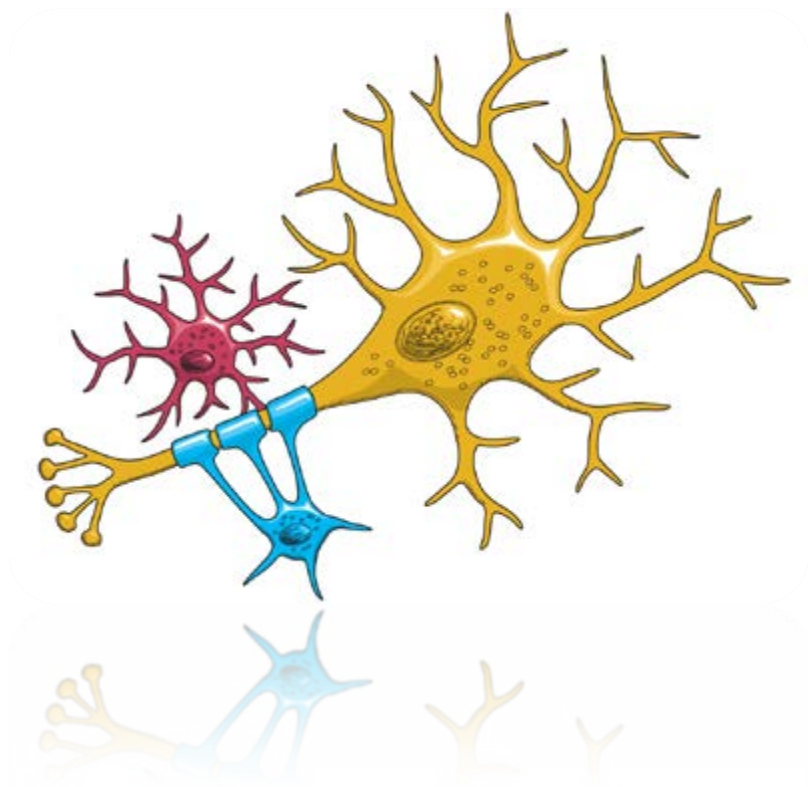


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Jerusalem, ISRAEL Ancient Roman Road

“Is it paved by the Lord”? Archaeologists in Jerusalem unearthed a part of ancient stone road stretched 26 feet (8 meters) across and was bound on either side by curbstones, said by the Israeli Antiquities Authority (IAA). This is a finely preserved section of the road, one of two imperial arteries that connected

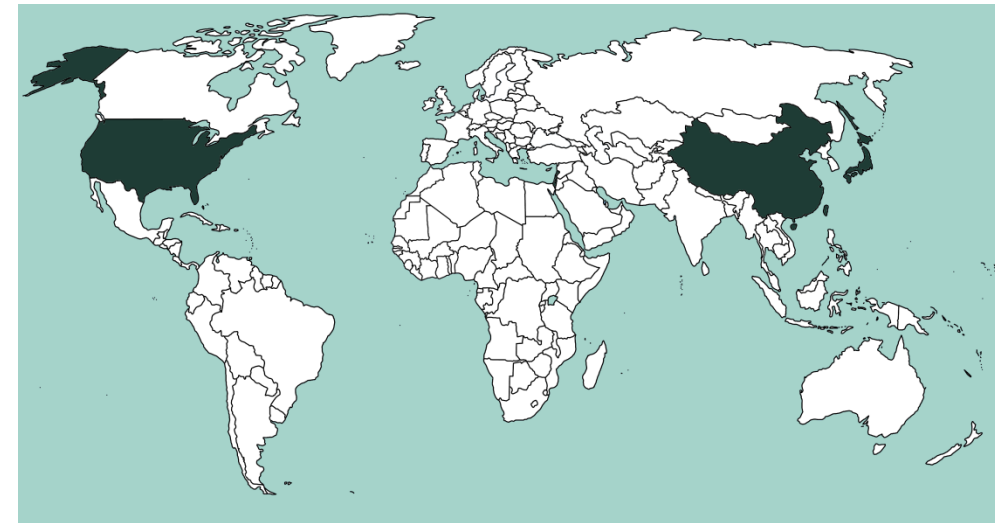


Jerusalem to the ancient coastal city of Jaffa, now part of Tel Aviv about 1,800 years ago. Israel, a God-loved country needs consider how to reserve the historic spots not for the nation itself, but for the world. ■

<http://www.livescience.com/37732-ancient-roman-road-exposed-in-jerusalem.html>

Tokyo, JAPAN Space Robot

Japan wants to be the first in space robot communication. Kirobo, named after "kibo" or hope in Japanese and "robot", is ready to be launched into space first, the Kirobo project aimed to have the space “man” speak with us on earth. In fact, it seems not



that difficult. Because Kirobo does not need to perform physical activities, it is smaller than most robots that go into space. Kirobo is about 34 centimeters tall and weighs about 1 kilogram. This talking space robot will be launched from the Tanega-shima Space Center, Japan on August 4, 2013. ■

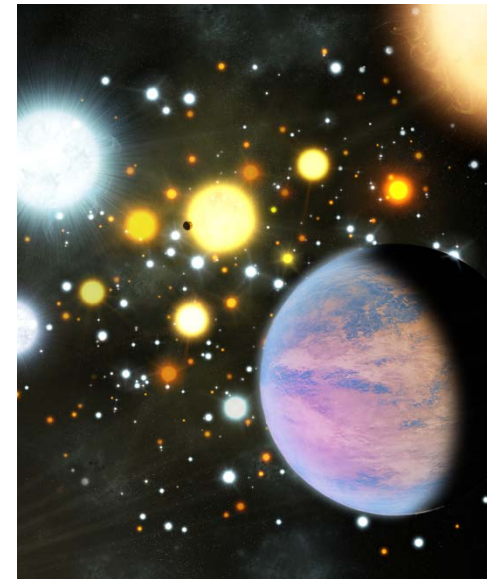
<https://twitter.com/auchikura>

Washington DC, USA Alien Planets

Astronomers using the planet-hunting Kepler spacecraft have found two planets circling different stars in the violent environment of an ancient open star cluster called NGC 6811 located about 3,300 light-years from Earth. The planets, Kepler-66b and Kepler-67b, are both smaller than the planets previously found in clusters. These types of planets could be just as commonly found orbiting stars in clusters as they are around other kinds of stars. These two planets are going around their stars over a time of 15 and 17 days respectively, and both the frequency and the properties in terms of size and orbital period

are consistent for these planets. It is possible for them to grow life there, but still need confirm. ■

<http://www.space.com/21729-mini-neptune-alien-planets-discovered.html>



Guangzhou, CHINA Do Not Be a Governor

It is so popular in China for college graduates to sit tests of Public Officials. Even it was considered as the only way to become rich and comfortable because it can give the tester successors chances to be a governor. However, some scholars like Yuanping Chen gave a

speech at Sun Yet-Sen University to the would-be graduates – college students should not only want to be a governor. In the



lecture, Dr. Chen said it is impossible for universities to produce governors; on the contrary, high schools should be the places

for talents and knowledge spreading. If universities become the machine of governors, that means it is really the time for the government to consider the education system. ■

<http://edu.163.com/13/0625/11/927AJDRA00294JA1.html>

Rehovot, ISRAEL Brain: Past and Future

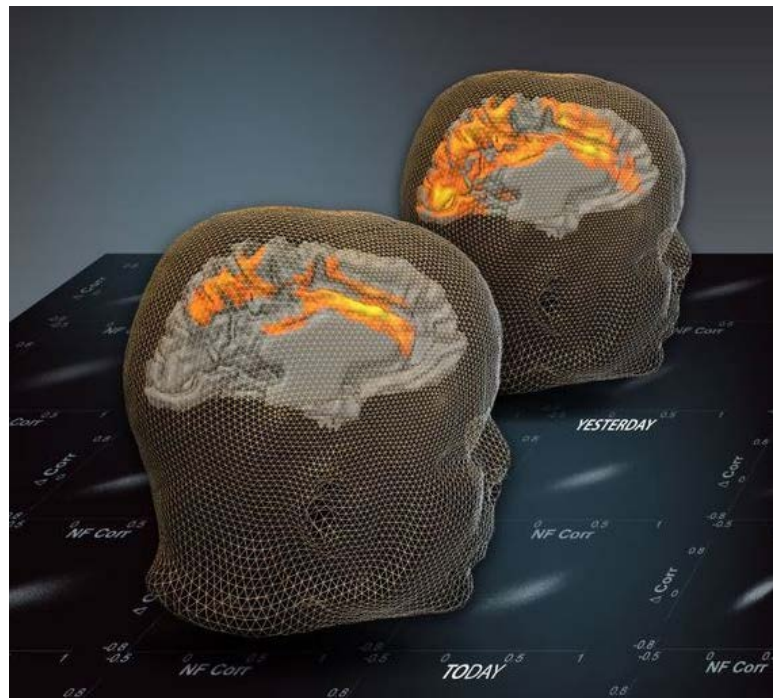
What will happen if scientists could one day be able to uncover your personal history and predict your future just by looking at your brain? It would be. Scientists from the Department of Neurobiology - Weizmann Institute of Science in Israel have recently discovered that the human brain bears the imprint of earlier events for at least 24 hours after the experience has taken place. They used our brainwaves to do all of these. Spontaneous brainwaves are easy to spot. The brainwaves are complex, but highly organized and symmetrical, and they always travel through the same part of the brain – the

outer layer or cortex. Functional magnetic resonance imaging (fMRI) scanner was used to monitor the subjects' brain activity. The researchers found that the experience of undergoing the training activity not only changed the resting brain-wave patterns right after it occurred, it actually strengthened new links between brain cells, even 24 hours later. Such alterations could display not only information about recent events but, if monitored over time, could also reveal a sort of personal profile of that person's brain. They also believe that such profiles would be especially useful in diagnosing or learning the brain pathologies associated with a wide array of cognitive disabilities. ■

<http://news.yahoo.com/brainwaves-reveal-past-might-predict-future-160530216.html>

New York, USA Bugs: the Real Sustainable Foods

Is it possible to eat insects as foods? Yes, even it sounds strange to the Western population, but the United Nations' Food and Agriculture Organization has weighed in favor of entomophagy, the practice of eating insects. Many Westerners



may react to the idea of bug-eating with disgust, whereas insects make up a part of the traditional diets of some 2 billion people, the report estimates. These include the larvae of the palm weevil, a type of beetle, in a number of tropical regions; mopane worms in southern Africa; yellow jacket wasp larvae in Japan; and grasshoppers known as chapulines in Oaxaca, Mexico. Good news is that a



company, Utah-based Chapul, has taken this approach and sells energy bars made of cricket flour. Humans aren't the only creatures who could stand to eat more insects. ■

<http://www.livescience.com/37816-eating-insects-helps-feed-hungry-world.html>



EVOLUTION

Carbon Isotope and Early Diets

In human evolution, diet has long been implicated as a driving force. Stable carbon isotope analysis is a relative newcomer to early hominin dietary studies. Carbon isotope studies of early hominins from southern Africa showed that their diets differed markedly from the diets of extant apes. Researchers from the United States of America, Kenya and United Kingdom presented their findings in the *Proceedings of the National Academy of Sciences of USA* that early hominin diet has changed since the first carbon isotope study of early hominins was published in 1990s. Isotopic and other lines of evidence are now the researchers to consider adding foods to early hominin menus that few people would have contemplated 15 years ago. The authors gave an example that a hominin that ate grass, or other

animals that ate grass, would have used the environment, interacted with the broader mammalian community, and weathered changing habitats in very different ways. Thus as the researchers concluded that hominin carbon isotope ratios increase with postcanine tooth area and mandibular cross-sectional area, which could indicate that these foods played a role in the evolution of australopith masticatory robusticity. - KH

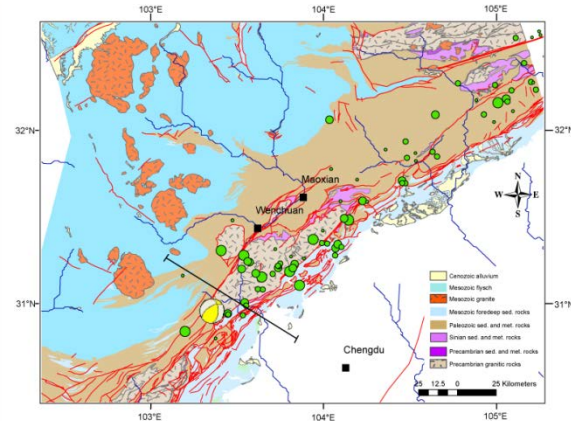
PNAS 2013; 110(26): 10513

GEOLOGY

Earth: Healing by Herself

Our earth, like us human, can heal herself after earthquake identical to the healing process of tissue injury. Reported by Sino-American scientists on 28 June 2013 in *Science* that a process of punctuated recovery exists as healing and damage interact in the aftermath of

a major earthquake through studying the fractures of the underground fault zone resulted from the 2008 Mw 7.9 Wenchuan earthquake in Sichuan, China. In their study, several wells were drilled in and around the fault zone to understand



the mechanics of the earthquake. The findings, although were not telling us the final question, at least in part evoked questions that we can and should focus on this area by which we can predict earthquake more accurately. - FW

Science 2013; 340(6140): 1555.

NEUROSCIENCE

LKB1-NUAK1 and Terminal Axon Branching

How to branch of the terminal axon plays an essential role in the formation of the functional neural circuits. The



studying group headed by Dr. Franck Polleux reported in their present publication in *Cell* that the kinases of LKB1 and NUAK1 are required for cortical axon branching *in vivo* through immobilizing mitochondria specifically at nascent presynaptic sites. This gives

at nascent presynaptic sites. This gives

hope to targeting on the kinases to regulate branching of axon that would benefit the patients with nerve injury or degenerative diseases. As the authors pointed out that Future investigations will determine how LKB1-NUAK1-regulates the capture of mitochondria to nascent presynaptic sites and how this capture regulates axon branching through control of ATP production and/or Ca²⁺ homeostasis or through other unknown mechanisms. – FW

Cell 2013; 153(7): 1510.

MEDICINE

Lithium and Suicide

Mood disorders are a leading cause of global disability and suicide. It is difficult to regulate the rate of suicide by medication. Studies showed that long term lithium reduced the risk of suicide in mood disorders compared with placebo or other drugs. However, the precise relationship between lithium and suicide is unknown. Dr Andrea Cipriani and colleagues pooled and analyzed the data related to the lithium treatment on sui-

cide, and found that lithium is an effective therapy for reducing the risk of suicide in people with mood disorders. It means that the clinical decision making will need to take a balanced view of the likely benefits and harm of lithium in the individual patient. – EE

BMJ 2013, 346: f3646.

BIOLOGY

Carotenoid and Oxygenic Photosynthesis

Carotenoids are critical cofactors for the photosynthetic process. Carotenoids achieve their functions through the electronic properties, which arise from their linear conjugated polyene chain. A group led by Dr. Bruno Robert from Université Paris Sud, France, determined the factors that underlie differences in the electronic properties of these carotenoid molecules. In addition, they tried to relate these differences to the 3-D structures of these proteins, as determined by X-ray crystallographic studies. For this the authors proposed a mechanism by which their



process, allowing for an optimization of the excitation energy cascade in these complex light-transducing structures. – FW

J Biol Chem 2013; 288(26): 18758.

PSYCHOLOGY

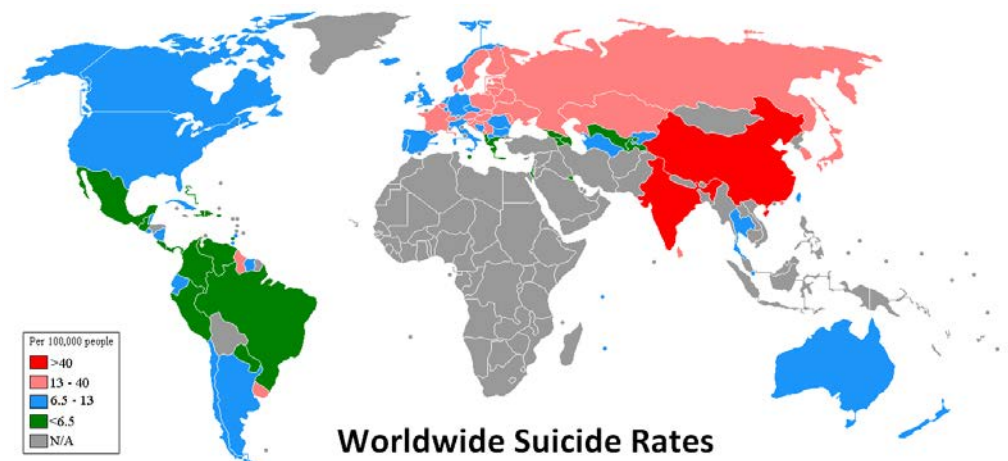
Risk Factors for School

Victims

School is the most important place for education, but school victim is unavoidable. Recent data showed an increase in

viewing bullying as a social process. In school, a notable minority of children and adolescents are affected by school bullying as targets of abuse by peers, which possesses negative effects on students learning and development. Dr. Silja Saarento from the University of Turku, Finland, reported student-, classroom-, and school-level risk factors for victimization. In their study, social anxiety and peer rejection at the student level, and negative social outcome expectations of defending the victim at the classroom level, and students perceived their teachers to have less disapproving attitudes toward bullying at the school level were found the risk factors for the victimization. The study gives hope in maximizing the effectiveness of the interventions and in enhancing the wellbeing of school-aged children and adolescents. – MPW

J School Psychol 2013; 51(3): 421.



Worldwide Suicide Rates

binding pockets may impose specific conformations on carotenoids to modulate their electronic structure and thus tune their absorption spectra. The meaning of this property may explain the recruitment of carotenoids with conjugated end cycles in the photosynthetic

Homeostatic Synaptic Plasticity: Balanced by COX2-PGE₂ System to a New Setpoint^{PC}

Xiaofeng Shen, * Hongmei Yuan, * Wei Wang, * Shiqin Xu, * Haibo Wu, * Xirong Guo, † Fuzhou Wang *^Δ

THE SETPOINT OF neural activity plays a critical role in maintaining the complex neural circuits into stable activities. Homeostatic synaptic plasticity is a major component of the setpoint theory that dynamically adjusts synaptic strengths. Cyclooxygenase 2 (COX 2) is rapidly upregulated in inflammatory episodes after nervous injury and its product prostaglandin E₂ (PGE₂) exerts contrast functions in the nervous system by working on the homeostatic plasticity. New data revealed that COX2-PGE₂ system takes an essential part in balancing excitation and inhibition of the synaptic activities at a new setpoint that finally is maintained by the homeostatic synaptic plasticity.

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NEURONS are functionally connected with each other to transmit excitatory or inhibitory information produced by internal or external stimulation, which is a crucial property endowed with the neural synaptic transmission. Activity-dependent enhancement or depression in the efficacy of synaptic communication has been proposed to play a critical role in the ability of modifying neural circuitry. Although such activity-associated refinement on synaptic connectivity initially defined as Hebbian assembly is of fundamental importance throughout the brain development, this plasticity tends to destabilize the activity of neural circuits through neuron-to-neuron activa-

tion in sequences. In fact, activity-dependent synaptic plasticity occurs physiologically where specific types of neural activity result in changes in neural excitability and synaptic efficacy. However, the so-called “setpoint” of neural activity kept through self-regulating by neurons plays an important role in maintaining the complex circuits into stable activity states in facing the destabilizing stimuli. Homeostatic synaptic plasticity is a major component of the setpoint theory that dynamically adjusts synaptic strengths in the correct direction to promote stability (1). Consistent with homeostatic regulation, excitatory synaptic transmission can be increased after neural activity deprivation in the

cultured hippocampal slices, and even leading the hippocampus to generate seizure-like activity (2). While such a consequence of epileptogenesis from homeostatic plasticity is unwanted, it somehow suggests that injury-induced epilepsy may be a state maintained by the homeostatic synaptic plasticity at a new setpoint.

Previous work has long recognized the function of inflammatory mediators in plasticity stability, and suggested they should be treated as neuromodulators in normal or/and injured brain. Cyclooxygenase 2 (COX 2), the inducible isoform of cyclooxygenase is rapidly upregulated in inflammatory episodes after nervous injury, of which consequently

leads to downstream prostaglandins (PGs) production functioning pathologically in promoting further nervous injury. Among the four PGs, PGE₂ exerts contrast functions in the nervous system because divergent results obtained in different types of context of nerve injury, during which either neurotoxic or neuroprotective role was observed depending on distinct downstream PG receptor signalings. These seem to be associated with an elevated regulation at a higher-than-normal level by the homeostatic plasticity. This link between PGE₂ and homeostatic synaptic plasticity was investigated by Koch et al. (3) using organotypic slices, in which a series of *in vitro* experiments indicated that PGE₂ reduces excitatory synaptic transmission and depresses network activity when applied acutely in neocortical slices, but long-term exposure to PGE₂ results in a hyperexcitable network state displaying paroxysmal depolarization shifts (PDSs), a result of a homeostatic response that may lead to epileptogenesis.

Organotypic slice preparations have been increasingly used for the study of synaptic plasticity, where the hippocampus is removed after 5 days of postnatal experience and subsequently develops in the total absence of sensory input. Nonetheless, acute slices are prepared from animals with over 2-week postnatal experience mainly because in which development occurred *in vivo* (4). When analyzing spontaneous synaptic activity, tetrodotoxin (TTX), a blocker of the sodium action potentials, is used to inhibit the occurrence of spontaneous action potentials, and thus generating data for all miniature currents, whether carried by glutamate (excitatory postsynaptic currents, mEPSCs) or GABA (inhibitory postsynaptic currents, mIPSCs). In some cases, bicuculline, a blocker of GABA_A re-

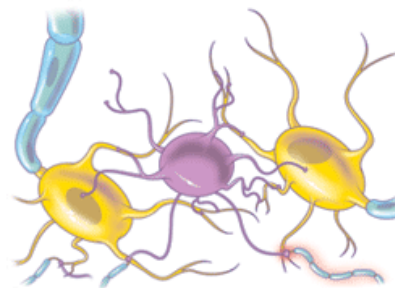
ceptors, is added to the TTX solution to block GABAergic activity, which finally allows a study of mEPSCs in isolation. Theoretically, changes in the amplitude of mEPSCs display a postsynaptic mechanism, but presynaptic effect can be explained with the changes in the frequency of mEPSCs.

Using acute and organotypic slices, Koch et al. (3) performed three parts of experiment to approve their hypothesis that traumatic brain injury leads to a homeostatic response that constitutes the first step in a process that will eventually result in seizures and epilepsy, during which COX2-PGE₂ system may be involved in the activity-dependent regulation on the homeostatic plasticity to excitable or inhibitable responses. First of all, acute effects of PGE₂ on synaptic electrophysiological patterns were tested when TTX was added 48 h to produce activity deprivation leading to increase in peak and mean amplitudes of PDSs and mEPSCs in organotypic preparations [Koch et al. (3), their Fig. 2 and 3], and then the effect of PGE₂ on extra potassium-induced network bursting activity was observed in acute and organotypic slices [Koch et al. (3), their Fig. 4 and 5]; subsequently, the authors found that PGE₂ decreased the amplitudes of excitatory postsynaptic potentials (EPSPs) and/or mEPSCs in both kinds of cultures [Koch et al. (3), their Fig. 6], leading the authors to suggest that PGE₂ postsynaptically inhibits excitatory synaptic transmission in acute and organotypic slices.

Following these observations, the authors then investigated the long-term effect of PGE₂ on PDSs' up state activity and mEPSCs in organotypic slices, and found PGE₂ exposure 48 h increased the amplitude of PDSs and the frequency of mEPSCs [Koch et al. (3), their Fig. 7 and 8]. This appears diverse compared with the acute effect of PGE₂ in that a mainly presynaptic effect was pro-

duced when the organotypic slices were exposed to PGE₂ in a relatively long-term duration. Then the authors examined the possibility that similar homeostatic mechanisms are involved in the PGE₂-induced synaptic plasticity through occlusion experiments by exposing organotypic slices to PGE₂+TTX up to 48 h. The combined exposure showed distinct forms of homeostatic plasticity expressed as the increase in amplitude and frequency of both the PDSs up state activity and mEPSCs [Koch et al. (3), their Fig. 9 and 10]. Finally, the authors determined the role of TTX or/and PGE₂ in apoptosis using immunofluorescence staining for active caspase-3, and found that chronic exposure of organotypic cultures to TTX or PGE₂ induced increased apoptosis [Koch et al. (3), their Fig. 11]. Together, these key findings led the authors to come to the conclusion that the hyperexcitable state together with the permanent changes associated with cell apoptosis may contribute to a change in the balance between inhibition and excitation that could eventually become permanently manifested in epileptic patients.

In the light of above interesting findings, Koch et al. (3) provided fundamental data through which a link between homeostatic synaptic plasticity and PGE₂ was established, while several concerns on experimental methodology should be acknowledged. Firstly, Koch et al. (3) used isoflurane as anesthetic to their animals. The reasons for putting this forward are as follows: 1) isoflurane possesses anti-epilepsy property; 2) isoflurane inhibits neuronal degeneration; 3) isoflurane inhibits presynaptic R-type calcium channel resulting in inhibition of synaptic transmission; 4) isoflurane enhances GABA_A receptor-dependent excitability, and suppresses glutamate-mediated excitatory currents (for review, see reference 5). Thus deep anesthesia with isoflurane before decapitation is similar to pre-



conditioning that might produce unwanted influence on synaptic plasticity especially in the immature brains used in this study. Secondly, the authors performed experiments using samples from male or female animals. Although sexual hormones might play no significant role in synaptic development at such an early period of the study animals investigated, it still cannot preclude the sex influence on impending *in vitro* study on synaptic electrophysiology because gender difference exists in synaptic density (6) and it is remarkably similar between the *in vitro* and the *in vivo* development of synapses which largely independent of environment when comparing acute slices with organotypic ones (4).

Determining the mediators of homeostatic synaptic plasticity is of great interest. As Koch et al. (3) presented that acute exposure of PGE₂ reduced electrophysiological activity postsynaptically, but long-term stimulation with PGE₂ increased presynaptic plasticity. However, the homeostatic plasticity of the nervous system is such complex that the whole molecular or cellular events involved in this process cannot be figured out totally. Synaptic connectivity is a complex network forming through neuron-to-neuron, astrocyte-to-neuron, microglia-to-neuron and neuron-to-effector organs, and the homeostatic plasticity occurs among these patterns of synapse. Although Koch et al. (3) provided evidence of pre- or/and postsynaptic plasticity after PGE₂ exposure, they did not present any clue that which kind of synapses were involved in this process. Additionally, the effect of PGE₂ on synaptic plasticity, in fact, is an integrative result detected with experimental means, of which may result from the combined influence of afferent neurons, astrocytes, microglia and inhibitory interneurons (Figure 1). Of the four subtypes of PGE₂ receptor, EP₃ was found to be involved in the regulation of PGE₂-associated synaptic plasticity in acute slices (3). Nonetheless, what about the downstream signaling pathways related with EP₃-Gi activation is not defined by Koch et

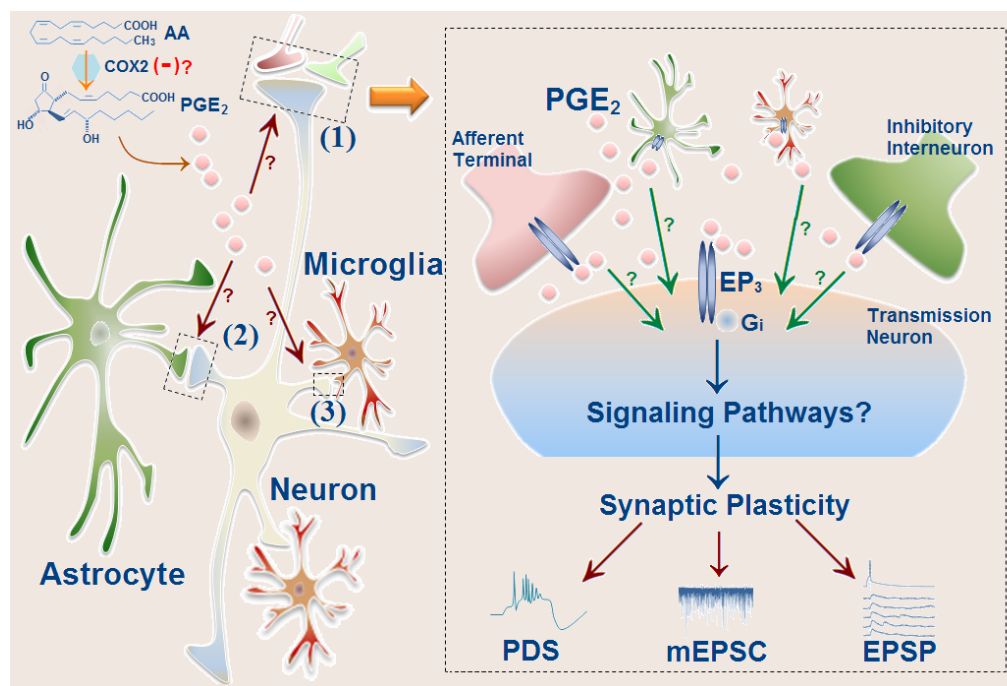


Figure 1. Schematic of COX2-PGE₂ system in neural synaptic plasticity.

Arachidonic acid (AA) is converted to prostaglandin E₂ (PGE₂) by cyclooxygenase 2 (COX2) physiologically, and pathologically increased after nervous injury evoked by following inflammatory responses, and the secreted PGE₂ involves in the regulation of synaptic plasticity at sites of neuron-to-neuron (1), astrocyte-to-neuron (2), and microglia-to-neuron (3) connections. On micrographic display at neuron-to-neuron synapse, PGE₂ exerts function through binding to its subtype receptor EP₃, one type of G protein coupled receptor, lying within the membrane of afferent terminal, inhibitory interneuron, transmission neuron, astrocyte and microglial cell, which results in activation of unknown downstream signaling pathways and, finally displays with synaptic plasticity including changes in paroxysmal depolarization shift (PDS), miniature excitatory postsynaptic current (mEPSC) and/or excitatory postsynaptic potential (EPSP). In the light of role for PGE₂ in synaptic plasticity, the upstream enzyme COX2 possesses therapeutic potential by using corresponding inhibitors. Question mark (?) refers to untested or uncertain effects as indicated.

al. (3) and needs to be guaranteed by further studies (Figure 1).

Although the study from Koch et al. (3) suggests a therapeutic potential for PGE₂ in epileptic patients, dissatisfactory results reported when the PGE₂ upstream enzyme COX2 was focused on as therapeutic target (7). Therefore, the data from Koch et al. (3), on another side, may reveal a role for COX2-PGE₂ system in balancing excitation and inhibition of the synaptic activities at a new setpoint that finally is maintained by the homeostatic synaptic plasticity. ■

Acknowledgements

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Conflict of Interests

None

References

1. Turrigiano GG, Nelson SB. Homeostatic plasticity in the developing nervous system. *Nat Rev Neurosci* 2004; 5: 97-107.
2. Trasande CA, Ramirez JM. Activity deprivation leads to seizures in hippocampal slice cultures: is epilepsy the consequence of homeostatic plasticity? *J Clin Neurophysiol* 2007; 24: 154-64.
3. Koch H, Huh SE, Elsen FP, Carroll MS, Hodge RD, Bedogni F, Turner MS, Hevner RF, Ramirez JM. Prostaglandin E₂-induced synaptic plasticity in neocortical networks of organotypic slice cultures. *J Neurosci* 2010; 30: 11678-87.

4. De Simoni A, Griesinger CB, Edwards FA. Development of rat CA1 neurones in acute versus organotypic slices: role of experience in synaptic morphology and activity. *J Physiol* 2003; 550: 135-47.
5. Larsen M, Langmoen IA. The effect of volatile anaesthetics on synaptic release and uptake of glutamate. *Toxicol Lett* 1998; 100-101: 59-64.
6. Alonso-Nanclares L, Gonzalez-Soriano J, Rodriguez JR, DeFelipe J. Gender differences in human cortical synaptic density. *Proc Natl Acad Sci USA* 2008; 105: 14615-9.
7. Holtman L, van Vliet EA, Edelbroek PM, Aronica E, Gorter JA. Cox-2 inhibition can lead to adverse effects in a rat model for temporal lobe epilepsy. *Epilepsy Res* 2010; 91: 49-56.

Paper Discussed in This Journal Club

Koch H, Huh SE, Elsen FP, Carroll MS, Hodge RD, Bedogni F, Turner MS, Hevner RF, Ramirez JM. Prostaglandin E₂-induced synaptic plasticity in neocortical networks of organotypic slice cultures. *J Neurosci* 2010; 30:11678-87.

PICTURE STATION



By **Frei Cristovao de Lisboa** in the 17th Century (1625-1631), Brazil. He draws birds, mammals and plants while he was in Brazil as a missionary. The original drawings, in pencil and covered in ink, are part of a manuscript "Historia dos animais e árvores de Maranhao" that is kept in an archive in Portugal. This is a Yellow-rumped Cacique, *Cacicus Cela* (a passerine bird) and a *Crimson-crested Woodpecker* (*Campephilus Melanoleucos*).