Stem Cells of the Brain and Their Ability to Repair Damage

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Abstract

Stem cell therapy is a promising and relatively new advancement in healthcare. The human brain possesses the ability to continuously generate stem cells throughout the lifespan. It has been shown in studies that these new neurons travel to sites of injury or damage in what is believed to be an attempt at repair. This repair mechanism is not very successful on its own. By speeding the rate at which this occurs along with helping these neurons increase in number and functional abilities, perhaps degenerative brain disease as well as significant injuries can become a thing of the past.
Stem Cells of the Brain and Their Ability to Repair Damage

The human brain is complex and intricate. It has the capacity to grow, learn, remember, coordinate movements, and regulate every function the body has. It is the powerhouse. One of the most interesting features of the brain is its ability to create stem cells which can be sent out to areas of damaged tissue. By definition a stem cell has "a dual functional criteria...the capacity to self-renew indefinitely and to differentiate into specialized cells with limited proliferative capacity" (Williams & Keating, 2008, p.301). These stem cells have the ability to not only become activated when damaged has occurred, but also the location where they are needed.

Unfortunately, the amount of stem cells sent to these areas is not sufficient for any significant repair and/or restoration of function. The hope is that with a way to help the number of stem cells in the brain grow, therapies will emerge that can repair damaged areas and improve the quality of life on those it affects.

Location and Function of Stem Cells

Stem cells in the adult body can be found in all the tissues such as bone marrow, brain, liver, blood, etc. (Paspala, Murthy, Mahaboob, & Habeeb, 2011). Neural stem cells (NSCs) have been studied as early as the 1990s and when engrafted into neonatal mice they proliferated, migrated, and differentiated (Paspala et al., 2011).
There are two areas in the brain where NSCs reside, the subgranular zone (SGZ) of the hippocampal dentate gyrus, and the subventricular zone (SVZ) of the lateral ventricle wall (Landgren & Curtis, 2010). (See Fig.1) While these stem cells have the capabilities to aid in recovery from injury and disease, they are restricted in how much they can grow and for how long (Roh, Jung, & Chu, 2008). Among the cell types of the SVZ are immature neurons, ependymal cells, transit-amplifying cells, and neural stem cells (Nakaguchi, Masuda, Keneko, & Sawamoto, 2010). (See Fig.2) The neural stem cells are able to migrate as new neurons via the adult rostral migratory stream and are sent to the olfactory bulb (OB) (Nakaguchi et al., 2010). It remains unclear what happens next to these new neurons, but the fact that they are created continuously in the adult brain is both intriguing and promising. It seems this process simply needs a nudge in its capabilities to self-renew the brain.

Animal Studies

A few studies on the capacity of neurogenesis have been done on animal subjects, particularly mice. Interestingly, when a human dissected brain is examined alongside that of a rodent it is noted that neurogenesis in the SVZ occurs more often in the rodent's brain (Nakaguchi et al., 2010). When a rodent has an infarction of the brain, the new neurons created...
in the SVZ travel to the site of injury. Similarly, when a human has a stroke the new neurons travel from the SVZ to the damaged area. According to Conover and Shook (2011), “the cell types are essentially similar and as in the rodent model there is an increase in proliferating cells within the SVZ following stroke” (p 55). Though the amount of neurons that make it to the site of injury cannot make up for the damage, the mechanism by which they travel to the site is in place and simply needs to incorporate a way to improve and speed up this process. As Nakaguchi et al. (2010) stated:

The spontaneous regeneration response of the adult SVZ to pathological neuronal loss does not lead to the regeneration of the lost neurons, because of limitations in the numbers of neurons generated and the fates they adopt. However, many studies support the idea that interventions to increase the production of new neurons in the SVZ and promote their migration, maturation, and survival in the damaged area could be beneficial for treating a variety of neurological deficits (p.6).

In essence, being able to use the brain’s already existing ability to respond when it is damaged alongside therapies that can increase this natural response would be a groundbreaking advancement in healthcare.

A study done by Yun, Wei-Min, and Ting-Hua (2011) used rat subjects to engraft neural stem cells following a surgical procedure in which the spinal cord was cut at the level of T9. Improvements were shown in all the rats in their hind limb locomotor functions (Yun et al., 2011). In addition, when NSCs are implanted they have the ability to provide cytokines and neurotrophic factors that aid in the rebuilding of the nervous system (Yun et al., 2010). This study shows that NSC transplantation is a viable method of rebuilding and replacing the neurons that are lost after a spinal cord injury. Also, it was discovered in the study that the timing after a
spinal cord injury is key to the success of NSC engraftment. The best window of opportunity is between 7 and 14 days (Yun et al., 2011). Whether this window is the same amount of time in humans is unknown, but it makes sense that the sooner treatment can commence the sooner recovery will begin. If functional recovery was made during this experiment then the same success happening in human patients is very achievable.

**Stem Cell Therapy**

Therapies and treatments can expand to cover minor brain injuries to more serious traumatic injuries. The number or new neurons necessary to facilitate healing in the affected areas would be significantly higher for the traumatic injuries and it is unknown how well the more serious injuries would benefit, if at all, from such therapies. Other factors affect successful therapy as well such as time after the occurrence of an injury, the area that is damaged, and the amount of inflammation.

There are two ways in which NSC can be used for therapy. One is in vivo where the cells are differentiating on their own within the body and the other is in vitro when the NSCs are harvested and taken outside of the body to be cultured, differentiated, and then reimplanted (Lowenbruck & Storch, 2011).

This therapy could also aid in the treatment of stroke victims. After a stroke brain tissue is damaged and essentially dead, but it could be replaced if the timing is right. (See Fig.3) Previous investigation into recovery after a stroke has uncovered that the timing after a stroke
has occurred is very important. If a therapy can be incorporated after a stroke has happened it is best to begin treatment as soon as possible. The reasoning is because this is the time that the brain is more open to conforming and changing in order to reorganize itself. The treatment of implanting stem cells into a damaged area has been shown some promising recovery for strokes in studies done on rodents (Srivastava, 2009).

The stem cells that already exist in the brain of both human and animals are not sufficient enough to repair damage alone. In order to help the brains’ ability to repair itself granulocyte stimulating factor can be administered to speed up the process by which the cells travel, and they also have the added benefit of being neuroprotective (Srivastava, 2009).

Stem cell therapy and how effective it can be depends on many factors besides timing such as how much damage there is, the degree of severity, and inflammation (Liu, Lang, Baskaya, Dempsey & Vemuganti, 2009). Even so, the approach of enhancing the already existing stem cells of the brain will aid in the recovery of an individual following a stroke. As Liu et al. (2009) state “The ability to isolate, grow and transplant stem cells is a promising approach which in the near future might help to restore the lost neurons in the post-ischemic brain” (p.474-476).

As more studies are conducted on how the existing stem cells of the brain can be further improved upon, the number of diseases and damage that can be slowed, stopped, or wiped out increases. There remains much to learn about the mechanics of how the neurons proliferate and what triggers them to be formed.

**Parkinson’s and Alzheimer’s Patients**
Patients with Alzheimer’s disease are good candidates for NSC therapy because the main problem in the disease is neurodegeneration. It begins in the cortex and progressively spreads to the temporal, frontal, and parietal lobes (Rodriguez & Verkhratsky, 2011). Interestingly, the hippocampus is affected early on in the disease and this area is also one of the neurogenic niches of the brain (Rodriguez & Verkhratsky, 2011).

From the onset of Alzheimer’s the areas in the brain that could possibly regenerate neural stem cells is attacked. Perhaps the production of new neurons can be reintroduced in these areas that are wiped out so early. This could effectively delay the disease in order to find ways to recover the mental and functional difficulties.

Similarly to Alzheimer’s, Parkinson’s disease is also a neurodegenerative disorder. (See Fig.4) It is also a very frequent one. The reason that motor movement breaks down in this disease is because the highly specialized cell population degenerates (Lowenbruck & Storch, 2011).

The neural stem cell niche

Within the adult brain the area where the stem cells reside is referred to as the ‘neural stem cell niche’.
This area has a special microenvironment which maintains the neurons and helps them to remain at the ready in case something goes wrong and they are needed to replace lost neurons. The downside is that as a person continues to get older, this niche tends to degrade. A study done on mice showed that there is a correlation between a decline in neurogenesis and an increase in age (Conover & Shook, 2010). The main contributing factor to why this happens has to do with the cells’ DNA. Telomerase needs to be active for the strands to maintain their length and regular functions. As Conover and Shook (2010) noted: “cells that remain proliferative require telomerase activity to maintain telomere length, preventing replicative cellular senescence…expression and telomerase activity are reduced in an age-dependent manner in the SVZ” (p.52).

This may make the outlook of using the bodies’ own brain stem cells bleak but in actuality the proliferative ability of these cells does not decrease with age (Conover & Shook, 2010). This very fact means that regardless of the age of the brain the neurons that reside within it have the potential to multiply in order to carry out their function as a repair mechanism.

**Potential Risks**

With most treatments in the medical world there are associated risk factors when it comes to stem cell therapy. Among these risks are the site of injection, how the cells are handled, the culturing history of the cells, and the fact that multiplying cells make for candidates of malignant transformation (Herberts, Kwa & Hermsen, 2011). Many of these risks are considered ones if the cells are prepared outside of the body. The risks are lessened if there is a way to enhance these cells ability to multiply within the body.
Another factor is that in order for stem cell therapy to be effective a large number of cells are needed. If administered from the outside world to the inside these cells could accumulate and cause embolisms and infarctions (Herberts et al., 2011).

Though there are risks the benefits are far more numerous. Just as victims of cancer undergo chemotherapy to eradicate cancerous cells, so would a victim of a stroke or a disease process undergo a therapy to increase the response of their neuronal stem cells. Risks are also at a minimum with this type of therapy because the cells being improved upon are those belonging to the patient themselves. Adult NSCs avoid that danger of graft rejection and the ethical concerns that are tied in with the use of embryonic stem cells (Lowenbruck & Storch, 2011).

**Conclusion**

Like any advancement in the medical world there will be plenty of testing and retesting. Studies and experiments will continue to be made on animal models until neuronal stem cell therapy is better understood. Eventually, with caution, human trials can begin and a whole new world of opportunity will open up. The benefits far outweigh the risks or any setbacks that will be encountered along the way.

If existing neuronal stem cells that reside in the human brain can be improved upon to enhance their inherent abilities, then perhaps other stem cells in the body such as those residing in the bone, adipose tissue, etc. have the same ability to repair other parts of the body. The human body is already capable of healing itself and defending itself when attacked by an outside source or even an internal threat. Being able to perfect the brains’ ability to self-heal can be the forerunner in future studies and successes in harnessing the power the body has to offer to regenerate itself.
References


