The subtle onset of neuronal loss following exposure to neurotoxins, environmental pollutants and by aging is irreversible and irreparable as neurons in the adult mammalian central nervous system (CNS) do not have the ability to divide or regenerate. Such perturbations in the central nervous system lead to variety of functional deficits particular of many neurodegenerative diseases such as Parkinson's, Alzheimer's, Huntington's chorea, dementia and amyotrophic lateral sclerosis. The lack of adequate medical therapy and severity of symptoms in such conditions have prompted the introduction of cell transplantation as a possible treatment for such disorders. Recent advances in the technology of neural grafting in the adult CNS have provided an experimental way to alleviate neuronal loss by replacing missing neurons with young, post mitotic neurons, taken from isogenic embryos.

The ability of intracerebrally implanted fetal neurons in promoting functional recovery in brain damaged animal recipients has raised speculations of how these implants potentiate restoration. Mechanistic studies on the functional effects of grafted neurons have shown that diffuse release of active compounds such as trophic factors may be sufficient to restore defective neurotransmission in a denervated brain region.
Electrophysiological and ultrastructural studies of grafted brain regions have shown that the transplants establish synaptic connectivity with the denervated or neuron depleted host brain and become integrated into the host neuronal circuitry. Grafted fetal neurons have also been shown to reconstruct the functional circuitry of the host brain by restoring the normal synaptic neurotransmitter release. Thus, the potential of fetal neural grafts to induce or improve functional recovery in brain damaged recipients rests on a multitude of trophic, transmitter specific or synaptic mechanisms that may allow the transplanted tissue to promote host brain function and repair.

The hippocampus lies in a strategic position to process information derived from its associated regions and to redistribute them to regions involved in cognition and behavioural reactivity. The hippocampus has been shown to modulate a variety of behavioural functions such as motor coordination, reactivity and learning and memory. Any damage to the hippocampus leads to irreparable alterations in behavioural functions controlled by it. Studies have been carried out extensively on hippocampal damaged animals to understand its function in coordinating complex behaviours and also to develop animal models of neurodegeneration which mimic similar deficits in humans.

Colchicine (a classical neurotoxin) and trimethyltin (an industrial pollutant) are known to selectively damage specific regions of the hippocampus. Direct administration of colchicine destroys the granule cells, whereas trimethyltin (TMT) is known to selectively kill the pyramidal neurons of the hippocampus. The formation of amyloid precursor protein plaques in both cases suggests them as a tool for developing an animal model for Alzheimer's disease. The primary target of colchicine appears to be the cholinergic pathway with alterations in cholinergic muscarinic receptor functions, while TMT is believed to exert its action by affecting multitransmitter systems, leading to diverse functional abnormalities in both cases.

Intra-hippocampal fetal neural transplantation in animal models has been shown to partially restore such type of functional deficits. However, the transplanted fetal neurons themselves have been found to degenerate due to lack of trophic support and improper integration with the host. Supplementing the grafted fetal neurons with
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Exogenous nerve growth factor (a neurotrophin known to potentiate neuronal survival, maturation and differentiation) could enhance their viability and restorative potential.

Modifications in the grafting technique by distributing the fetal neurons in the form of small microtransplants at multiple sites so as to repopulate maximum area of degeneration could also influence better recovery of function. Such type of microtransplants could potentiate interconnections between the transplanted cells as well as between the transplants and the host and thus influencing better and long-term benefits following transplantation.

Detailed behavioural and biochemical studies are required to assess the functional recovery following fetal tissue grafting.

Therefore, the present investigations were aimed to study:

1. Neurobehavioural, neurochemical and morphological effects of colchicine (a classical neurotoxin) and trimethyltin (an environmental pollutant).
2. Restorative potential of fetal intra-hippocampal transplants in ameliorating functional deficits caused by the two chemicals.
3. The effect of nerve growth factor infusions in increasing the efficacy of the transplants.
4. The comparative restoration of neurobehavioural, neurochemical and morphological parameters using micro (multiple) and macro (single) transplantation techniques.