category of mental aspects. Thus, patients suffering from other neurodegenerative disorders, such as Huntington's disease, might be more adequate transplantation candidates than patients with Parkinson's disease. However, it is clear that this argument should not be used to hastily carry out clinical transplantation studies on patients with Huntington's disease, particularly because the anatomical and pathological situation is much more complicated in Huntington's disease than in Parkinson's disease (50,55).

In conclusion, it is clear that clinicians and research teams, as well as ethicists, could benefit greatly if they entered into a common, interdisciplinary exchange of ideas. With respect to neural tissue transplantation research, this exchange of views could increase the attention paid to questions concerning the use of human fetal tissue and the personality and personal identity of the graft recipients.

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