Biological Clock and Wake-up Call in Mammals

Almost all organisms ranging from single cell bacteria to humans exhibit a variety of behavioral, physiological and biochemical rhythms. This biological phenomenon better known as Circadian rhythm Biological clock controls the timing of many physiological processes over a twenty four hour period, including body temperature, feeding, hormone production and sleep-wake cycles in mammals. Although, we know fairly well about the biochemical processes that make us sleep, very little is known about what makes us wake up.

Scientists at the Salk Institute of Biology in La Jolla, San Diego, California, USA have discovered a gene that helps people wake up, much in the way that a key turns on the engine of a car. This discovery unmasked an aspect of circadian rhythm that's important in human health. Their study identified a new component of the biological clock, a gene responsible for starting the clock from its restful state every morning. This clock ramps up metabolism early each day initiating important physiological functions that tell our bodies that it's time to rise and shine.

"Our body is essentially a collection of clocks," says Dr. Satchidananda Panda, associate professor in Salk's Regulatory Biology Laboratory, who led the research along with his post-doctoral associates. The discovery fills in a missing link in the molecular mechanisms that control daily wake-sleep cycle. The central player of the cycle is a protein called PERIOD (PER). Cells use the level of PER protein as an indicator of the time of the day and tell our body when to sleep or be awake. The number of PER proteins in each of our cells rises and falls every twenty-four hours and two genes, CLOCK and BMAL1, serve as the key drivers for increasing PER protein levels.

As the level of PER protein rises during the daytime, reaching its peak around evening, it puts a brake on CLOCK and BMAL, thereby reducing its own level during nighttime. Falling PER protein levels at night cause our biological systems to slow down. Our blood pressure drops, our heart rate slows and our mental processes wind down. But, until now, the precise nature of this night time brake and what lets CLOCK and BMAL proteins overcome this brake to raise PER protein levels each morning was a mystery.

In their search, Dr Panda identified an enzyme JARID1a as the molecular bugle for cells and organs to get back to work each morning. By studying the genetic mechanisms underlying circadian rhythms in human and mouse cells and in fruit flies, the researchers discovered a new protein JARID1a that is required for normal cycling of PER protein, both at the cellular level and behavioural level. This enzyme serves as an activation switch in the biochemical circuit.

In human and mouse cells that were genetically modified to under-produce JARID1a, PER protein did not rise to its normal peak each day. Fruit flies that were similarly genetically altered also had low levels of PER protein. The flies lost track of time: they did not know when to sleep or wake up and took frequent naps throughout the day and night. Digging deeper into the molecular workings of the clock, Dr. Panda and his colleagues found

Mathematics is Neither Hardwired, Nor 'Out There'

Representations that map numbers onto space and in a way that magnitude differences can be ascertained – or the concept of a number line – are ubiquitous around us. Examples of these include rulers, measuring tapes, graph sheets and electricity meters. Understanding the number line is one of the most basic concepts in learning mathematics, as we all may remember from our lower school and middle school days. Education scholars have thought that the number line was an innate concept, an ability that human beings were naturally endowed with (though they may have acquired it through evolution and human progress). Now, challenging this majority scholarly position, a new study suggests at least some of it is learned.

A study, published in the April 2012 issue of the journal *Plos One*, tested this hypothesis in an experiment with an indigenous group in Papua New Guinea. The researchers included cognitive scientist Dr. Rafael Nunez of University of California at San Diego and his collaborators: student Dr Kensy Cooperrider and anthropologist Dr. Jurg Wassmann, an anthropologist at the University of Heidelberg.

The researchers conducted the study in the Finisterre Range of Papua New Guinea. The indigenous people in this region, known as the Yupno, are subsistence farmers, and number about 5000. The Yupno have little to no formal schooling. They have a native counting system, with precise number concepts and specific words for numbers greater than twenty. The researchers, however, did not find any evidence of measurement.

After confirming the Yupno participants' understanding of numbers with piles of oranges, the researchers asked Yupno adults to complete a task that has been used widely by researchers interested in the source of basic mathematical intuitions. This task was as follows: people were shown a line and asked to place numbers onto the line according to their size, with "1" going on the left endpoint and "10" (or sometimes "100" or "1000") going on the right endpoint. Since many in the study group were illiterate, Nunez and the researchers adapted the task using groups of one to ten dots, tones and spoken instructions, instead of written numbers. The experimental group consisted of fourteen adults with no schooling and six adults with some formal schooling. There was also a control group of participants in California for comparison.

that each morning, JARID1a reactivates the wake up cycle by countering the action of a brake protein that inhibits the action of CLOCK and BMAL1.

To support their findings about the clock's workings, the researchers studied genetically altered mice cells and fruit flies that lacked the JARID1a gene. They inserted JARID1a into the flies' DNA, which released the brake so the flies returned to a normal cycle. They treated mouse cells with a drug that mimics JARID1a, which allowed their biological clocks to operate normally. Their result has further been confirmed by genetic and pharmacogenetic approaches.

The biological clock also appears important to the development of disease, most likely due to its daily influence over metabolic cycles. The cellular mechanisms of diabetes are also tied to metabolic cycles controlled by the biological clock. Conversion of sugar into fat, which normally occurs only at certain times of day, often seems to occur all day long in diabetics' bodies, suggesting the clock has lost control. Similarly, with age the biological clock seems to decline, often causing older people to suffer from sleeping difficulty. There is also strong evidence that shift workers, such as nurses and emergency personnel, who work long shifts that break them out of the normal twenty-four hour cycle of waking and sleeping, are at much higher risk for certain diseases.

Due to this discovery, a whole new avenue opens up to explore sleep disorders and chronic diseases. Discovery of this mechanism by which JARID1a starts the clock everyday may help explain the genetic underpinnings of sleeplessness, aging and chronic illnesses, such as cancer and diabetes.

Circadian clock: time governing sleep and wake up in mammals
(Source: Science photo Library)

Contributed by Dr Prasanta K Dash, Pradeep K. Jain, Kishor Gaikwad and Rhitu Rai. Dr Prasanta K Dash (prasanta01@yahoo.com) is fellow of Howard Hughes Medical Institute and a scientist at NRC on Plant Biotechnology, Pusa Campus, New Delhi-110012. Drs. Pradeep K Jain, Kishor Gaikwad and Rhitu Rai are scientists at NRC on Plant Biotechnology.

Researchers found that unschooled Yupno adults placed numbers on the line using only the endpoints: putting small numbers on the left endpoint and the mid-size and large numbers on the right. In other words, they did not demonstrate the understanding of a number line – a serial arrangement of numbers with uniform magnitude difference. Like their native counting system, the study participants understood only a categorization of numbers as large or small. The Yupno study participants with some schooling used the concept more, but not to the extent of the control group.

"Our study shows, for the first time, that the number-line concept is not a 'universal intuition' but a particular cultural tool that requires training and education to master," Nunez said. "Also, we document that precise number concepts can exist independently of linear or other metric-driven spatial representations."

The study has important implications for mathematics education. Earlier, language was thought as an innate ability of human beings, but many studies have shown that human beings acquire language skills from their environment. Even more than language, mathematics is considered an innate ability, and often taught in a dogmatic way.

The Yupno people show an understanding of mathematics that is close to their native counting system. By considering the way that people acquire mathematical concepts from their society, education can serve to strengthen those concepts and ways of learning. This will ensure that people can readily apply mathematics learning to their everyday lives. A study of people's natural mathematical conceptions can also help shed light on how misconceptions in understanding arise.

Adapted from UCSD news release at http://ucsdnews.ucsd.edu/pressreleases/study_finds_twist_to_the_story_of_the_number_line/

Researcher confirming a Yupno participant's understanding of numbers
(Source: http://ucsdnews.ucsd.edu/pressreleases/study_finds_twist_to_the_story_of_the_number_line/)

RISING TEMPERATURES IMPACT MAJOR PEST OF RICE

Rice crop plaguing insects may struggle to survive in a warming climate, scientists from the University of Birmingham have found. The brown planthopper is the most serious rice pest across the world, widespread in tropical climates, and commonly devastates rice fields across Asia. The insects not only damage rice directly through feeding but by transmitting viruses, which stunt the growth of the crop.

During the study, the researchers exposed the insects to high temperatures to determine their upper thermal thresholds at which they become immobilised by heat stress and those that were fatal. Experiments were carried out on both young and adult brown planthoppers collected in Pilau Pinang in Malaysia, where the annual mean temperature is approximately 27.5 degrees Celsius (81.5 F).

Results from the study indicate that the brown planthopper is living at temperatures close to its upper thermal limits in parts of its current distribution. For that reason, climate warming in tropical regions and occasional extreme high temperatures are likely to become important limiting factors affecting the survival and distribution of the insect.

Aside from the lethal effects, the research shows that higher temperatures impact the insects' mobility meaning that the annual migratory behaviour could be affected. Professor Jeffrey Bale, Professor of Environmental Biology, at the University of Birmingham, said: "It seems that in most countries, summer high temperatures are lower than those that would kill brown planthoppers, but high enough to limit their mobility. We have a basis by which to identify rice-growing regions in Asia where the insect is likely to become more or less of a problem through future changes in climate. We are now researching whether insects, such as the brown planthopper, will be able to adapt and survive the further heat stress, and whether reproduction will still be possible."

LHC TEAM DISCOVERS NEW ELEMENTARY PARTICLE

Physicists Claude Amsler, Vincenzo Chiochia and Ernest Aguiló from the University of Zurich have detected for the first time a baryon denoted as Xi_b^*. This discovery comes as a prelude to the definitive confirmation (or lack thereof) of the elusive Higgs Boson.

The baryon family refers to particles that are made up of three quarks. Quarks form a group of six particles that differ in their mass and charge. The two lightest quarks, the so-called "up" and "down" quarks, form the two atomic components, namely protons and neutrons. All baryons that are composed of the three lightest quarks ("up," "down" and "strange" quarks) are known. Very few baryons with heavy quarks have been observed.

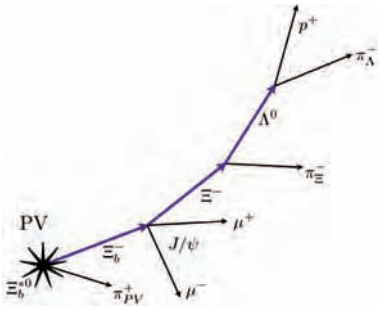
In the course of proton-proton collisions in the Large Hadron Collider (LHC) particle accelerator, physicists have managed to detect a baryon with one light and two heavy quarks. The particle Xi_b^* comprises one "up," one "strange" and one "bottom" quark (usb), is electrically neutral and has a spin of 1.5. Its mass is comparable to that of a lithium atom.

Very few baryons with heavy quarks have been detected directly, as they tend to be very unstable. Xi_b^* is no exception. As is now customary in particle physics research, conceptual strategies are used to overcome this challenge. Xi_b^* breaks up in a known cascade of decay products. Ernest Aguiló, a postdoctoral student from Professor Amsler's research group, identified traces of the decay products in the measurement data and was able to reconstruct the decay cascades starting from Xi_b^* decays.

The physicists' calculations are based on data from proton-proton collisions at energy of seven Tera electron volts (TeV) collected by the Compact Muon Solenoid (CMS) detector at the Council for Nuclear Research (CERN) between April and November 2011. A total of 21 Xi_b^* baryon decays were discovered, which was statistically sufficient to rule out a chance incident or a statistical artifact.

The discovery of baryon Xi_b^*confirms the theory of

Schematic showing how the excited neutral Xi-b baryon (bottom left) decays into other subatomic particles that could be detected (Source: http://www.msnbc.msn.com/id/47217745/ns/technology_and_science-science/t/super-collider-team-discovers-new-subatomic-particle/)



how quarks bind and therefore helps to understand the strong interaction, one of the four basic forces of physics theory about the structure of matter. The new discovery also means that two of the three baryons predicted by theory have now been observed.

Adapted from http://www.mediadesk.uzh.ch/articles/2012/uzh-forschende-entdecken-neues-teilchen-am-cern_en.html