Satisfying brain metabolism at high altitude

At sea level, we bathe in air compressed by Earth's atmosphere, replete with oxygen molecules. At this low altitude, most of us can walk easily without huffing and puffing and we can exercise with some huffing and puffing because we're used to it. However, at 5050 m above sea level, the air is thin, the oxygen more scarce – we need to work harder just to supply energy for essential functions, let alone exercise.

The brain, arguably the most essential organ in the human body, is one of the greediest when it comes to oxygen consumption. It requires the steady delivery of a large supply of oxygen: merely being at high altitude causes blood flow to the brain to increase to meet oxygen demands. Of course, when people exercise at high altitude, they need even more oxygen – fuelling efficient metabolic reactions in many systems, in addition to the constant drain of the brain. The scarcity of oxygen at high elevations forces us to breathe harder, or slow down; and yet mountain climbers exist. Somehow, they manage to extract enough oxygen from the thin atmosphere to fuel their physical exertions and their greedy brains.

Kurt Smith, a graduate researcher at the University of British Columbia, Canada, and a team of international collaborators from the USA, Canada, New Zealand and UK, wanted to know how oxygen consumption and other metabolic supply chains to the brain are sustained during exercise at high altitude. To answer this question, the researchers took a group of plucky participants to perform a series of gruelling experiments both at sea level and at the base of Mount Everest, 5050 m above sea level. The team fitted the athletes with internal jugular vein and radial artery catheters, among other devices, so that they could measure a series of physiological and metabolic factors – cerebral blood flow, intracranial arterial blood velocity, extra-cranial blood flow, and substrate differences between arterial and venous blood to the brain – during rest, exercise and recovery periods.

At high altitude, the partial pressure of oxygen in the subjects' arterial blood during exercise was reduced from both rest and sea level values. Despite the drop in blood oxygen, cumulative oxygen delivery to the brain was maintained via increased cerebral blood flow during and after exercise. Furthermore, at rest at high altitude, the brain increased its uptake of lactate and glucose, suggesting that it may have switched some of its metabolism from an oxidative to a non-oxidative pathway.

The rate of oxygen metabolism in the brain only changed from the resting rate during maximal exercise at both sea level and high altitude – but the magnitude of this change in metabolic rate, and the way the change was effected, differed between the two conditions. At sea level, the brain supports its increased oxygen metabolism by increasing oxygen extraction from the blood. At high altitude, the brain's oxygen metabolic rate increases only half as much as it does at sea level, and this increase is facilitated by an increase in cerebral blood flow, not by increasing oxygen extraction.

Taken together, these findings suggest that in response to the multifaceted physiological challenges of high altitude, the body comes up with creative ways to maintain oxygen delivery to the brain. By increasing blood flow and using multiple metabolic pathways, the greedy brain can sate its hunger for oxygen, even atop mountains.

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Lizard colour changes to a daily rhythm

The ability to change one's skin colour is an extremely useful trait. Some species use dynamic changes in pigmentation to signal to potential mates or rivals. Others use it to camouflage themselves to fit in with their surroundings and avoid predators. Colour change can also assist in body temperature regulation by allowing for greater (or lesser) amounts of heat absorption as required. This last function is especially important in ectotherms, organisms that rely almost exclusively on external sources of heat to maintain an optimal body temperature. Darker pigmentation has a lower reflectance, which allows the animal to absorb more heat from the sun; conversely, lighter skin has a higher reflectance, which can reduce the amount of heat gained. As such, some ectotherms have been shown to change colour throughout the day, visibly darkening to assist in morning basking and lightening as temperatures increase and the need to absorb heat declines. While the existence of such regular changes in pigmentation is well known, what triggers these changes remains under-studied.

To test the hypothesis that photoperiod (daily cycles of light and dark) is a cue for colour change in lizards, Marie Fan and her colleagues at the University of Melbourne, Australia, acclimated inland bearded dragons (*Pogona vitticeps*) to four different

photoperiods (full dark and 6, 12 and 18 h of light per day). Bearded dragons are a rather large and charismatic Australian lizard and are known from previous work to use colour change to assist in thermoregulation, making them the ideal animals to test the scientists' theory. Fan and colleagues also wished to discern whether the changes in pigmentation occurred immediately in response to environmental cues, such as changes in light, or whether they occurred under regulation from a circadian (daily) clock. The team captured lizards from the wild, brought them into the lab and placed them at a constant temperature for 3 days under one of the four experimental photoperiods. Then, on the third day, the researchers measured the reflectance of the animal's skin once every 3 h for 72 h, to allow them to visualize the changes that occurred in the lizard's skin pigmentation throughout the day and night, and to determine whether there was a distinct rhythm to any pigmentation fluctuation.

The team found that the lizard's pigmentation consistently changed along with the light cycle: lightening in the dark and darkening during the day. Under the variable light conditions, the timing of the colour changes reflected the artificial day and night times with peak reflectance (lightest colouring) occurring after the start of the dark phase. The circadian rhythms persisted even for lizards kept under 24 h of darkness. These findings show that not only does the skin colour of bearded dragons respond to an internal clock but also the clock can be manipulated and entrained by changes in photoperiod. The presence of a circadian rhythm allows the lizards to change colour in anticipation of changes in environmental cues. That changes in pigmentation occur in a manner that would be conducive to increasing body temperature during the daytime active phase is indicative of a control for thermoregulatory purposes. But it remains to be seen exactly what triggers the changes and whether the circadian clock would react differently under variable environmental conditions.

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Bat's jamming sonar tricks echolocation in rivals

Insectivore bats are perfectly adapted to hunt for insects at night using an elaborate biosonar system for echolocation. To avoid sonic interference in situations where many bats fly together, some bats modulate the frequencies of the emitted acoustic signals. Mexican free-tailed bats (*Tararida brasiliensis*) live in huge colonies with more than a million individuals. The bats communicate amongst themselves with the help of at least 15 social calls that have different meanings, but not all of them have been identified. To decipher the function of one of the unexplored calls, named 'sinusoidal frequency modulated (sinFM)', Aaron Corcoran and William Conner from Wake Forest University and the University of Philadelphia, USA, performed field observations and elaborate playback experiments. They recently published their discovery that these bats send out jamming signals deliberately to paralyse the biosonar of their bat competitors in *Science* magazine.

As it was only possible to record sinFM signals when another bat was generating ultrasonic sounds during the final stage of an attack (known as the 'feeding buzz'), the scientists speculated that the sinFM signals may be emitted to jam the calls of other bats to increase hunting success – some insects, such as the tiger moth, make ultrasonic clicks to confuse bat echolocation systems. To test this hypothesis, the duo recorded bats hunting at two foraging sites in Arizona and New Mexico using highly sensitive cameras and ultrasonic microphones to reconstruct the complex 3D flight paths of the bats and correlate them with the emitted calls. Indeed, they observed that hunting bats were usually off target when another bat was sending the jamming sound: the jamming call appeared to have disrupted the attacker's final approach. Interestingly, sinFM call duration and the number of sound intervals within a call (syllables) correlated with the duration of the competitors' feeding buzz. This finding suggested that the bats modulate their sinFM signals to optimize sonic interference and stimulate FM rate-sensitive auditory neurons in the rival's brain that process information about prey localization.

Next, the scientists performed sophisticated playback experiments to test the effect of the jamming signals during an attack. They encouraged bats to capture moths hanging on very thin fishing line and played different ultrasonic sounds while the bats pursued the insects. These artificially synthesized jamming calls deranged the bats only when they were emitted at precisely the right time and frequency, and prevented insect capture only when they overlapped with the rival's feeding buzz.

Corcoran and Conner have provided compelling evidence supporting the existence of a novel strategy in food competition that involves sonic interference. This type of jamming has only been observed in Mexican free-tailed bats so far. However, other animals that rely on echolocation, such as other bat species or toothed whales, may also employ jamming sonar to trick their rivals.

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Muscles antagonize their neighbors' spindles

Because of the practical and ethical problems of experimenting on humans, it is very difficult to directly study the physiology of the intact human nervous system. However, there is one unusual (but safe) method for recording from single neurons in humans. This technique, called microneurography, requires impaling a peripheral nerve with a fine

tungsten electrode. The electrode is then finely repositioned until the spikes of an individual sensory axon are isolated. Microneurography was invented by Swedish neuroscientists Karl-Erik Hagbarth and Åke Vallbo, who boldly worked out the technical details by experimenting on themselves. The majority of microneurography studies are still performed by Hagbarth and Vallbo's successors in Sweden, presumably because of the technical challenges and obvious hazards of recording from human nerves.

One of the first applications of microneurography was to investigate mechanosensory neurons called muscle spindles. Deeply embedded within skeletal muscles, muscle spindles are proprioceptive sense organs that monitor the lengthening of surrounding muscle fibers. The muscle spindle itself contains specialized muscle cells, called intrafusal fibers. While skeletal muscles are controlled by alpha motor neurons, intrafusal fibers are innervated by a separate class of gamma motor neurons. The role of the gamma motor neurons is to adjust the mechanical sensitivity of the muscle spindle when the surrounding muscle contracts. Recording from human subjects, Vallbo discovered that alpha and gamma motor neurons often fire at the same time. Thus, when the primary muscle contracts and shortens, the intrafusal fibers also contract, increasing the tension on the muscle spindle organ. This phenomenon, called alpha–gamma co-activation, increases the ability of the muscle spindle to detect subsequent changes in muscle length.

In order to smoothly control the movement of joints, skeletal muscles often work together as antagonistic pairs: for example, when you point a finger, the extensor digitorum muscle contracts while its antagonistic partner, the flexor, relaxes. But are muscle spindles influenced by the activity of antagonistic muscles? In other words, does contraction of a flexor muscle affect the sensitivity of the extensor muscle spindle?

To answer this question, Michael Dimitriou, of Umeå University, Sweden, used microneurography to again record from human muscle spindle axons. After he isolated signals from a muscle spindle that controlled extension of a specific finger, Dimitriou asked his subjects to slowly and continuously wag that finger up and down. In some cases, an opposing force was applied to the finger, which required the subject to either increase or decrease muscle output. Although the finger movement kinematics remained constant across conditions, the activity in the flexor and extensor muscles varied, depending on the direction and amplitude of the applied external load. This allowed Dimitriou to compare trials in which the flexor muscle activity was the same, but the extensor muscle activity was variable, and vice versa.

Surprisingly, Dimitriou found that activity within an antagonistic muscle was negatively related to muscle spindle output. For example, extensor muscle spindles exhibited lower firing rates during contraction of antagonistic flexor muscles. This inhibitory relationship suggests that muscle spindle sensitivity actually reflects the balanced activity of both muscles within an antagonistic pair. Because antagonistic muscle pairs function together, adjusting spindle sensitivity based on the activity of both muscles may increase the ability of the muscle spindle to detect and encode muscle movements across a wide dynamic range.

How do signals from muscle spindles contribute to motor control? Many of our basic stretch reflexes, such as the knee-jerk response, result from direct muscle spindle feedback on to motor neurons. In the mouse, ablating muscle spindle neurons profoundly disrupts locomotor rhythms like walking and swimming. Finally, muscle spindle feedback might also be critical for the execution of fine motor skills, such as guiding a tungsten electrode into the radial nerve of a young Swedish student.

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Correction: The hormone battle behind 'eau de snake'

There were a number errors in the Outside JEB article, "The hormone battle behind 'eau de snake'". The affiliations of Rockwell Parker and Robert Mason were incorrect. Rockwell Parker is affiliated with Washington and Lee University, USA, and Robert Mason is affiliated with Oregon State University, USA. The article also stated 'These snakes solve the problem of telling males and females apart through pheromones, secreted hormones that serve as chemical signals.' However, this species secretes methyl ketones, not modified hormones, as pheromones. Finally, the snakes were not injected with testosterone as stated in the text. Instead they were implanted with long-lasting steroid hormone (testosterone) implants. We apologise for the errors.