appeared on 28th May 2007

Brain recovers like computer disk

It looks like loss of memory is only loss of the mechanism to access the memory, says S.Ananthanaryanan.

Li-Huei Tsai and others at MIT, Cambridge, USA describe in this week's ***Nature***, their work which shows that loss of old memories can be recovered. The work was done with mice, but the results should be equally valid for humans with degenerative brain disease.

Brain and cells

Brain cells communicate through extensions known as dendrites (or branches) at junctions known as synapses. At synapses, nerve cells are able to signal each other and a series of cells form pathways or circuits. Synapses also enable communication with other cells, like muscles, so that nerves can carry signals that result in action.

Loss of such mechanisms, which takes place due to ageing, leads to break-down of the circuits and loss of learning and recall ability, an early symptom of many neurodegenerative diseases. Ready instances are where patients are able to relate to recent events, but are unable to remember old acquaintances or even conversations a few days old. A question of interest has been whether memories lost in such cases are lost forever or are still there and only out of reach.

Li-Huei Tsai and colleagues made use of a mouse model to try out therapeutic agents and they have found that paths to old memory records can be rebuilt!

Transgenic mouse

CK-p25 Tg is a mouse that has been developed using gene manipulation, with the quality that a particular protein that affects the brain processes can be switched on or off with the help of a particular diet. P25 is the protein, which has been noticed to be around at the site of many neurodegenerative diseases. It was seen that if p25 was induced in these mice for 6 weeks, with the help of the diet, the mouse displayed learning and memory disability, and this was accompanied by severe loss of synapses and neurons in the forebrain.

The method to test this was to create a long term memory record in the mice, by a traumatic event, which caused 'fear conditioning'. The mice then showed characteristic 'fear' reaction when exposed to the particular stimulus.

When the mice were then fed the diet that made them 'p-25 induced', for 6 weeks, it was found that they no longer displayed the 'fear' reaction, indicating that the memory had been lost or the lesson unlearned.

Regenerating synapses

The next step was to try regenerate the communication between neurons by a known device of the 'enriched environment' (EE). This consists of housing the mice in a large cage with a maze, toys and an exercise wheel. It is established that putting mice in such

an environment leads to increase in the indicators of more dendrites and synapses in the nerve cells and is accompanied by increased learning ability.

The mice that had lost memory were then placed in EE for 4 weeks. It was found that there was marked recovery of the ‘fear’ reaction, unlike control mice not exposed to EE. This indicated that EE had positively rebuilt communication channels between neurons and established afresh the pathways to access the record of the fearful experience learned over 10 weeks ago!

Clinical EE

The next step was to see what chemical changes EE seemed to create and whether these elements could be administered so that regeneration of learning and memory could be controlled. Study of the changes set in motion by EE showed that specific genes that promote synapse formation were activated and, more important, changes in chemicals that had been found to help synaptic development were brought about in the cortex and hypothalamus parts of the brain. It was also known that injection of sodium butyrate (SB), a reagent that provoked these changes, also did facilitate associative learning.

The scientists hence tried out the effect of SB in helping revive lost long term memory. Carefully controlled experiments have clearly shown that EE and its chemical equivalents markedly promote recovery of memory, apart from other learning ability benefits. The findings are significant in the context of recent report of the recovery of a brain injured man who was minimally conscious for twenty years.