WILL EMBRYONIC STEM CELLS BE WIDELY USED IN THE FUTURE TO TREAT PARKINSON’S DISEASE?

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ABSTRACT
Ever since the discovery led by James Thomson (1998) to isolate and grow human embryonic stem cells in cell culture, there have been high medical expectations for them in the future. Stem cells offer huge potential as they can become any type of cell in the human body. However, many ethical reasons arise against embryonic stem cells research as some people believe this involves destroying a life. Furthermore, scientists face many hurdles in their research method. One example is experimenting on animals which can produce inaccurate results as there are many factors that differentiate humans from animals. Therefore scientists face the danger of making false assumptions. These factors are a few of many that will contribute to whether embryonic stem cells will be widely used in the future to treat Parkinson’s disease. It is this question which will be my main focus in this report.

INTRODUCTION
Embryonic stem cells can be used in medicine as an effective treatment for medical problems that can not be treated by drugs or surgery. Current research shows that scientists have been successful in treating Parkinson’s disease in mice (Fleming, N (2011)).

Parkinson’s disease is a neurodegenerative disease, which means it is the result of progressive and selective degeneration of neurones in the brain by 80% (Dupret, D (2011)). These neurones are called dopamine neurones which, when we age, begin to stop working efficiently. This is because the nerve cells that produce dopamine, a chemical messenger, gradually decrease in numbers. As a result the neurotransmitter is unable to carry out its central roles in the brain such as movement and thought. Therefore, people who suffer from Parkinson’s disease can become paralysed, as they cannot start movement easily and they can experience tremors or small repetitive movements of the limbs at rest (Dupret, D (2011)).

Already the treatment for Parkinson’s disease is dopamine replacement therapy. This is when a patient takes a synthetic drug called L-dopa that is converted in the brain to dopamine (Dupret, D (2011)). However, L-dopa can cause serious side effects such as dyskinesia. This is when the patient suffers from excessive and abnormal involuntary movements. Unfortunately, L-dopa has little effect on patients who suffer the late stages of Parkinson’s disease and thus they are subjected to deep-brain stimulation, in order to control the motor neurones. This new procedure involves implanting electrodes into the basal ganglia, which continuously sends small electric shocks (Dupret, D (2011)).

The number of stem cells present in an adult is far fewer than the number seen in early development because most of the stem cells have differentiated and multiplied. This makes it extremely difficult to isolate stem cells from an adult organism, which is why scientists hope to use embryonic stem cells for therapy because embryonic stem cells are much easier to obtain. These embryos, used with consent of the donors, are leftovers from IVF clinics. Separated from the other parts of the early developing embryo, primitive cells can be grown in a culture medium to become embryonic stem cells (Kelly, E (2007)).

The stem cells undergo cell proliferation by mitosis, in the laboratory for many months. At this stage it is totipotent (Kelly, E (2007)). As the egg becomes a blastocyst and before it implants in the uterus, it develops a clump of cells- the inner cell mass- and become pluripotent (Kelly, E (2007)). Embryonic stem cells needed to grow into nerve cells are harvested exclusively from this inner cell mass from the ectoderm layer (Kelly, E (2007)). The cells are used to differentiate into dopamine-producing neurons by introducing the gene Nurr1 in vitro (Kelly, E (2007)). By culturing the cells in suspension embryoid bodies are formed. These cells differentiate into various types of cells spontaneously, including nerve cells. The initial steps for obtaining the cells are conducted under a dissecting microscope (Kelly, E (2007)). Under the microscope, the colonies are mechanically dispersed.
There have been clinical trials with embryonic stem cells to improve the locomotor recovery in spinal-cord injured rats in 2009. The results were promising as it showed that transplanting these stem cells can improve the quality of life.

DISCUSSION

Ethical reasons
The most obvious ethical reason against embryonic stem cell research is that it involves the destruction of an embryo. Permission must be granted by the parents in either case before the embryo can be used for research. Many people believe that such research is immoral, and that stopping it is righteous and necessary. Using the embryo as a tool of research cheapens the value of human life, and conflicts with religious and moral views held in our society. "A life is a life and that should never be compromised. A fertilized egg should be valued as a human life even if it is in its very first weeks. Destroying a human life in the hopes of saving another human life is not ethical." (Experiment-Resources.com (2008)). It is this argument that could delay the use of embryonic stem cells as a treatment for Parkinson’s. However, others believe that the potential for this research to provide treatments and possibly cure debilitating illnesses overrides this concern.

Another ethical issue associated with stem cell research ties in with the combination of embryonic stem cell and cloning technologies, leading to generation of an embryo that is a genetic clone of the donor of the nucleus. This means that embryos will be purely produced for the purpose of generating tissue for transplantation. This is unethical and is not acceptable to some people as the embryo generated could have been allowed to continue development and thus could potentially lead to the birth of a new human if implanted into a willing mother. Therefore, there are serious ethical concerns associated with the process of somatic cell nuclear transfer to reproduce humans and this is why it is illegal in Australia, UK and the USA to conduct any research into reproductive cloning of humans.

Therefore, Australia has the Prohibition of Human Cloning Act (2002), which prohibits all types of human cloning by any method (The Australian Stem Cell Centre). In addition, the Research Involving Human Embryos Act (2002) was made to allow approved research programs to use a regulated number of excess embryos that would assist reproductive technology (The Australian Stem Cell Centre). This ensures that each embryo will be used with the utmost care, rather than some being discarded without valid reasons.

Furthermore, Australia has a policy in which all research involving humans must be approved by Human Research Ethics Committee. The legislation states that no embryo may be created for the purpose of this research or to generate stem cell lines (The Australian Stem Cell Centre). The embryonic stem and germ cells are obtained from either donated embryos not required for an IVF procedure that would otherwise be destroyed, or from pregnancies that were terminated for medical or social reasons. This is a sensible decision as it gives an embryo, which would have been thrown away, a purpose in life without being created for the sole role of helping research.

All scientists are aware that they must undertake their work ethically and within the boundaries of the law, and these can vary from country to country. It is this task which can provide a problem to some research programs as the U.K, China, Korea and Singapore are competing with one another to become the epicentre of stem cell research. Such competition, especially between the U.K and China which are both high-developing countries, can degrade the care scientists take in their work.
Fortunately, for scientists, the argument for embryonic stem cell research is increasing due to new successful research being carried out. The reason why embryos are destroyed is because the aim the research is to achieve a beneficial end. In addition, with so much attention focusing on research problems and the significant expense of developing new drugs, stem cell cultures that are created solely for this purpose would enable pharmaceutical companies to conduct tests for toxicity in humans that cannot be accomplished with animal experiments. Clones could be used to counter the argument of those who believe that life begins at conception, because nuclear transfer is not fertilization.

Therefore, due to the significance of embryonic stem cell research, the ethical reasons against the research will be outweighed when the beneficial aspect of it is shown to the public through successful research. This is especially important now, as the life expectancy of humans is increasing and thus the rate of people getting Parkinson’s disease in a population is increasing. As a result, there will be more people wanting proper treatment than those who are against stem cell research and decide to undergo less effective treatment with serious side effects, such as L-dopa.

**Treating Parkinson’s disease in animals**
Before the embryonic stem cells can be grafted into the human brain, animal studies have to be carried out to ensure there are no side effects and most importantly if the stem cells will actually carry out their role.

Mouse embryonic stem cells have already been used in rat models of Parkinson’s disease. These rats were treated with chemicals so that they became models of Parkinson’s disease (Fleming, N (2011)). One of the aims of this study was to see if any immune problem in the brain would occur. It was thought that the immune system would not attack the tissue transplanted into the substantia nigra (Kelly, E (2007)). However, a recent report disagreed with this hypothesis and so autologous cells are now thought to be a safer alternative.

Another thing scientists wanted to check was whether there would be an overproduction of new brain cells. This would be harmful and potentially critical to the brain. Furthermore, it was important that the cells introduced did not suddenly form the incorrect cell type.

Initially, the new dopamine-producing cells showed improvements in the movements of the rats. However, the cells did continue to grow and some even transformed into tumours called teratomas (Fleming, N (2011)).

Some of these mice died from the brain tumours, creating more ethical problems as the research was a form of animal cruelty. As the result of this experiment, researches used a different procedure to differentiate the stem cells into nerve cells, which eliminated the ability to cause tumours. The cells were transplanted however into monkeys. The new nerve cells did not form tumours and improvement of Parkinson’s became apparent (Fleming, N (2011)).

The results from the monkeys are even more crucial, as the monkeys have more neurons in their brain than rodents. If possible, clinical trials conducted on guerillas should be carried out before human clinical trials as they are more closely linked to us than monkeys. Nevertheless, humans’ brains are far more complex than any other species as we have the ability of speech. Therefore, we are still a long way from our goal treating Parkinson’s with embryonic stem cells.
Problem with Human Clinical Trials

In the 1990s, there was a scenario where Parkinson’s patients were transplanted with foetal brain tissue (Fleming, N (2011)). The results varied as some patients got better but others actually got worse. Scientists found out that transplanting the tissue too early provided side effects, and transplanting too late had no beneficial effect. Therefore, we can learn from this report when to transplant the dopamine-producing nerve cells and so now it is not a problem that researchers have to face.

The real problem is what happens when the new nerve cells are attached to the brain. There have been no human clinical trials using embryonic stem cells to treat Parkinson’s disease. However, there has been a safety trial of using human embryonic stem cells to produce retinal cells, which were injected into the back of the eye of sufferers of Stargardt’s disease (Walsh, F (2012)). After treatment they showed some slight improvement in vision. There was no abnormal proliferation, teratomas formation or graft rejection. Even though this opens up a door of possibility of doing the same in the basal ganglia, both the eye and the brain are different organs.

Transplanting the stem cells in humans already has many risks of complications. One way embryonic stem cells can be delivered to the brain is via a lumbar puncture (Chinese Stem Cell Transplant Department). This method is already used for bone marrow stem cells. The patient has a spiral injection in the lower back into the cerebral spinal fluid. A small amount of cerebral spinal fluid is collected and mixed with the stem cell fluid. The cerebral spinal fluid circulates the brain and this circulation takes between 6-7 hours. It is within these hours that the stem cells flow into the brain. However, the dopamine-producing nerve cells need to be in the substantia nigra, which is in the middle of the brain and so this raises more complications for researchers getting the cells there. Another method is to directly inject the neuronal stem cells into substantia nigra, just like they did in their animal studies. However, any type of surgery for humans involves the patient being awake throughout the whole procedure. This is to ensure that no essential neurons are damaged during the procedure.

Finding people to take these trials is another hurdle researchers face. Since this is the brain we are talking about, people will be reluctant to be part of an experiment. The brain is of course the most delicate organ in the body as it contains around 100 billion neurons, so any side effects can cause serious damage to the patient’s lifestyle.

However, suffering from Parkinson’s disease is already a challenging ordeal so the patient may experience no fear in volunteering. There is always the possibility of being cured which can provide hope for volunteers. Nevertheless, there is also a chance of having increasingly worse symptoms, like in the 1990s’ clinical trial. Thus a huge amount of courage is required from volunteers.

Be that as it may, there is a high probability that there will be more volunteers than anticipated. This is because of the growing population and the increasing life expectancy. This means there will be more people suffering from Parkinson’s disease. Therefore, more people will be adamant for a permanent cure for the disease.

This leads me on to my next point that the pressure on researchers by the public will increase due to the increasing number of cases of Parkinson’s disease. Therefore, the ban in some countries against embryonic stem cell research is likely to be lifted as the need to prevent the death of humans is more important than an embryo that cannot speak, see nor hear. This also means that opinions will change and be more in favour of embryonic stem cell research.
Conclusion

Overall, looking at both sides of the argument in each of my three main discussions I am sure that embryonic stem cells will be widely used in the future to treat Parkinson’s disease. The main reason for this is because of the growing number of people with Parkinson’s disease due to the growing population and so there will be volunteers for the human clinical trials. The ethical reasons against embryonic stem cell research explained in my report will decrease as the need for survival becomes more and more important as people begin to realise that embryonic stem cell research is only carried out for the benefit of humans.

The research that has already happened over the past couple of decades has provided invaluable knowledge, but there is still a long way to having the first person being treated for Parkinson’s disease with embryonic stem cells. However, the wait may not be as long as expected because there has been an increase in discoveries in the past couple of months about nerve cells.

However, it must be noted that treating patients with Parkinson’s disease will cause a strain on environmental factors as we are extending the lives of people, thus encouraging the growing size of the population. Therefore, other cases of diseases will become increasingly apparent and more people will get them. This is something that we will have to face and more importantly something the government and the NHS will have to discuss, as a growing population means a more expensive healthcare for each person.

Furthermore, as stated in the animal study section of my report, humans have more neurons in their brain, thus it is more difficult to find where the dopamine-producing nerve cells are, even though it was found in animals. Therefore, researchers are unsure were exactly can the new nerve cells be injected into. It is important that the cells are injected in an area where there is no immune system so that white blood cells don’t start attacking the foreign cells.

With more research into the structure of the brain at a cellular level, we will be sure to know where exactly the new dopamine-producing nerve cells must be transplanted in the substantia nigra. This means that we will be one step closer into using embryonic stem cells to treat Parkinson’s disease on a large scale.

Despite all these developments, it is important to remember not to force woman to suddenly become egg farms (Kelly, E (2007)) and eggs should not become fertilized for the purpose of them being used in research. This is because we should not make the moral of this embryonic stem cell research, which is to improve the life of Parkinson’s patients, to be overcast by these negative factors all because of time and public pressure. This is why it is important for researches and governments to know where to draw the line in embryonic stem cell research.

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