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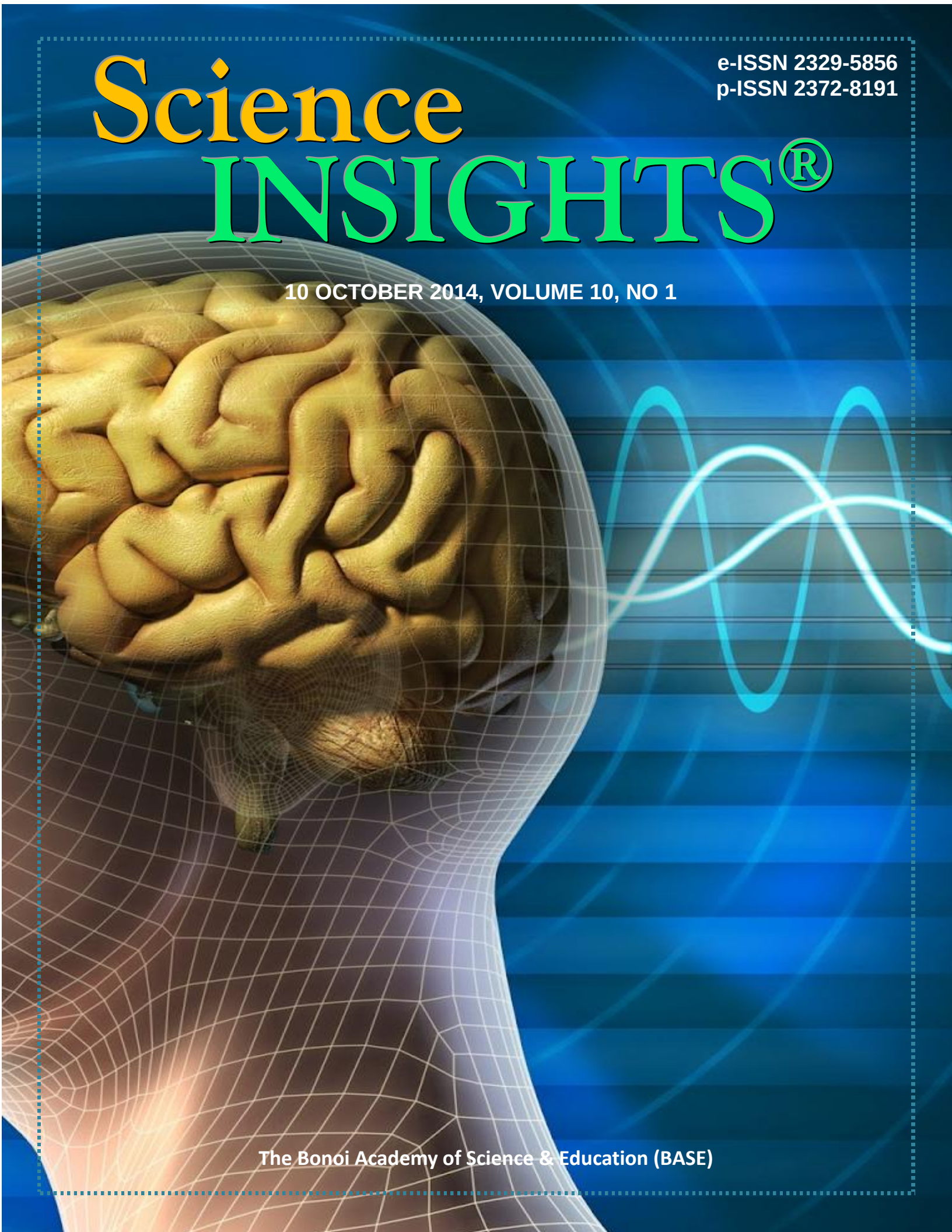

The Bonoi Academy of Science & Education (BASE)


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The Official Journal of The Bonoi Academy of Science & Education (BASE)

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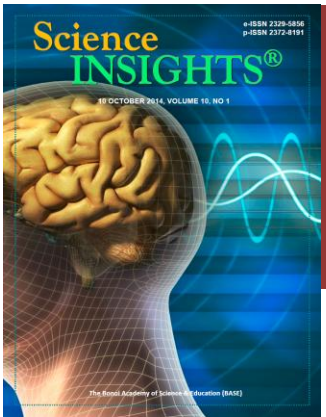


**COVER**
The pontile GABA signaling plays an essential role in sevoflurane-induced adulthood cognition impairment, and further evaluation is needed on the exact interaction among sevoflurane, GABA, glutamate, receptors, corresponding signaling mediators, and cognition alteration in the pontine region. See page 273.
*Image: BASE illustrating group*

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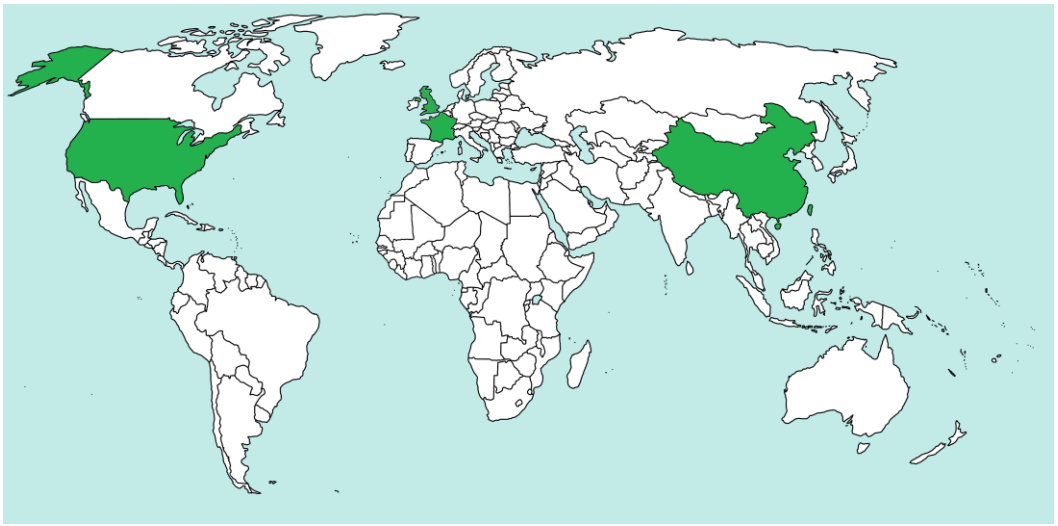

## Leicester, UK

## Ancient Skeletons Found Holding Hands in England

Archaeologists from the University of Leicester, UK, uncovered remains of two skeletons holding hands believed to have been resting that way for at least 700 years. The archaeologists, who said there are likely to be more skeletons in the ground, were not certain why the people were buried there rather than in the main church in the village. They said it was possibly a special place of burial for pilgrims. Among the other skeletons was an older male apparently killed by a sharp implement, such as a pole axe, to the head, according to Vicki Score, project manager for University of Leicester Archaeological Services. A young male was buried in a pit with his legs raised to his chest, which archaeologists said was possibly the result of a disease, she said.■

## Paris, FRANCE

## Close-Up Look at A Comet

Ten years ago the European Space Agency launched Rosetta, a first-of-its-kind spacecraft on a mission to meet a comet. It finally accomplished that goal earlier this month — getting into the comet's orbit. But it's not done yet. This November, Rosetta will deploy a small probe that, if successful, will land on the comet — the first time we've ever made contact with a comet (intentionally). Before Rosetta, we knew comet 67P/Churyumov-Gerasimenko as just a speck of light — as we do most comets. It's hard to really see what a comet is like because comets are extremely small. But as soon as Rosetta reached the space rock, it started snapping pictures of the comet, unveiling for the first time the ominously alien, mountainous world, the likes of which humans have never seen before. Part of the Rosetta craft with the dumbbell-shaped comet in the background. Rosetta will continue to lower its orbit ever closer to the comet until it is about one kilometer, less than a mile, away from the surface of the space rock. And that's when it will dispatch a tiny lander, named Philae. Rosetta is getting closer by the day to the surface of the comet. This image was taken just 38 miles from the surface — you can clearly see the jagged cliffs and boulders of the dumbbell-shaped comet. Another close up, taken Sunday, was shot about 19 miles from comet 67P/Churyumov-Gerasimenko. Scientists were surprised they found no traces of water ice on the comet's black-as-coal surface. The comet only looks grey because of the intense blackness of space behind it.■

## Boston, USA

## Fluid Mechanics Suggests Alternative to Quantum Orthodoxy

The central mystery of quantum mechanics is that small chunks of matter sometimes seem to behave like particles, sometimes like waves. For most of the past century, the prevailing explanation of this conundrum has been what's called

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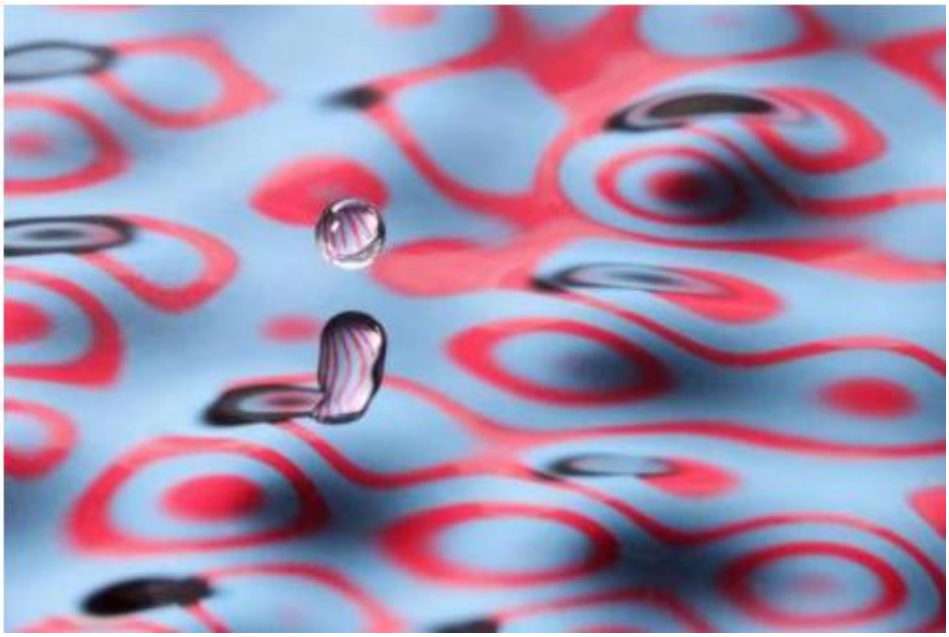


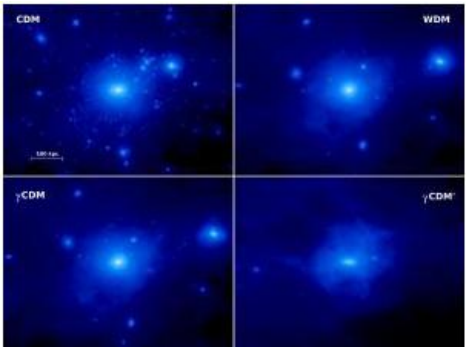
the "Copenhagen interpretation"—which holds that, in some sense, a single particle really is a wave, smeared out across the universe, that collapses into a determinate location only when observed. But some founders of quantum physics—notably Louis de Broglie—championed an alternative interpretation, known as "pilot-wave theory," which posits that quantum particles are borne along on some type of wave. According to pilot-wave theory, the particles have definite trajectories, but because of the pilot wave's influence, they still exhibit wavelike statistics. John Bush, a professor of applied mathematics at MIT, believes that pilot-wave theory deserves a second look. That's because Yves Couder, Emmanuel Fort, and colleagues at the University of Paris Diderot have recently discovered a macroscopic pilot-wave system whose statistical behavior, in certain circumstances, recalls that of quantum systems. Couder and Fort's system consists of a bath of fluid vibrating at a rate just below the threshold at which waves would start to form on its surface. A droplet of the same fluid is released above the bath; where it strikes the surface, it causes waves to radiate outward. The droplet then begins moving across the bath, propelled by the very waves it creates.

"This system is undoubtedly quantitatively different from quantum mechanics," Bush says. "It's also qualitatively different: There are some features of quantum mechanics that we can't capture, some features of this system that we know aren't present in quantum mechanics. But are they philosophically distinct?"■

## Durham, UK

## Modified Theory of Dark Matter

Dark matter is an aspect of the universe we still don't fully understand. We have lots of evidence pointing to its existence (as I outlined in a series of posts a while back), and the best evidence we have points toward a specific type of matter known as cold dark matter (CDM). One big downside is that we have yet to find any direct detection of dark matter particles. In fact, many of the likely candidates for dark matter have been all but eliminated. Another is that cold dark matter doesn't agree with our observations of dwarf galaxies. Now a new paper presents a solution to the second problem that might even help with the first. The main problem with dwarf galaxies is that there are fewer of them around spiral galaxies than dark matter predicts. When we do dark matter computer simulations, the results always have more dwarf galaxies than we observe. This has been taken to mean that either the simulations are somehow flawed, or dark matter isn't the complete solution we've thought. This new work looks at a modified version of dark matter, and how it affects these kinds of computer simulations. Normally, it is assumed that dark matter doesn't interact with light directly at all. This means we can see its gravitational effects, but we don't see anything such as absorption lines and the like, which we observe with regular matter. The reason for this is that dark matter makes up the majority of matter in the universe. About 90% of the mass in our own Milky Way consists of dark matter. If it interacted much with light, then we would have seen its effects on light by now. This new work proposes that dark matter does interact with light, but only very, very slightly. Now you might think that if dark matter interacts so slightly with light that we don't see its effect, then it certainly can't differ that much from standard dark matter, but the team showed that this very small effect can build up over time, so that modern galaxies have fewer dwarf satellites, just as we observe. You can see this in the image above. The top left image is standard dark matter model, with too many satellite dwarf galaxies. The top right is a warm dark matter model that solves the dwarf galaxy problem but doesn't agree with other observations. The bottom left is this new,



light interacting dark matter model, and the bottom right is what happens when you make the light interaction too strong and get no dwarf galaxies. So by modifying dark matter to include slight interactions with light, the predictions match dwarf galaxy observations. It should be noted that just because this modification works, that doesn't mean it is the solution. Tweak theories are weak theories, as I've said before. This type of dark matter could also affect other things such as large scale structure, and this would need to be studied before we could be confident about this particular model. But the work does show that dark matter models can address some of the known problems with dark matter.■ Read more at: http://phys.org/news/2014-09-theory-dark.html#jCp

## Shenyang, CHINA

## Ancient 'Dragon' Beast Flew Right Out Of 'Avatar'

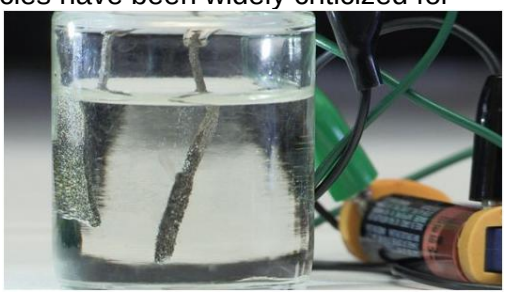
A sprawling ancient flying reptile looked so much like a dragon that could have flown alongside the aerial predators called "ikran" in the film "Avatar" that its discoverers named the newfound beast after these mountain banshees. The pterosaur, now called *Ikrandraco avatar*, may have stored food in a throat pouch like a pelican does, the researchers said. Pterosaurs were the first vertebrates to flap wings to fly. Before pterosaurs went extinct in the catastrophic impact that also ended the Age of Dinosaurs, they were the biggest animals that ever flew, with wingspans measuring up to 39 feet. Scientists investigated two partial skeletons of *Ikrandraco* dating back about 120 million years ago to the Early Cretaceous Period. They unearthed these fossils in arid hills in northeastern China's Liaoning province, which has become famous for the trove of feathered dinosaurs unearthed there over the last decade. Back when this reptile was alive, the area where it was found

was a large freshwater lake with a warm climate that was home to many kinds of animals, such as fish, frogs, turtles, other pterosaurs, feathered dinosaurs, birds and mammals, as well as many plants, such as ferns, conifers, gingkos, cycads and some flowering plants. The pterosaur was about 2.3 feet long and had a wingspan of about 4.9 feet. It had an elongated skull and a unique crest or bladelike bulge of bone on the tip of its lower jaw. The head of this newfound pterosaur is different from that of any other known pterosaurs, "but similar to [the head on] a flying creature, 'ikran,' in the movie 'Avatar,'" said lead study author Xiaolin Wang, a vertebrate paleontologist at the Institute of Vertebrate Paleontology and Paleoanthropology at the Chinese Academy of Sciences in Beijing. The back of Ikrandraco's jaw crest had a little hooklike structure. The researchers suggested this notch may have served as an anchor for soft tissue, and they proposed that *Ikrandraco* had a throat pouch like the one a pelican uses to store food. The researchers said that *Ikrandraco* might have sometimes foraged for food by hovering over water and scooping up prey near the surface. However, *Ikrandraco* is larger than modern skimming birds, so it may not have skimmed regularly, instead usually standing in shallow water to hunt, Wang said. The researchers plan to conduct experiments to see whether *Ikrandraco*'s jaw crest might have supported a throat pouch.■

## Stanford, USA

## Scientists Create Water Splitter That Runs on a Single AAA Battery

A new emissions-free device created by scientists at Stanford University uses an ordinary 1.5-volt battery to split water into hydrogen and oxygen at room temperature, potentially providing a low-cost method to power fuel cells in zero-emissions vehicles and buildings. The water splitter is made from the relatively cheap and abundant metals nickel and iron. It works by sending an electric current from a single-cell AAA battery through two electrodes. "This is the first time anyone has used non-precious metal catalysts to split water at a voltage that low," chemistry professor and lead researcher Hongjie Dai says. "It's quite remarkable, because normally you need expensive metals like platinum or iridium to achieve that voltage." The technology has huge potential as a source for powering hydrogen fuel cells, long held as a likely successor to gasoline. Unlike gasoline combustion, which emits large quantities of the greenhouse gas carbon dioxide, fuel cells combine stored hydrogen gas with oxygen from the air to produce electricity, leaving only water as a byproduct. Fuel cell vehicles have been around since the 1960s, albeit mostly as research projects and demonstration cars and buses. But we may soon see them in commercial production, with Toyota and Honda both committed to selling fuel cell cars in 2015 and Hyundai already leasing fuel cell vehicles in Southern California. Fuel cell vehicles have been widely criticized for



their high cost, the lack of infrastructure around their fuel delivery, and their low energy efficiency after accounting for the effort it takes to produce compressed hydrogen (often involving large industrial plants that use an energy-intensive process that combines steam and natural gas). But the new Stanford research, which latches onto a previously unknown method for splitting water, could help account for all these issues. "It's been a constant pursuit for decades to make low-cost electrocatalysts with high activity and long durability," Dai explains. "When we found out that a nickel-based catalyst is as effective as platinum, it came as a complete surprise." The nickel-metal/nickel-oxide catalyst, discovered by Stanford graduate student Ming Gong, also requires significantly lower voltages to split water when compared to pure nickel or pure nickel oxide. This new technique is not quite ready for commercial production, though. "The electrodes are fairly stable, but they do slowly decay over time," Gong says. "The current device would probably run for days, but weeks or months would be preferable. That goal is achievable based on my most recent results." The next step is to improve that decay rate and to test a version that runs on electricity produced by solar energy instead of the AAA battery. The researchers believe that their water splitter could save hydrogen producers billions of dollars, and the electrolytic device could be used to make chlorine gas and sodium hydroxide as well as hydrogen fuel cells.■

## College Station, USA
## Msida, MALTA
## Aix-en-Provence, FRANCE
## Oldest Shipwreck in the Mediterranean Discovered Near Malta

Dr. Timmy Gambin with the GROplan Project and researchers from France, the United States, and Malta announced the discovery of the oldest shipwreck in the Mediterranean that has been found to date. The discovery was announced in the Times of Malta on Aug. 25, 2014. The exact location of the vessel will not be released until all of the ship and its contents have been recovered. This measure is necessary to prevent theft of ancient artifacts for sale to individual collectors. To date the archaeologists and anthropologists have recovered 20 lava grinding stones that weigh about 77 pounds each and 50 wine storage vessels called amphorae. The ship is located roughly one mile off Gozo Island. The artifacts date to 700 B.C.E. and are thought to be Phoenician. The scientists estimate that the ship was possibly 50 feet in length. The wreck is about 400 feet deep. The cargo indicates the ship was sailing from Sicily to Malta when it sank. The Phoenician civilization was one of the first that was dependent on trade. The Phoenicians developed the galley and the two decked bireme. The Phoenicians are credited with developing the first known alphabet. The Phoenician civilization lasted from 1550 B.C.E. to 300 B.C.E. The Phoenicians are considered to have a Canaanite origin. The civilization was conquered by the Persians and then by the Greeks. Tyre and Lebanon are considered to be the centers of Phoenician civilization. The Phoenicians are documented to have sailed from the coast of Lebanon to the Pillars of Hercules. Ancient texts including Egyptian, Greek, and the Hebrew Bible reference the Phoenicians as a thriving trade culture that existed as city-states. The ship may be the oldest and most complete Phoenician ship ever recovered.■

## Washington DC, USA
## Hypersonic Weapon Detonated After Lift-Off: US Military

The US military had to detonate a hypersonic weapon seconds after lift-off Monday due to a technical problem, cutting short a flight test for the experimental project, officials said. "Less than four seconds into the lift-off phase, we terminated the flight," Pentagon spokeswoman Maureen Schumann said. The decision to abort the flight test in Alaska was due to a technological "anomaly," she said, without providing more details. The launch of the "Advanced Hypersonic Weapon" occurred after 4 am local time at the Kodiak Launch Complex in Alaska, Pentagon officials said. The weapon is part of the Pentagon's "prompt global strike" program designed to build conventional weapons that could take out targets anywhere on the planet within an hour's notice. "Due to an anomaly, the test was terminated near the launch pad shortly after lift-off to ensure public safety," the Pentagon said in a statement. There were no injuries in the incident, it said, adding that officials are conducting an "extensive investigation" to determine what went wrong.■

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# Call for Subcommittee Members

The Bonoi Academy of Science & Education (BASE) is composed of 20 different scientific and educational divisions. All these divisions are consisted of Director, Co-Director, Standing Committee, and Office Members. Some of the divisions are enrolling above positions. If you are interested in science or education work and if you think that is of great value for your career development, please send us your application asap. Given the BASE is a non-profitable organization, these positions then are also non-profitable, the BASE is not responsible for the salary or any other benefits. If you are approved as a member of one of the subcommittees, you automatically become a member of the BASE, which means you do not need to pay for the membership fees during the term. Of course, you are also eligible for applying for the BASE awards and funding, and also suitable for the member benefits. Come on with us to spread science knowledge to the far corner of the world by education.

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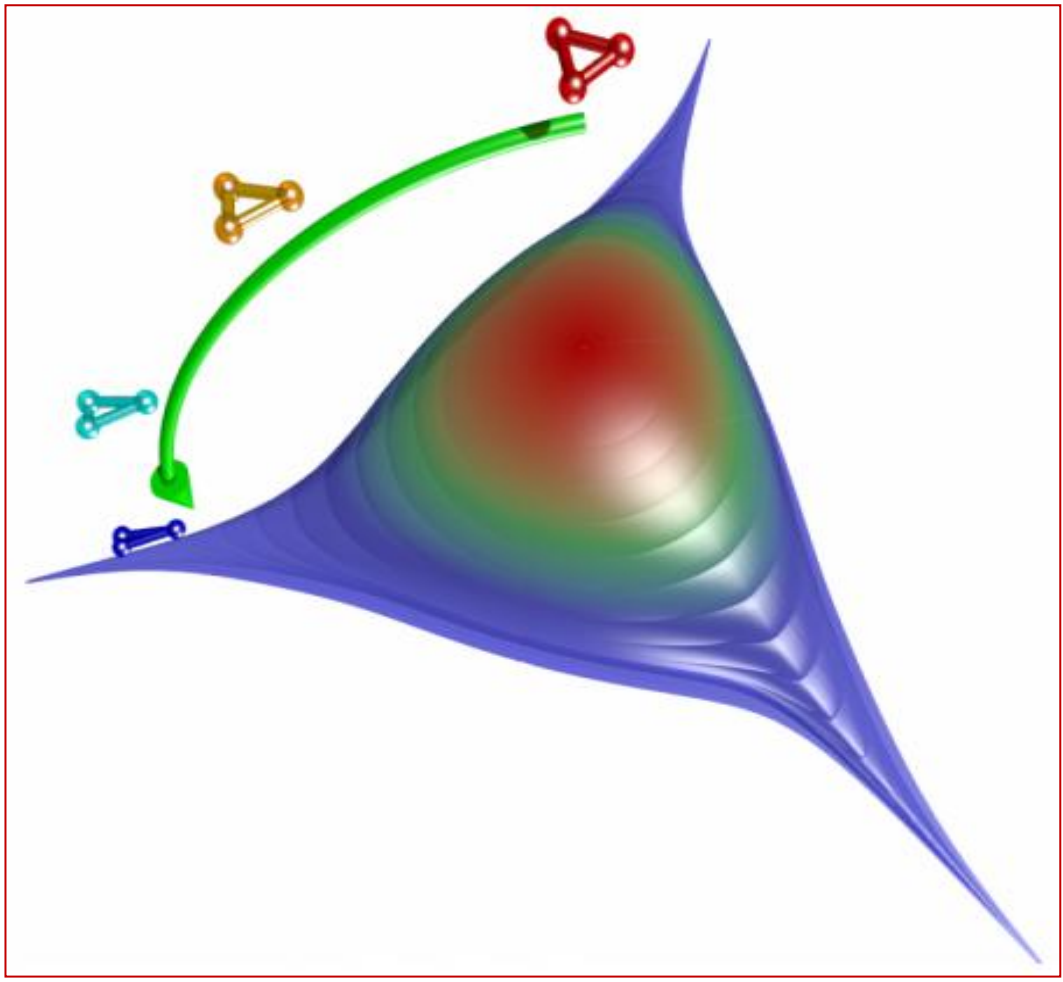
## PHYSICS

## Removes Outcome Unpredictability of Ultracold Atomic Reactions



Findings from a physics study by a Kansas State University researcher are helping scientists accurately predict the once unpredictable. Yujun Wang, research associate with the James R. Macdonald Laboratory at Kansas State University, and Paul Julienne at the University of Maryland, looked at theoretically predicting and understanding chemical reactions that involve three atoms at ultracold temperatures. Their findings help explain the likely outcome of a chemical reaction and shed new light on mysterious quantum states. The scientific journal *Nature Physics* recently published their findings in the article "Universal van der Waals Physics for Three Cold Atoms near Feshbach Resonances." In the theoretical study, Wang and Julienne developed a robust yet simple model that successfully predicts what happens in atomic reactions at ultracold temperatures. Their model, which is considered the best available, accounts for spin physics of the atoms as well as the van der Waals force—the attractive long-range forces between the forming molecules. "For a long time there has been the belief that this kind of reaction in three or more particles is too difficult to predict because the interaction is so complicated," Wang said. "Now, this research has shown consistent observations that indicate and imply that theoretical prediction is possible." These findings can guide research in chemical engineering, molecular physics and other fields because the model gives scientists a largely accurate idea of how the atoms will bind to form a molecule, Wang said. Additionally, their work may help scientists understand the Efimov effect. The Efimov effect, which was first predicted in the early 1970s, is what happens when two atoms that normally repel each other become loosely bound when a third atom is introduced. The result is three atoms that all stick together despite trying to repel each other—a reaction that defies conventional knowledge. "It's a very bizarre mechanical phenomenon in quantum mechanics that cannot be understood using the classical model of physics," Wang said. "The details of the Efimov effect are seemingly random and therefore complicated to study. But, because we showed that our atomic model and calculations can pretty accurately predict the position of such molecular states, we have new knowledge that may help us bypass those old barriers."■

**Nature Physics 2014; DOI: 10.1038/nphys3071**

## GEOPHYSICS

## World's Tectonic Plate Movement Mapped

A group of geophysicists is testing the hypothesis that the rate of "supercontinent assembly"—or tectonic plate movement—changes over time. Study co-author Professor Sergei Pisarevskiy says plate tectonics is the study of the horizontal movement of tectonic plates over the Earth's surface. "This is not uniform movement," he says. "Sometimes there are periods where there was very quick movement all together globally, and some-


times very slow movements. "We try to analyse that and to populate the mean angular velocity of the average plate movements on the surface of the earth." He has come to the tentative conclusion that the average rate of tectonic plate movement does change. "Right now for example it's slower than it was half a billion years ago—but approximately the same as it was one and a half billion years ago," he says. "But there are many problems to be resolved before the final answer. "It's sort of half guessing I would say at this stage." He says beside the uneven level of the same analysis in different countries, he and lead author Kent Condie are addressing various other problems. One is the inconsistent rate at which plates appear to move, both individually and relative to each other. "For example Africa moved very slowly for the last few hundred million years, on the other hand India as you probably know moved very fast," he says. "When you calculate the average movement of the continents of the earth you cannot just average the movement, the speed of a continent like Africa and some very small block like Madagascar for example. "They must be weighted, so we normalise the speeds by the area of that particular continental block." "When talking about the average speed, we also found some quieter periods, not exactly the periodicity but some maximums and minimums." Another problem is the way in which evidence tends to deteriorate over time with more recent "overprints" creating statistical "noise". "The older the rocks, the less information you will have," he says. "This noise increases—going back in time it's more difficult to extract this information." They are also contending with the phenomena of "passive margins" between plates. One of these is thought to exist beneath the ocean south of Australia—it shows little or no movement for at least a billion years. "There are no major tectonisms here or seismicity, it's just accumulations of sediments mostly," he says.■

**Precambrian Research 2014;**
**DOI:**
**10.1016/j.precamres.2014.07.015**


Who feeds us?


When you face the eruption
Do you feel the ending of the world?

# “God” and “Angel” in Photograph of Clouds over Cape Coral, Florida

**By Fiona Finn (2014)**

Definitely, this is an awesome picture but is it really a message from heaven? Is this striking image of majestic man wearing robes God? You be the judge. The cloud above was spotted in Cape Coral, Florida by my boss on his way home from work. And what was immediately obvious was the fact that this cloud was shaped in the image of the Lord. Also look to the far right and you'll see another cloud that looks like an angel with a trumpet in hand. Maybe it's the angel Gabriel blowing a trumpet blast to indicate the Lord's return to Earth, or maybe not...I realize that some may see this as a sign, an act of God if you will. There will be others, those who will doubt. And that's okay. But one thing's for sure, and that's how remarkably clear this image in the sky really is. Believe it or not, God is said to work in mysterious ways. Regardless of your belief system, it's your God-given right to judge this photo for yourself, isn't it? So, I ask you is the image above just a group of cumulus clouds? Or are those noticeable clouds with clearly defined edges the Almighty himself? Still, no matter the answer, lots of us will continue to look to the sky, searching for life's deeper meaning. Or are we searching in vain, deluding ourselves while involving our senses that random images are actually miracles or signs from above? Why do we look to the skies above in relation to God? Sure, as children we stare at the sky and see shapes appear in the swirling clouds but as adults some of us look upwards reaching for a higher power. Are we waiting for signs? Or proof of God? I for one was blown away by this photo and yes, I believe it's a real snapshot of God in the clouds. Although personally, I'll admit it is hard to digest this image as I am living a hell-on-earth type of life, wishing daily that I didn't feel so hollow, so broken. I was raised a Catholic, so sure I believe in God -- but lately, I have to wonder how much he really believes in me, or my family. God only knows why I was one of the first to see this photo. And since I believe that he made me human, I believe he won't condemn me when I behave like one. That said I've spent my fair share of time blaming him for my actions and inactions. Yes sir, I've projected my fears, insecurities, and failures onto Him. Blaming God has been easier than blaming myself. Okay, I'm sure you're thinking that's not the typical reaction of someone who just seen God manifest himself in the clouds. But God forbid in these turbulent times anyone of us gets real? You know raw, I have -- by opening up my life, my struggles, and my insecurities with my story. Although, I still struggle with what I'm doing here on this planet and why there's so much unfairness and evil in this world. Still, I do see this picture as proof that God is speaking to all of us. So who among us is willing to listen? Please share your opinions below. I'd love to hear them. Follow Finn’s Twitter Twitter@fionaburkefinn.■


Working like a worker bee?
Relax yourself.....

# Inhibition of Pontine CaMKII Alleviates Sevoflurane-Induced Long-Term Memory Impairment in Rats

Yusheng Liu*, Wei Wang*Δ

**SUMMARY** General anesthesia-associated cognition impairment has been becoming one of the major issues derived from medical procedure, particularly when it was performed in younger patients. Our previous data noted that early exposure of sevoflurane impaired the adulthood spatial memory function in dose and time-dependent manner. Gamma aminobutyric acid (GABA) is the key inhibitory neurotransmitter in the central nervous system, and functions through mediating Wnt signaling pathway. The pontine GABA takes a special part in keeping awakening. We in this study investigated the role of pontine GABA signaling pathway activation in sevoflurane anesthesia-related long-term cognition in infantile rats via intracranial microinjection of CaMKII inhibitor KN-93 into the pons under different minimum alveolar concentrations of seveflurane. Morris Water Maze (MWM) was used to detect the spatial memory changes after speculated interventions. The results showed that pontile inhibition of GABA-Wnt-CaMKII through blocking CaMKII substantially alleviated sevoflurane-induced long-term special memory, which demonstrated dose- and time-dependent association. These preliminary observations indicated that the pontile GABA signaling plays an essential role in sevoflurane-induced adulthood cognition impairment, and further evaluation is needed on the exact interaction among sevoflurane, GABA, glutamate, receptors, corresponding signaling mediators, and cognition alteration in the pontine region.■

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**Keywords**: Sevoflurane – Cognition – Pons – GABA – Wnt – CaMKII

THE CHILDREN younger than 3 years are more than 35% in all children experienced general anesthesia each year, account for 4-7% of all children and the number is more than 80 million (1). Recent clinical cohort studies and meta-analysis suggested that the infants younger than 3 years exposed to the anesthetic were followed by long-term cognitive function and learning ability markedly reducing (2,3). At the same time, animal studies have found that early life exposure to the anesthetic causes degenerative change of brain neurons and spatial cognitive dysfunction (4,5). But the mechanism of anesthetic impairing learning and cognitive function is not yet clear. Most studies demonstrated that neuronal apoptosis induced by anesthesia is the main reason (6). There is also other research thinking that is because of cerebral energy metabolism disorder (7).The "central inhibition" theory is a new hotspot new, on which some researchers have carried out a series of studies involving ion channels, synaptic plasticity, glial cells inflammatory reaction, relevant signal pathways activation, etc. and have gained some progress (8,9,10,11,12).

Sevoflurane, a new type inhalational general anesthetic, is now the most common agent for pediatric patients due to its sweet-smelling property as well as fast onset plus recovery. Our recent studies found that early-life rats undergone sevoflurane anesthesia possessed long-term learning and spatial cognitive function serious damage. The damage degree was closely related to sevoflurane exposure duration, repetitions, weeks age of rats. The longer sevoflurane exposure duration, the more repetitions, the smaller weeks age, the more serious impairment was (8,13). Through literature review, the general anesthesia mechanism of sevoflurane mainly focused on that sevoflurane activates gamma aminobutyric acid (GABA) neural pathways in hippocampus to lead to unconsciousness (9,10,11,14,15,16). It is known now pontine reticular formation as an important part of the uplink reticular activation system also plays an important role in the process of awakening. But interestingly, pontine reticular formation activates GABA neural pathways to achieve awakening (12,17). Earlier studies have found that sevoflurane inhibits the activity of GABA neural pathways in pontine reticular formation (13,18), so we speculated that the activity inhibition of GABA neural pathways in pontine reticular formation may be one of the mechanisms by which early life undergone sevoflurane anesthesia leads to long-term learning and cognitive function damage.

## MATERIALS AND METHODS

### Animal care and ethics

After approval by the Institutional Committee of Animal Care and Use, male Sprague-Dawley rats aged 3 days (postnatal 3 days, P3D) were used for pontine injection and sevoflurane intervention and behavioral tests. The pups (P3D) were housed with maternal rats to a same plastic cage with soft bedding on a reverse 12:12 h light/dark cycle with lights on at 8:00 AM and maintained in climate with 23±1 ℃ housing temperature and free access to food and water. The pups were returned to their mother cage after sevoflurane anesthesia. Three weeks after birth, the offspring were separated from maternal rats and housed one animal to one cage until the completion of behavior tests. The littermates were randomly assigned to each testing group. The random numbers were generated by means of the QuickCalcs (GraphPad Software Inc, La Jolla, San Diego, CA; Online Calculators for Scientists, available at http:// www.graphpad.com/quickcalcs/RandMenu.cfm. Last accessed April 03, 2014.). Anesthesia and pontine injection were conducted during the light phase between 08:00 AM and 05:00 PM in a quiet room maintained at 22–24 ℃. Each animal was used for the same anesthesia and pontine injection regimen and was euthanized after completion of the water maze behavioral experiment by administering a lethal dose of pentobarbital.

### Pontine medicine injection procedures

This methods of pontine medicine injection used at the present study referenced to the methods by David I. et al. (19), and were modified somewhere accordingly. Before sevoflurane exposure procedures, the rat's head was secured in a stereotactic frame. The rat's head position was adjusted within the stereotactic frame to facilitate the appropriate trajectory for cannula insertion into the target site within the pontine tegmentum. The place was selected as the target site because of its relatively large size, the predominance of surrounding white matter, and the absence of cranial nerve nuclei or major ascending and descending fiber tracts. To obtain the appropriate trajectory for this target, the anterior portion of the animal's head was elevated 3 mm above a horizontal plane, and the skull target point was located within the bregma area at 0.6 mm to the right of the sagittal suture and 0.4 mm anterior to the lambdoid suture. After antisepsis with 2% iodine solution, a 25-gauge needle was used to puncture through the skine and the dura mater under the skull target point gently to make a channel for cannula inserting. The infusion cannula apparatus was secured in the clamping device of the stereotactic frame and inserted to its target depth in the brain (2.6 mm below the skull) though the channel.

The infusion cannulas were prepared by inserting 33-gauge internal cannulas into 26-gauge guide cannulas with a 1.5-mm projection of the internal cannula tip. The space between the distal end of the guide cannula and the projecting portion of the infusion cannula was sealed by applying methyl-2-cyanoacrylate to prevent backflow of infusate into the space between the guide cannula and the internal cannula. The sealed guide

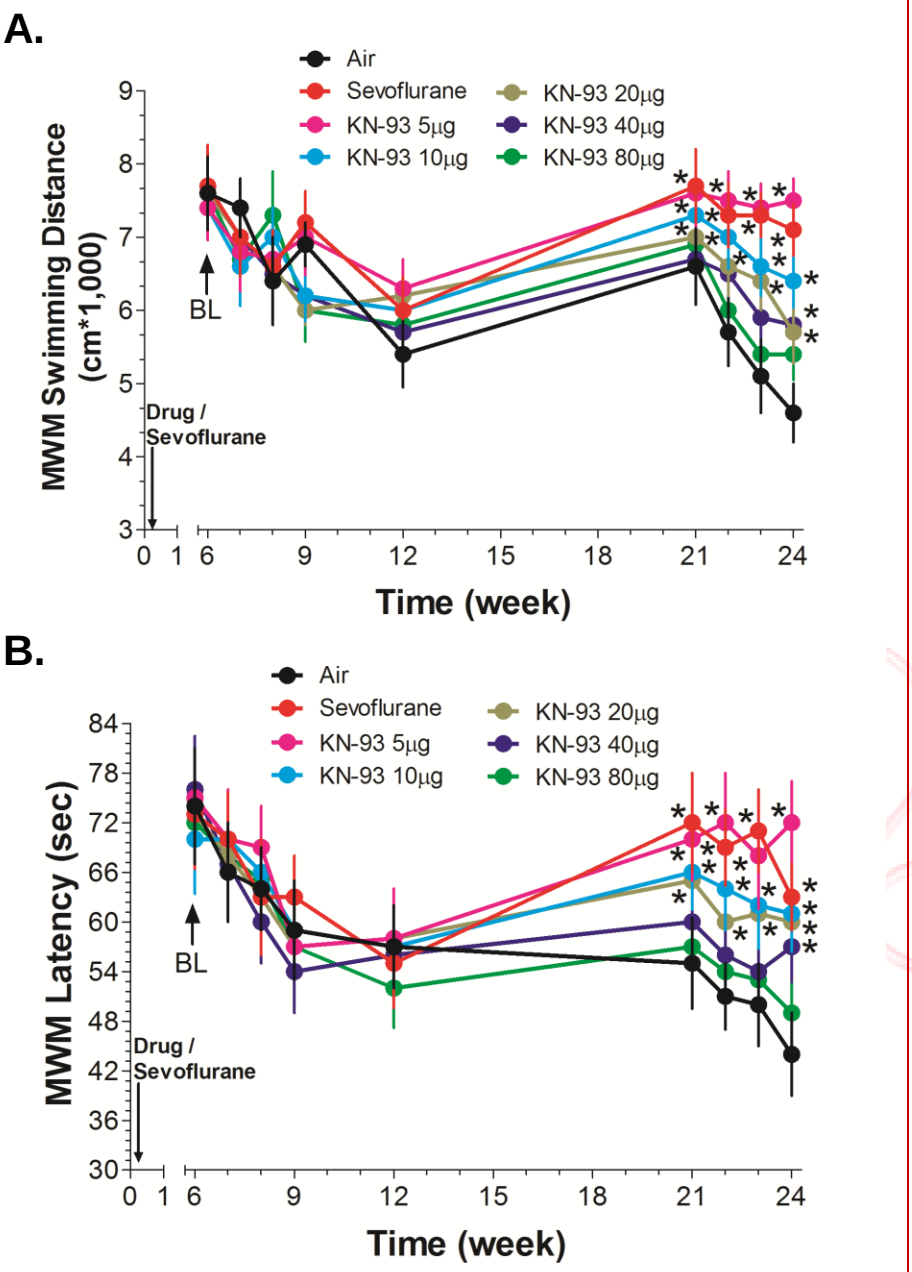


**Figure 1. The effect of pontine injection with different doses of CaMKII inhibitor KN-93 on the long-term spatial memory impairment induced by sevoflurane exposure.** The p3d rats were undergone 2% sevoflurane exposure for thirty minutes once after pontine medicine injection of different doses of CaMKII inhibitor KN-93 respectively 5, 10, 20, 40, 80μg / 5μl or no pontine medicine injection, and trained with MWM at the forth week after birth followed by spatial memory detection from the 6th to 24th week after birth. The pontine KN-93 injection improved the impaired long-term spatial memory induced by sevoflurane exposure dependently on the doses of KN-93, i.e. the larger dose, the more obvious the improvement was, including the swimming distance (A) and latency (B) of the rats. Data are depicted as mean±SEM, n = 8. Compared with Air Group, *$P$ < 0.05. Air Group only breathed air without sevoflurane exposure.

cannula and the internal cannula were attached to the connector assembly, which consisted of a polyethylene supply tube encased in tough vinyl tubing, and the free end of the tubing was attached to a 10-μl syringe. The infusion system was sterilized before use and preloaded with the infuscate corresponding to the experimental design to eliminate air bubbles before injection.

All infusions were administered at a constant rate of 0.3 μl/min via a syringe pump attached to the connector assembly. The duration of the infusions was 5 min. In rats receiving infusions, cannulas were removed 5 minutes following completion of the infusion. Burr hole site bleeding was controlled by applying gentle pressure with a cotton-tipped applicator, then coated with erythromycin eye ointment to protect from infection. The animal was then removed from the stereotactic frame and put into its cage, and observed thirty minutes. If its behavior was normal, the animal continued to participate in the subsequent experiment.

### Sevoflurane exposure procedures

Animals were exposed to sevoflurane (Abbott Laboratories, Animal Health Division, IL, USA) through a specific vaporizer (Penlon Sigma Delta Sevoflurane Vaporizer; Kent Scientific Co., Torrington, CT, USA). A total of 150 rats aged P3D were used in different exposure sessions. Sevoflurane was given through conical tubes with apropriate size to the pups under 100% oxygen.

### MAC determination and survival rate

The minimum alveolar concentration (MAC) of sevoflurane for P3D rats have been measured in our previous studies (13). The results were referenced in the present study. The MACs displayed an exposure time-dependent decrease, exposure, duration 1, 2, 3, 4 hours, the MACs corresponding to about 8%, 6.5%, 4%, 3.5%. When exposed for 4 hours at 1 MAC, the P3D rats survival rate was 40%. In our study, we set the exposure-duration 30 minutes each time at 2% concentration of sevoflurane, so the survival rate was 100% for P3D rats.

### *Session 1: The effect of pontine*

***injection with different doses of CaMKII inhibitor KN-93 on the long-term spatial memory impairment induced by sevoflurane exposure***

A total of fifty-six P3D rats were randomly divided into seven groups consisting of eight animals each (n = 8). The rats in negative control group weren't undergone sevoflurane exposure and pontine medicine injection (Air Group). The rats in positive control group were undergone 2% sevoflurane exposure for thirty minutes only once without pontine medicine injection (Sevoflurane Group). The rats in the other groups (KN-93 5, 10, 20, 40, 80 Group) were administrated pontine medicine injection with different doses of CaMKII inhibitor KN-93 (Sigma) respectively 5, 10, 20, 40, 80μg in volume 5μl by the different group, after thirty minutes, undergone sevoflurane exposure as Sevoflurane Group. After sevoflurane anesthesia, the animals were returned to maternal cages for three weeks and then separated into individual cages until the water maze test was performed at the 24th week after birth. The Morris Water Maze (MWM) training was given once a day for three consecutive days at the forth week after birth and followed by measurement at 1, 2, 3, 4, 7, 16, 17, 18, and 15 weeks after training (Fig. 1).

***Session 2: The effect of pontine injection with 30μg KN-93 on the long-term spatial memory impairment induced by sevoflurane exposure***

In session 1, we found that there was the tendency of improvement in KN-93 20 Group, and more obvious improvement in KN-93 40 Group at the 21, 22, 23th week after birth compared with Sevoflurane Group about the impaired long-term spatial memory induced by sevoflurane exposure in the rats. In this session, we wondered how about the pontine injection with 30μg KN-93.

A total of twenty-eight P3D rats were randomly divided into 4 groups consisting of eight animals each (n = 8). The rats in negative control group weren't undergone sevoflurane exposure and pontine medicine injection (Air Group). The rats in positive control group were undergone 2% sevoflurane exposure for thirty

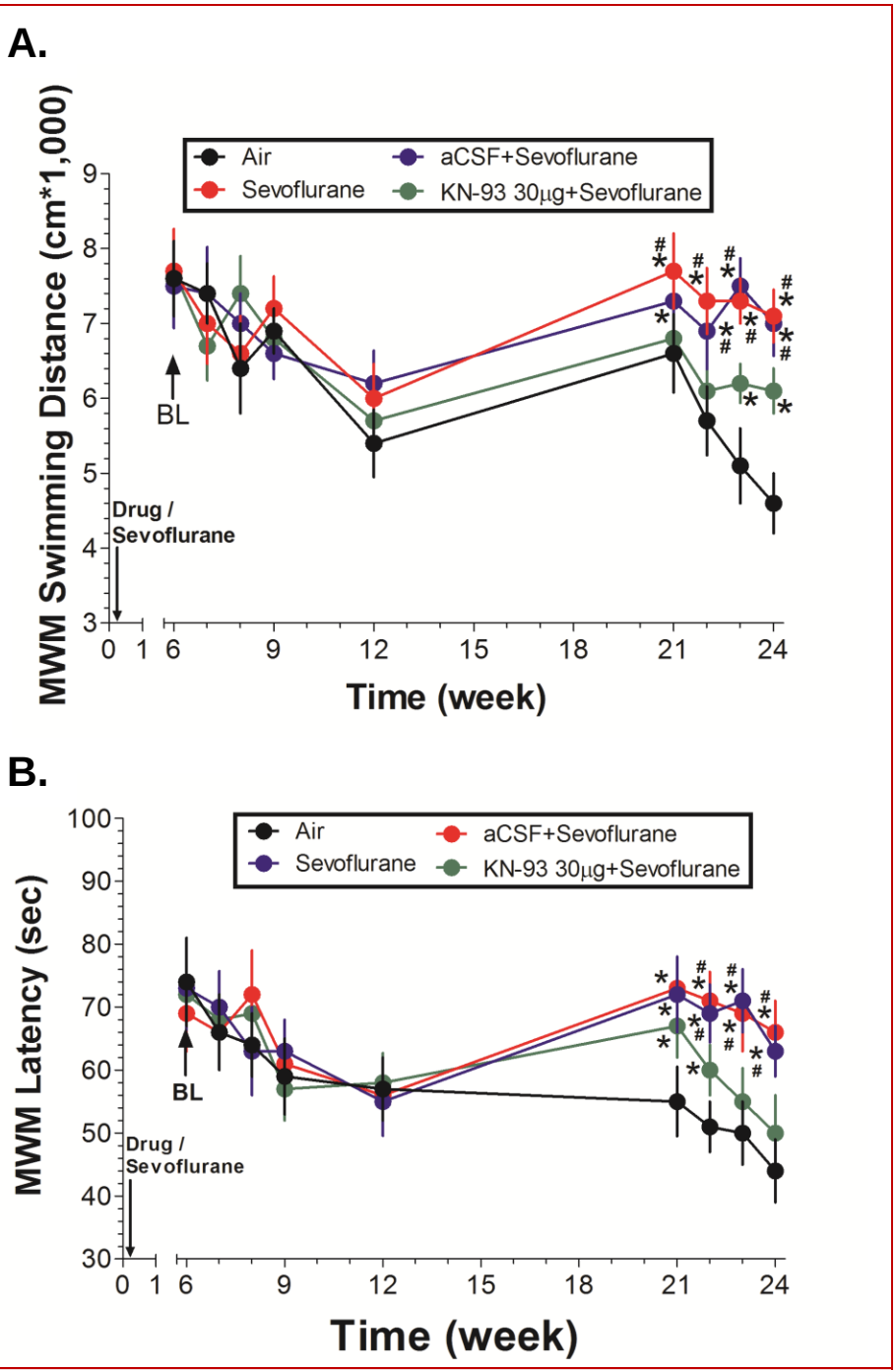


**Figure 2. The effect of pontine injection with 30μg KN-93 on the long-term spatial memory impairment induced by sevoflurane exposure.** The P3D rats were administrated pontine injection with 30μg KN-93 or artificial cerebrospinal fluid before exposed to 2% of sevoflurane for thirty minutes, and trained with MWM at the forth week after birth, then measured their spatial memory from the 6th to 24th week after birth. The pontine injection with 30μg KN-93 also improved the impaired long-term spatial memory induced by sevoflurane exposure, including the swimming distance (A) and latency (B) of the rats. Data are depicted as mean ± SEM, n = 8. Compared with the Air Group, $^{*}P < 0.05$. Compared with the KN-93-30 Group, $^{\#}P < 0.05$. Air Group only breathed air without sevoflurane exposure.

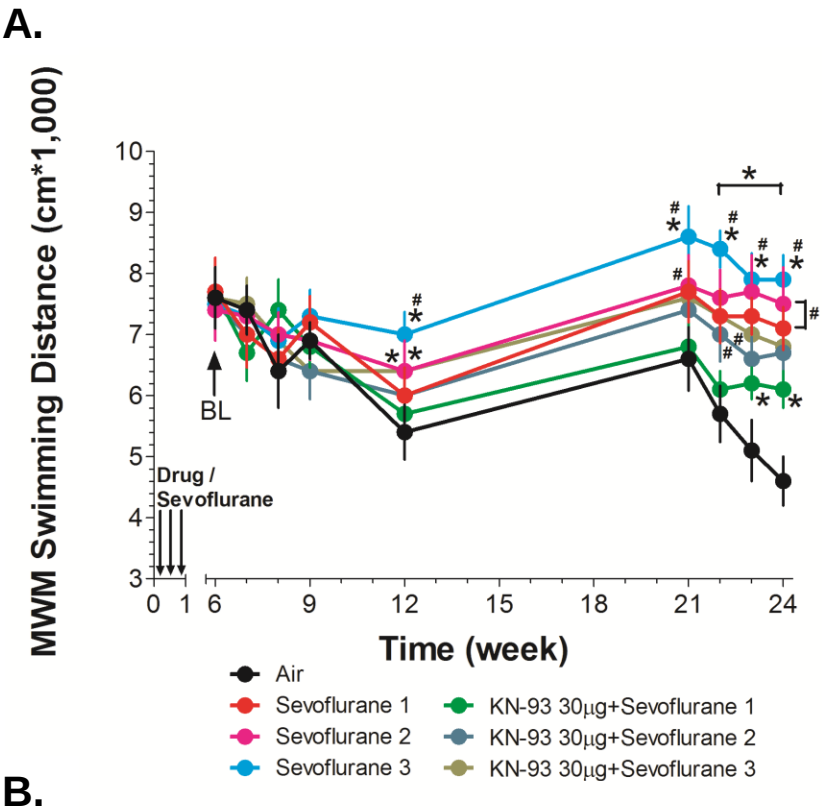


**Figure 3. The effect of pontine injection with 30μg KN-93 on the long-term spatial memory impairment induced by repeats sevoflurane exposure.** The P3D rats were administrated pontine injection with 30μg KN-93, then exposed repeatedly to 2% of sevoflurane for thirty minutes, and trained with MWM at the forth week after birth, then measured their spatial memory from the 6th to 24th week after birth. The protection of pontine injection with 30μg KN-93 for the damaged spatial memory induced by once sevoflurane exposure was better than repeats sevoflurane exposure, including the swimming distance (A) and latency (B) of the rats. Data are depicted as mean ± SEM, n = 8. Compared with the Air Group, $^{*}P < 0.05$. Compared with the KN-93 30μg + Sevoflurane 1 Group, $^{\#}P < 0.05$. Air Group only breathed air without sevoflurane exposure. 1, 2, 3 means sevoflurane exposure times. BL means base line.

minutes only once without pontine medicine injection (Sevoflurane Group). The rats in the rest groups, were administrated pontine medicine injection with 5μl artificial cerebrospinal fluid (aCSF + sevoflurane Group), or 30μg KN-93 in volume 5μl (KN-93 30μg + sevoflurane Group) by different group, after thirty minutes, undergone sevoflurane exposure as Sevoflurane Group. Then the animals were managed as mentioned above in Session 1.

### *Session 3: The effect of pontine injection with 30μg KN-93 on the long-term spatial memory impairment induced by repeats sevoflurane exposure*

A total of fifty-six P3D rats were randomly divided into seven groups consisting of eight animals each (n = 8). The rats in negative control group weren't undergone sevoflurane exposure and pontine medicine injection (Air Group). The rats in three positive control groups were undergone 2 % sevoflurane exposure for thirty minutes, repeated respectively once, twice, thrice by the different group once a day for three days, withour pontine medicine injection (Sevoflurane 1, 2, 3 Group). The rats in the rest three groups were administrated pontine medicine injection with 30μg KN-93 in volume 5μl, thirty minutes later, undergone sevoflurane exposure as the three positive control groups (KN-93 30μg + Sevoflurane 1, 2, 3 Group). Then all the animals were managed as the mentioned above in Session 1.

### Spatial memory detection

The Morris Water Maze (Shanghai Jiliang Software Technology Co. Ltd., China) was used as we have previously reported. In brief, the MWM was performed to detect sevoflurane-induced changes in animals' spatial memory and cognitive function after different interventional procedures. A circular tank 100 cm in diameter and 30-cm deep was filled with water to a depth of 25 cm. A transparent round platform 10 cm in diameter was

placed at 0.5 cm below the surface of the water. During the test of spatial memory, the animals learned to use distinctive distal visual cues surrounding the pool to navigate a direct path to the hidden platform. The platform remained in a constant location during the acquisition phase. Animals were placed on the platform for 30 s preceding the start of each training session. Animal training took place during a 3-day acquisition phase with three massed trials administered each day. Rats were allowed to swim freely for 90 s or until the platform was reached. If the platform was not located within the 90 s, the rats were guided to the platform and allowed to remain there for 30 s. After completion of three consecutive trials, the rats were placed in their home cages under a heat lamp for 10 min. A video camera mounted to the ceiling directly above the center of the maze was used in conjunction with a computerized animal tracking system to monitor latency to the platform and distance swam.

### Statistical analysis

The MWM data are presented as the means ± standard error of the means (SEM), and were compared with two-way ANOVA. The ANOVA tests were followed by Bonferroni *post hoc* tests if applicable. GraphPad Prism v5.0 (GraphPad Software Inc., San Diego, CA, USA) and PASW Statistics v18.0 (IBM Co., Armonk, NY, USA) were used for data analyses. All reported P values are two-sided and a P value of less than 0.05 is accepted for statistical significance.

## RESULTS

### The effect of pontine injection with different doses of KN-93 on the long-term spatial memory impairment induced by sevoflurane exposure

We exposed P3D rats to 2% of sevoflurane for thirty minutes after pontine injection with different doses KN-93, and trained them with MWM at the forth week after birth, then measured their spatial memory from the 6th to 24th week after birth. We found that pontine KN-93 injection improved the impaired long-term spatial memory induced by sevoflurane exposure dependently on the doses of KN-93, i.e. the larger dose, the more obvious the improvement was. The swimming latency and distance of the rats in KN-93 40, 80 Groups were both shorter significantly than that in Sevoflurane Group($P < 0.05$), and similar to that in Air Group ($P > 0.05$) at the 21, 22, 23th week after birth, even at 24th week so were that in KN-93 80 Group. There was also the tendency of the improvement in KN-93 10, 20 Groups at the 21, 22, 23th week after birth compared with Sevoflurane Group (Fig. 1).

### The effect of pontine injection with 30μg KN-93 on the long-term spatial memory impairment induced by sevoflurane exposure

We administrated pontine injection with 30μg KN-93 or artificial cerebrospinal fluid to the P3D rats before exposed to 2% of sevoflurane for thirty minutes, and trained them with MWM at the forth week after birth, then measured their spatial memory from the 6th to 24th week after birth. We found that pontine injection with 30μg KN-93 also improved the impaired long-term spatial memory induced by sevoflurane exposure. The swimming latency and distance of the rats in the KN-93 30μg Group were both shorter significantly than that in Sevoflurane Group at the 21, 22, 23, 24th week after birth ($P < 0.05$) or than that in aCSF Group at the 22, 23, 24th week after birth ($P < 0.05$), and the swimming distance in the KN-93 30μg Group was similar to that in Air Group at the 21, 22nd week after birth ($P > 0.05$), the swimming latency was also similar to that in Air Group at the 23, 24th week after birth ($P > 0.05$) (Fig. 2.).

### The effect of pontine injection with 30μg KN-93 on the long-term spatial memory impairment induced by repeats sevoflurane exposure

We administrated pontine injection with 30μg KN-93 to the P3D rats, thirty minutes later, repeatedly by the different group exposed them to 2% of sevoflurane for thirty minutes once a day for three days , and trained them with MWM at the forth week after birth, then measured their spatial memory from the 6th to 24th week after birth. We found that the protection of pontine injection with 30μg KN-93 for the damaged spatial memory induced by once sevoflurane exposure was better than repeats sevoflurane exposure. The swimming latency and distance of the rats in the KN-93 30μg + Sevoflurane 1 Group were both shorter significantly than that in Sevoflurane 1 Group ($P < 0.05$), but there were significant difference neither between that in the KN-93 30μg + Sevoflurane 2 and Sevoflurane 2 Group ($P > 0.05$), nor between that in the KN-93 30μg + Sevoflurane 3 and Sevoflurane 3 ($P > 0.05$), at the 21, 22, 23, 24th week after birth. and the swimming latency in the KN-93 30μg + Sevoflurane 1 Group was similar to that in Air Group at the 23, 24th week after birth ($P > 0.05$), the swimming distance in the KN-93 30μg + Sevoflurane 1 Group was also similar to that in Air Group at the 22, 23, 24th week after birth ($P > 0.05$) (Fig. 3.).

## DISCUSSION

GABA neural pathways action is mediated by Wnt signaling pathways (14,15,20,21). And there are three different ways to activate Wnt signaling pathways, i.e. the classic pathway by upregulating beta-catenin in cytoplasm, the Wnt/PCP pathway by activating c-Jun N-terminal kinase (JNK) , and the Wnt/$Ca^{2+}$ pathway depending on the activation of calmodulin protein kinase II (CaMKII) and protein kinase c (PKC) (16,22). Our previous studies showed CaMKII inhibitor KN-93 pontine injection in early-life rats significant-

ly inhibited the expression of CaMKII and $GABA_A$ receptor ($GABA_A$ R) in pontine reticular formation, shortened the anesthesia induction time of 1 MAC (minimum alveolar concentration effectively) sevoflurane, but β-Catenin inhibitor FH535, JNK inhibitor TAT-TI-JIP, PKC inhibitor Gö 6976 did not produce the similar effect as KN-93. So we speculated that sevoflurane works on GABA-Wnt-CaMKII signaling pathway in pontine reticular formation to produce general anesthesia effect. Based on these findings, the present studies observed the effects of sevoflurane exposure of young rats injected KN-93 to pons on the long-term spatial memory by MWM testing.

In sum, the data showed that pontile inhibition of GABA-Wnt-CaMKII through blocking CaMKII substantially alleviated sevoflurane-induced long-term special memory, which demonstrated dose- and time-dependent association. These preliminary observations indicated that the pontile GABA signaling plays an essential role in sevoflurane-induced adulthood cognition impairment, and further evaluation is needed on the exact interaction among sevoflurane, GABA, glutamate, receptors, corresponding signaling mediators, and cognition alteration in the pontine region.■

## Conflict of Interests

None

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When life starts,
It is so fresh.
Who knows the future?
Sunny
Rainy
Droughty
Or
……

# The History of China Has Been Rewritten by the Mysterious Ancient Artifacts of Sanxingdui

AMID THE once-tranquil village of Sanxingdui, in a quiet part of Sichuan province in China, a remarkable discovery took place which immediately attracted international attention and has since rewritten the history of Chinese civilization. Two giant sacrificial pits were unearthed containing thousands of gold, bronze, jade, ivory and pottery artifacts that were so unusual and unlike anything ever found in China before that archaeologists realized they had just opened the door to an ancient culture dating back between 3,000 and 5,000 years. In the spring of 1929, a farmer was digging a well when he discovered a large stash of jade relics. This was the first clue that eventually led to the discovery of a mysterious ancient kingdom. Generations of Chinese archaeologists searched the area without success until 1986, when workers accidentally found the pits containing thousands of artifacts that had been broken, burned, and then carefully buried. The discovery of the artifacts opened up a world of intrigue. The objects found in the sacrificial pits included animal-faced sculptures and masks with dragon ears, open mouths and grinning teeth; human-like heads with gold foil masks; decorative animals including dragons, snakes, and birds; a giant wand, a sacrificial altar, a 4-meter-tall (13-foot-tall) bronze tree; axes, tablets, rings, knives, and hundreds of other unique items. Among the collection was also the world's largest and best preserved bronze upright human figure, measuring 2.62 meters (8 feet). However, by far the most striking findings were dozens of large bronze masks and heads represented with angular human features, exaggerated almond-shaped eyes, straight noses, square faces, and huge ears, features which don't reflect those of Asian people. The artifacts were radiocarbon dated to the 12th-11th centuries BC. They had been created using remarkably advanced bronze casting technology, which was acquired

by adding lead to a combination of copper and tin, creating a stronger substance that could create substantially larger and heavier objects, such as the life-size human statue and the 4-meter-tall (13-foot-tall) tree. Some of the masks were enormous in size – one measures an incredible 1.32 meters (1.33 feet) in width and 0.72 meters (2.36 feet) in height, the largest bronze mask ever found. The three largest masks have the most supernatural features of all the Sanxingdui artifacts, with animal-like ears, monstrously protruding pupils, or an additional ornate trunk. Researchers were astonished to find an artistic style that was completely unknown in the history of Chinese art, whose baseline had been the history and

artifacts of the Yellow River civilization(s). The spectacular discovery at Sanxingdui in 1986 turned Sichuan into a focal point in the study of ancient China. The ancient artifacts found in the two pits date to the time of the Shang dynasty, in the late second millennium BC, when the primary civilized society was flourishing in the Yellow River valley, in north China, thousands of miles from Sichuan. No similar find has been made anywhere else, and there are no inscriptions at the Sanxingdui site to shed light on its culture, which was apparently a distinctive Bronze Age civilization, unrecorded in historical texts and previously unknown. The discovery contributed to a fundamental shift from the traditional understanding of a single centre of civilization in north China to the recognition of the existence of multiple regional traditions, of which Sichuan was clearly one of the most distinct. The culture that produced these artifacts is now known as the Sanxingdui Culture, and archaeologists are identifying it with the ancient kingdom of Shu, linking the artifacts found at the site to its early legendary kings. References to a Shu kingdom that can be reliably dated to such an early period in Chinese historical records are scant (it is mentioned in Shiji and Shujing as an ally of the Zhou who defeated the Shang), but accounts of the legendary kings of Shu may be found in local annals. According to the Chronicles of Huayang compiled in the Jin Dynasty (265–420 AD), the Shu kingdom was founded by Cancong. Cancong was described as having protruding eyes, a feature that is found in the figures of Sanxingdui. Other rulers mentioned in Chronicles of Huayang include Boguan, Yufu, and Duyu. Many of the objects are fish and bird-shaped, and these have been suggested to be totems of Boguan and Yufu (the name Yufu actually means fish cormorant). A metropolis of its time, covering about three square kilometers (1.8 square miles), Sanxingdui had highly developed agriculture, including winemaking

ability, ceramic technology and sacrificial tools and mining was commonplace. According to archaeological findings, the settlement at Sanxingdui was abandoned suddenly around 1,000 BC. For reasons that are still unknown, the prime of Sanxingdui Culture came to an abrupt end.

The sacrificial pits are believed to have been sites for the ancient Shu people to offer sacrifice to Heaven, Earth, mountains, rivers, and other natural gods. The human-like figures, bronze animal-faced masks with protruding eyes and flat bronze animal-faced masks may be natural gods worshiped by the Shu people. "Judging from the numerous bronze human images and funerary objects, the ancient Sanxingdui kingdom had unified and ruled the people through primordial religion. They worshiped nature, totems and their ancestors. The ancient Shu kingdom probably often held grand sacrificial activities to attract tribes with different religious beliefs to come from far and near to worship," said Ao Tianzhao from the Sanxingdui Museum, who has been studying the Sanxingdui culture for half a century. He believes the large number of bronze artifacts at Sanxingdui indicates that this site used to be a mecca for pilgrims. Since the discovery, these artifacts have received a great amount of international interest and attention. They have been exhibited at world renowned museums such as The British Museum, Taipei's National Palace Museum, National Gallery of Art (Washington), Guggenheim Museum (New York), Asian Art Museum (San Francisco), Art Gallery of New South Wales (Sydney) and Lausanne Olympic Museum (Switzerland). A selection of the artifacts are now making their way to the Bowers Museum in Santa Ana, California, where the exhibition, 'China's Lost Civilization: the Mystery of Sanxingdui', will be featured from 19th October 2014 to 15th March, 2015. The discovery of Sanxingdui shocked the world, but the history of the artifacts remains a mystery. Only the contents of two solitary pits reflect the immemorial and brilliant civilization of the Shu – no other artifacts like them have ever been found since. There are no historical records, and no ancient texts that speak of them, leaving experts asking what the purpose of the objects was, where the culture came from, and where they went after burying their most precious treasures. The Sanxingdui civilization is a unique page in China's long history and for now it remains an enigma.■

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