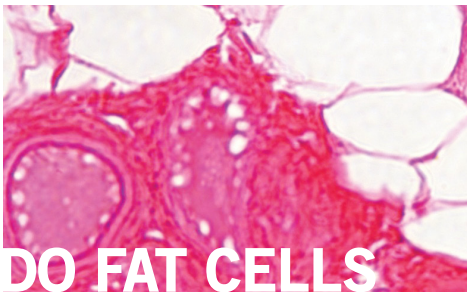
MEDBULLETIN



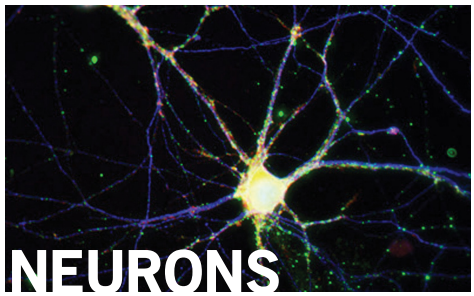
DO FAT CELLS NEED SLEEP?

KEITH LEE

Sleep deprivation has long been known to affect brain and immune function, causing deficits in learning, memory and wound healing.[1-2] A recent study also suggests that insufficient sleep may increase the risk of obesity and diabetes, through a reduction in fat cell sensitivity to insulin, a hormone that induces cellular uptake of glucose.[1]

To investigate this hypothesis, University of Chicago researchers conducted a randomized crossover study.[1] Seven healthy adults, aged 18 to 30, were tested under two experimental conditions in a randomized order: four consecutive nights of 8.5 hours of sleep, followed by four consecutive nights with 4.5 hours. After each four-day period, participants underwent an intravenous glucose tolerance test to measure total body insulin sensitivity. The researchers also biopsied abdominal fat cells from each participant to test their response to insulin. Food intake was strictly controlled and identical in both scenarios to ensure diet would not confound the results.

Results showed that total body insulin sensitivity was, on average, 16% lower after four nights of sleeping 4.5 hours compared to 8.5 hours. Similarly, insulin sensitivity in biopsied fat cells decreased by 30% under restricted sleep conditions. These results suggest that, through its effects on fat cells, sleep may play an important role in regulating whole-body metabolism, with potential implications in metabolic disorders such as diabetes. Future research can provide further insight into the importance sleep for our health.



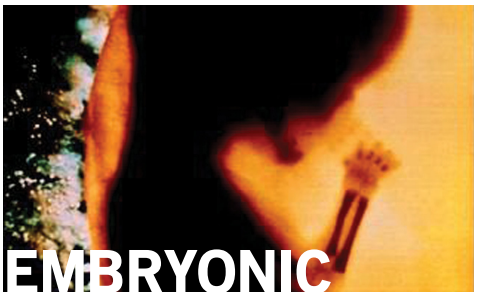
NEURONS FROM NON-NEURONAL BRAIN CELLS

BERNARD HO

Stem cell research has often involved programming somatic cells from other parts of the body to form neurons, which are then transplanted into the brain. Earlier this year, Stanford University researchers reported the successful conversion of mouse skin cells directly into neural precursor cells, which differentiate into the three main cell types of the nervous system.[1]

Recently, researchers at the Johannes Gutenberg University Mainz in Germany, led by Dr. Benedikt Berninger, converted non-neuronal cells in the brain into neurons.[2] They assert that neurons created from brain cells are better able to adapt compared to somatic cells, because their similar function and location implies a comparable differentiation pathway.[2] Berninger and colleagues focused on pericytes, which maintain the blood-brain barrier and play a role in wound healing. They manipulated two genes, *Sox2* and *Mash1*, to turn adult human brain pericytes into neuron-like cells. These genes, according to previous research, are powerful reprogramming factors for direct conversion of somatic cells into neuronal cells.[3] The researchers cultured mouse cerebral pericytes, employing retroviruses to insert the two genes. Within four weeks, the pericytes exhibited neuron-like properties such as the ability to produce electrical impulses and synapse with other neurons, two critical features for integration into neural networks.

This work raises the possibility of functional conversion of endogenous adult human brain cells into neurons. While much research is required before these results are applicable to humans, this is nonetheless another step in the search for neurodegenerative disease treatments.



EMBRYONIC INTERNEURONS RESTORE BRAIN FUNCTION

BHAVIK MISTRY

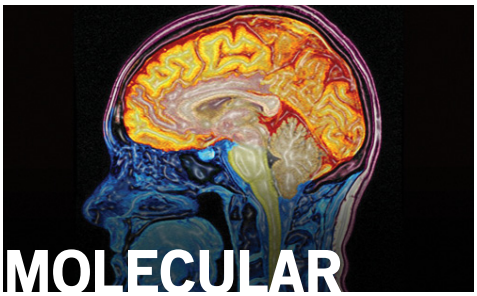
Scientists from the University of California, San Francisco, recently published a series of innovative experiments that suggest the possibility of transplanting embryonic neurons to treat multiple brain diseases. Led by Professor Arturo Alvarez-Buylla and former graduate student Derek Southwell, the researchers explored the properties of a special type of brain cell known as GABA-secreting interneurons. Deficiency in these cell types has been linked to several neurological disorders, including epilepsy, Huntington's disease and Parkinson's disease. These so-called GABAergic interneurons are critical due to their inhibitory function within the cerebral cortex, which counteract excitatory neurons.

The brain has a very limited capacity to accommodate additional cells, which is why the successful transplantation of interneurons into the brain has sent a shockwave throughout the neuroscience community. After discovering that these interneurons were able to survive, the researchers conducted further studies in which they varied the amount of interneurons transplanted. Results from these experiments showed that only a fixed and small number of transplanted embryonic interneurons would survive in the brains of adult recipient mice. The frequency of inhibitory synaptic events did not change with increasing number of transplanted interneurons. Interestingly, these transplanted interneurons did not require survival signals from other types of cells that are typically needed. The results from these experiments provide insight into brain plasticity, while suggesting a potential therapy for patients with neurological disorders.

DNA TRANSFER FOR MITOCHONDRIAL GENETIC DEFECTS

KIMIA SOROURI

Although both sperm and ovum contribute nuclear DNA to the genetic makeup of the offspring, the ovum also contributes DNA from the mitochondria – the energy-producing cellular organelle. Defects in the mitochondria occur in one in 4,000 individuals, and are involved in diseases such as Parkinson's and cancer.[1-2] Recently, a team of researchers led by Dr. Shoukhrat Mitalipov have used an innovative method to prevent genetic defects attributed not to nuclear DNA, but to mitochondrial DNA. The team successfully implemented a process called spindle-chromosomal complex transfer (ST) in rhesus macaque monkeys, in which nuclear DNA from an ovum containing defective mitochondria is implanted into a health enucleated ovum from a donor.[1] This effectively prevents the offspring from inheriting the defective mitochondrial genes from the mother.[2] Thus far, negative long-term effects have not been detected in follow-up studies.[1] It is interesting to note that offspring from the ST process possess DNA from three sources–the father, the mother (nuclear DNA), and the donor (mitochondrial DNA, comprising less than 1% of the offspring's genetic material).[3] Though this method requires further "tweaking", Mitalipov hopes this process will be available to women soon, despite scepticism from genetic specialists.[1] Regardless of the future hurdles to overcome in implementing ST, both parties agree that this new technology holds great potential for addressing certain genetic disorders.



MOLECULAR INSIGHT ON MEMORY FORMATION

HUMNA AMJAD

Protein kinase A (PKA) plays a critical role in memory formation.[1] Less understood, however, is how PKA interacts with other molecules, particularly its significance in forming short-, intermediate- and long-term memories. A team of neuroscientists from New York University and the University of California, Irvine, recently characterized the molecular interactions that may control the formation of memories.[2]

The neurotransmitter serotonin contributes to simple forms of learning such as sensitization and classical conditioning in *Aplysia* (sea slugs).[3] *Aplysia* was therefore used by Dr. Thomas Carew and colleagues to investigate the effect of molecules PKA and mitogen-activated protein kinase (MAPK) on memory formation. In their study, serotonin release was induced by tail nerve shock (TNS) to the sea slug, leading to activation of PKA and MAPK signaling cascades linked to learning and memory formation. The results suggest that variations in the interactions between MAPK and PKA cause different types of memories to form. For example, in short-term memories, no interaction with MAPK occurred; only PKA was active. In contrast, in intermediate- and long-term memories, both MAPK and PKA activity was present.[2]

The study provides insight into how MAPK and PKA are spatiotemporally arranged in a single neuron to facilitate synaptic plasticity, ultimately leading to memory formation. This research not only offers greater understanding into the molecular architecture of memory formation, but it also paves the way for the eventual development of therapeutics targeting related diseases, such as retrograde amnesia.

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