monkeys. This involved systematically testing each spinal segment once again, to identify the segments that should be targeted by TESS, and scaling their neuroprosthetic to match the larger anatomy of the monkey. Finally, and most remarkably, the group demonstrated that the prosthetic baroreflex could restore blood-pressure stability in a person who experienced disabling orthostatic hypotension following an SCI.

This bench-to-bedside study is unprecedented in many ways, and, as such, raises several questions. For instance, the sensory afferent neurons that are stimulated by the prosthetic device are unidentified, and the long-term effects of their stimulation are unknown. The spinal circuitry is reconfigured after spinal trauma[9], and reflexes are exacerbated such that formerly innocuous stimuli can trigger episodes of dangerously high blood pressure. Time and further animal experiments will be needed to determine whether chronic activation of these afferent neurons will mitigate or aggravate hyperactive reflexes. Indeed, unlike the real baroreflex, the prosthetic baroreflex is presumably much better at preventing bouts of low blood pressure than it is at mitigating rises in blood pressure.

In addition, it is possible that the neuroprosthetic will have adverse effects on gastrointestinal and kidney functions, which are regulated by lower thoracic sympathetic neurons. Finally, an invasive procedure is required for the placement of an epidural electrode in the spine, and its long-term efficacy is unknown.

Nonetheless, this latest attempt to treat the disabling hypotension that follows SCI is grounded in a large body of preclinical neuroscientific evidence. It is the most sophisticated strategy developed so far. The approach could conceivably replace currently available treatments — although it is much too early to say this for sure.

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Palaeontology

Lend an ear to a classic tale of mammalian evolution

Simone Hoffmann

Newly discovered fossil evidence has led to a re-evaluation of one of the fundamental transitions in mammalian evolution: the transformation of bones of the lower jaw into those of the middle ear. **See p.279**

Modern mammals have three tiny bones in their middle ear that aid hearing. Oddly, these bones evolved from remnants of jaw bones, and how they migrated to form the ear has fascinated biologists for 200 years[1]. The middle ear and lower jaw of mammals today differ strikingly from those of other vertebrates. In addition to the three bones of the middle ear (termed the malleus, incus and stapes), mammalian ears have an ectotympanic bone, from which hangs the tympanic membrane (also known as the eardrum) that is needed for hearing. But they have just one lower jaw bone (the dentary bone). By contrast, other vertebrates have only one bone in the middle ear (the stapes), but more than eight lower jaw bones.

Nineteenth-century biologists were the first to recognize the similarities in development between some of these extra elements of the lower jaw of non-mammalian vertebrates and the middle ear of mammals, and in doing so chronicled one of the most fundamental transitions in mammalian evolution: the transformation of lower jaw bones to form the middle ear. On the basis of new fossil evidence, Wang *et al.*[2] (page 279) now crucially revise this classic story of mammalian evolution.

Once the basic similarities in relative position and structure (homologies) between bones of the lower jaw and middle ear had been established, the question of how such a major transformation could have occurred baffled scientists. One way to gain insight is through fossil evidence, which provides the only direct evidence that can capture key evolutionary moments in deep time. Discoveries of early fossil mammals and their closest relatives (called mammaliaforms) originally indicated a gradual transition as the lower jaw bones

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Figure 1 | ***Vilevolodon diplomylos.*** Wang *et al.*[2] report a newly discovered specimen of this species that is 160 million years old. Tiny bones of the middle ear preserved in this fossil provide information that offers a fresh perspective on mammalian evolution. Scale bar, 2 centimetres.

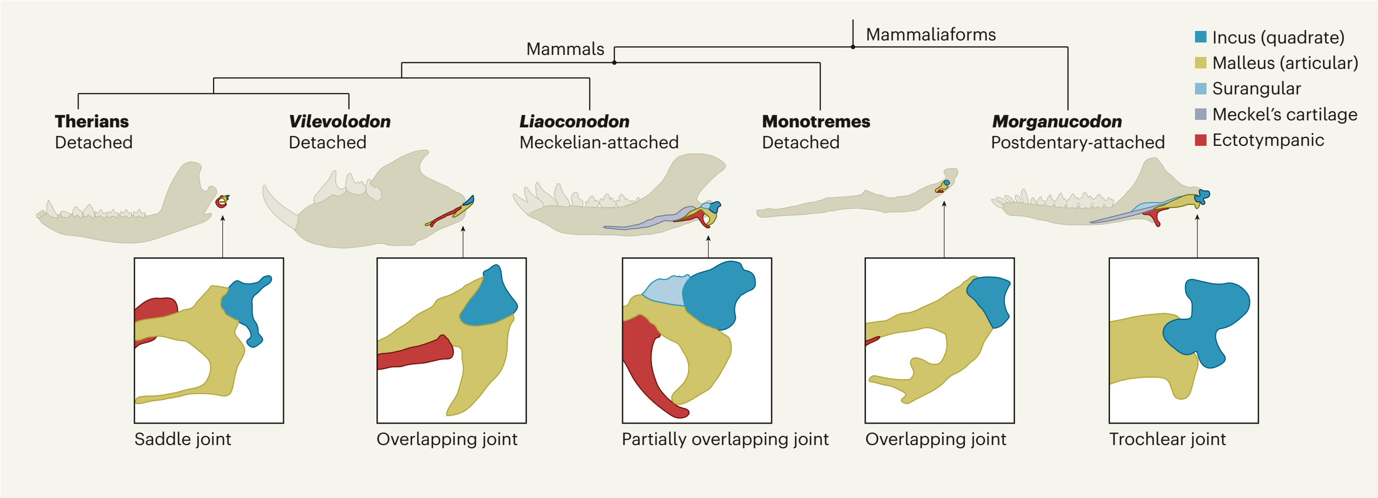

Figure 2 | Evolution of the middle ear. The middle ear, which comprises bones called the incus, malleus and stapes (not shown), arose from bones in the lower jaw during mammalian evolution. Elements of the ear, or the corresponding jaw bones from which they evolved, are shown in colour. Wang *et al.*[2] propose a new terminology system for classifying fossils depending on the connection between the middle ear and the jaw. This system describes the degree of direct attachment between the middle ear and the lower jaw, classifying fossil middle ears as either detached, Meckelian-attached (partially attached through Meckel's cartilage) or postdentary-attached (still part of the jaw). The authors present a fossil of the species *Vilevolodon diplomylos* that has a detached middle ear in which the incus and malleus form a flat, overlapping joint between these bones – an arrangement previously thought to be a specialized feature of monotreme mammals (such as the platypus). The authors find that this overlap is common in early mammals, and only the degree of bone overlap (full or partial) varies – for example, *Liaoconodon* has a partial overlap. In adult therians (marsupials and placentals, including humans), the incus instead lies behind the malleus in a saddle-shaped joint (which has convex and concave surfaces where the two bones interact, rather than a flat interaction surface). In the mammaliaform *Morganucodon* (an early mammalian relative), the bones corresponding to the incus (quadrate) and malleus (articular) remain connected to the jaw and form a specialized trochlear joint.

formed the middle ear[3]. This transition aligned with major groups of our evolutionary tree. On the basis of this initial fossil evidence, biologists coined the terms transitional mammalian middle ear (describing a partial detachment of the bones from the lower jaw) and definitive mammalian middle ear (describing the full detachment of the bones from the lower jaw).

However, subsequent fossil discoveries clouded this picture of a gradual transition[4–6]. Fossils discovered more recently show that the seemingly complex evolution that led to the detachment of the middle ear occurred independently at least three times in mammals[7]. Genetic evidence helps to explain these multiple origins of the middle ear, and what looks like a complex morphological (shape) transition is explained by relatively simple genetic mechanisms[8,9].

Given the current fossil and developmental evidence, it is clear that the established terminology is outdated. A definitive mammalian middle ear is neither a defining feature of mammals nor is it found in all mammals. Evidence from 200 years of research in various fields of biology has resulted in contradictory and inconsistent terminology and interpretations. The classification system used for evolutionary studies of the mammalian middle ear has therefore been in urgent need of revision.

Wang *et al.* have now provided exactly that, in the form of a detailed assessment of the fossil and developmental evidence. Their article combines the description of a new fossil (Fig. 1), a re-evaluation of previously reported fossil middle ears, and a discussion of the development of the middle ear in a wide range of modern mammals. On the basis of this much-needed, comprehensive comparison of the fossil and developmental data, Wang and colleagues have established a more-cohesive terminology system that is anchored in bone morphology (Fig. 2). This terminology identifies three types of middle ear: detached (the middle ear is completely separated from the lower jaw); Meckelian-attached (the middle ear is connected to the lower jaw through a structure called Meckel's cartilage); and postdentary-attached (the middle ear is not separated from the jaw).

At the core of Wang and colleagues' work is a fossil specimen from the Middle Jurassic epoch (160 million years ago), newly discovered in China. At first glance, the fossil itself is not spectacular; indeed, the species was described[10] in 2017. But, crucially, the middle ear of this new specimen is much better preserved than in the previously discovered fossil, and the insights it provides, even though based on only a few tiny bones of the middle ear, have broad implications.

The fossil, *Vilevolodon diplomylos*, belongs to a group called Haramiyida, or Euharamiyida, whose classification has been a source of contention, being placed either in or outside the class Mammalia (mammals)[10–12]. *Vilevolodon* was described originally as having its middle ear attached to the lower jaw[10]. This interpretation placed the species outside Mammalia in some previous studies. The new fossil suggests that *Vilevolodon* actually had a middle ear with all elements detached from the lower jaw (Fig. 2). Wang and colleagues' work thus places haramiyidans firmly within Mammalia in the evolutionary tree, and so favours an ancient origin for mammals, at least 215 million years ago (during the Late Triassic epoch). This is some 30 million years earlier than the timing of mammalian origins suggested by phylogenetic analysis in the original study of *Vilevolodon*[10].

In addition, as part of their broad evaluation of the morphology of the middle ear, Wang *et al.* determined that a morphology that was widely held to be a specialization of monotremes (egg-laying mammals such as platypuses) is actually more widespread than previously considered. Monotremes have a flat, overlapping joint (with a broad contact) between the malleus and incus (Fig. 2), whereas adult mammals in the therian group, comprising placentals (which includes humans) and marsupials, have a saddle-shaped joint, with the incus lying behind the malleus. Wang and colleagues indicate that the overlapping joint arrangement of monotremes seems to be present in all major early mammalian clades, as well as in the early developmental growth stages of marsupials and placentals.

The authors speculate that this joint shape might have balanced the needs for both increased auditory and load-bearing functions during ear evolution. It is unclear whether the overlapping morphology in different mammalian groups is a shared innovation in the ancestral animals that gave rise to Mammalia, or whether it evolved independently (by convergent evolution) in different groups as their middle ears became detached from their jaws.

Although their research is a major contribution to the understanding of Haramiyida, Wang and colleagues' study will not settle the debate about the placement and composition of this group. The striking increase in fossil discoveries, in particular new specimens from China, has fuelled routine revision of the mammalian tree of life during the past few years[10–12]. In the end, the lasting impact of Wang and colleagues' research will probably lie in their detailed evaluation of fossil and developmental morphologies of the middle ear, and the establishment of new terminology that is consistent with current evidence. Their work is a foundational reference for future studies that provides a framework on which to evaluate the evolution of the middle ear and new fossil discoveries.

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Astroparticle physics

Shedding squeezed light on dark matter

Igor G. Irastorza

Hypothetical particles called axions could constitute dark matter — the unseen component of the Universe. An experiment shows how quantum-manipulation technology can improve the sensitivity of axion detectors. **See p.238**

The Universe is filled with an invisible, unconventional form of matter, whose presence is betrayed by its gravitational attraction to ordinary matter. Scientists now have overwhelming evidence for the existence of such dark matter at galactic and cosmological scales. However, none of the known fundamental particles has the right properties to compose it. As a result, the nature of dark matter is one of the biggest puzzles in modern physics. For decades, researchers have struggled and failed to find signs of particles beyond the established catalogue. On page 238, Backes *et al.*[1] report an innovative way to accelerate future searches using quantum-manipulation techniques.

Among the particles suggested by theorists, the axion is a favourite for particle hunters[2]. Axions were originally proposed[3] to explain a somewhat obscure aspect of the current theory of particle physics, related to the fact that the dynamics of some particles seem to be unchanged when the arrow of time is reversed, contrary to expectation. More excitingly, axions are predicted to have the right properties to constitute dark matter. They would have been produced in large quantities after the Big Bang, and would permeate the Universe and behave exactly like dark matter.

If dark matter is made of axions, we would be embedded in a vast sea of these particles. An axion haloscope[4] is an instrument that looks for axions in our Galaxy's dark-matter halo (a roughly spherical region that extends beyond the stellar disk). In this device, a resonant cavity — a hollow metal structure that confines light of a particular frequency called a resonant frequency — is placed in a strong, uniform magnetic field. Inside the cavity, a potential axion can scatter from a quantum fluctuation of the magnetic field, known as a virtual photon, and produce a single real photon that has a frequency proportional to the axion mass (Fig. 1). If this frequency matches the resonant frequency of the cavity, the otherwise negligibly small axion signal will be amplified.

Even with this amplification, the signal expected for axions in the most realistic models of these particles is tiny and often buried under the 'noise' of the experiment. This noise has historically come from thermal radiation emitted from the cavity walls, or been introduced by the sensor technology used. Lowering the experimental noise is an effective way to improve the sensitivity to axions. As a result, the leading axion haloscopes[5–7] are cooled to cryogenic temperatures to reduce thermal emission, and use ultralow-noise sensor technologies. Unfortunately, until now, physics seemed to pose a fundamental barrier to this improvement.

Heisenberg's uncertainty principle of quantum physics[8] states that certain pairs of properties of a quantum system cannot be determined simultaneously with unlimited precision. Such properties are called complementary variables and include, for example, position and momentum. The uncertainty is sometimes referred to as quantum noise and is present even in the absence of any photons — a vacuum state. Consequently, quantum noise represents a limit to the achievable noise level in axion haloscopes. It is already a technological feat that the leading haloscopes reach noise levels extremely close to this quantum limit. But Backes and colleagues have now gone one step beyond the limit using a quantum state known as a squeezed state.

Squeezed states are specially prepared so that one of the properties in a pair has reduced uncertainty. To respect Heisenberg's principle, the complementary variable must then have larger-than-normal uncertainty. Squeezed states of light were first produced in the laboratory in the 1980s[9,10]. However, their potential to overcome the quantum limit in axion searches has been studied only in the past few years[11].

In the case of Backes *et al.*, the property being squeezed is the component of the quantum noise that resembles a mathematical curve called a sine wave, and the complementary variable receiving extra uncertainty is the component akin to a cosine wave. Fortunately, what is won by squeezing the former component is much greater than what is lost by 'unsqueezing' the latter. Therefore, preparing the vacuum state in the cavity of an axion haloscope in such a squeezed state enables the noise level to be reduced below the quantum limit.

Backes *et al.* have now implemented this concept in a real axion search. In doing so, they have proved that delicate quantum-manipulation technology is compatible with the environment of such a search. The authors report that a given region of axion parameter space (a plot of the axion–photon coupling versus the axion mass) can be explored in half the time when squeezing is included compared with when it is not.

This improvement might seem relatively modest, but it paves the way for further leaps forward in sensitivity. In principle,