

can we rely on a mouse model of social isolation to truly examine the underlying mechanisms of human loneliness? After all, loneliness and mental isolation are subjective, and a person might feel alone even when surrounded by other people. The traits exhibited by mice under prolonged social isolation greatly resemble those found in humans experiencing solitary confinement, so these animals do provide a good model for studying this process. What we currently lack are relevant animal models for other forms of human loneliness, such as social withdrawal or antisocial personality disorder. Expanding our research

toolbox — for example, by studying various species, including non-social and community-living animals, as well as humans — might bring us closer to understanding the biology of human loneliness. ■

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This article was published online on 20 June 2018.

ASTRONOMY

General relativity passes another test

Einstein's theory of gravity — the general theory of relativity — is based on the principle that all objects accelerate identically in an external gravitational field. A triple-star system provides a stringent test of this principle. [SEE LETTER P.73](#)

CLIFFORD M. WILL

All bodies in a given gravitational field are thought to fall with the same acceleration. This idea, known as the equivalence principle, is central to our understanding of gravitational physics. It was promoted by thinkers ranging from the sixth-century scholar John Philoponus to Galileo; it is the founding principle of Albert Einstein's general theory of relativity, and was famously demonstrated when Apollo astronaut David Scott dropped a hammer and a feather on the

Moon and saw that they hit the lunar surface at the same time. For decades, experimentalists have verified the equivalence principle using exquisitely delicate instruments. Now, on page 73, Archibald *et al.*¹ report the results of a remarkable test of the principle, in which the falling objects are two stellar remnants: a neutron star and a white dwarf.

A spinning neutron star that emits a beam of electromagnetic radiation is known as a pulsar. The emission seems to pulse because it can be seen only when the beam is pointing towards Earth. The pulses are so regular

that variations in their observed period can be readily interpreted as being due to the gravitational tug of another astronomical body on the pulsar. Such variations have been used to discover more than 220 binary systems containing a neutron star, and a handful of pulsars that have associated planets (go.nature.com/2mslfj4).

In 2014, astronomers reported a pulsar that is unusual because it has two stellar companions² (Fig. 1). The neutron star, weighing 1.4 solar masses, is in a close 1.6-day orbit with a 0.2-solar-mass white dwarf. This pair of objects is itself in a 327-day orbit with a 0.4-solar-mass white dwarf. The inner and outer orbits are nearly circular and exist in almost exactly the same plane.

If the neutron star and the inner white dwarf were to fall with different accelerations towards the outer white dwarf, there would be a tiny deformation of the inner orbit. Archibald and colleagues report an analysis of approximately six years of data showing no evidence of such a deformation. The accelerations of the two bodies differ by no more than 2.6 parts per million, in agreement with the equivalence principle.

Tests of this principle have a long heritage. In the late nineteenth century, the Hungarian physicist Roland von Eötvös devoted years to verifying that the accelerations of various laboratory materials in Earth's gravitational field differ by less than a few parts per billion³. His modern-day successors, the Eöt-Wash group⁴ in Seattle, Washington, pushed this bound to parts per 10¹³. And, in 2017, data from the French space mission MICROSCOPE⁵ moved the goalpost by a further factor of ten.

Given that a typical object in a physics lab consists of a swarm of elementary particles and their associated fields and energies, it is quite extraordinary that the responses of different materials to gravity should be so similar. In Einstein's unique imagination, there was a reason: gravity is not a force that acts on all of these particles in some fantastically fine-tuned manner, but is simply an effect of space-time geometry. The constituents of matter follow universal paths in a space-time that is curved by massive bodies, such as Earth or the Sun.

But does gravitational energy act in the same way as matter? The small objects used in lab experiments do not contain enough

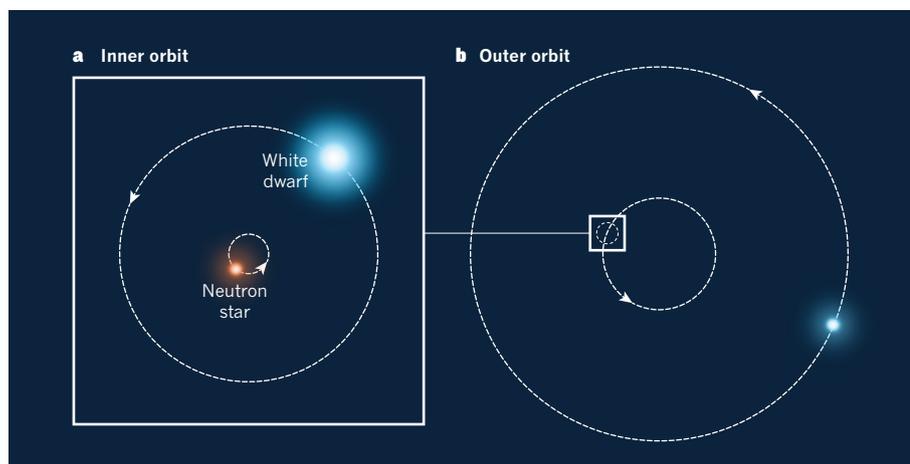


Figure 1 | Triple-star system. In 2014, astronomers reported a system that contains three stellar remnants: a neutron star and two white dwarfs². **a**, The neutron star is in a close 1.6-day orbit with one of the white dwarfs. **b**, This pair of objects is itself in a 327-day orbit with the other white dwarf. Archibald *et al.*¹ report no evidence of a deformation of the inner orbit, which would be expected if there were a difference between the accelerations of the neutron star and the inner white dwarf towards the outer white dwarf. The results provide support for Einstein's theory of gravity — the general theory of relativity.

gravitational energy to answer this question, but planets and stars do. With self-gravity in the picture, a concept called the strong equivalence principle comes into play. This principle singles out the general theory of relativity from its competitors. In Einstein's theory, all bodies — hammers, feathers, planets, neutron stars, white dwarfs and even black holes — fall with the same acceleration. But in most alternative theories of gravity, such as scalar–tensor theories⁶, the equivalence principle is violated for bodies that have self-gravity.

For almost 50 years, researchers have measured how long it takes for laser pulses to make the round trip from Earth to the Moon and back — a technique known as lunar laser ranging. Analyses of these data^{7,8} have verified the strong equivalence principle, by showing that the accelerations of the two bodies towards the Sun differ by no more than a few parts per 10^{13} . Because about 5 parts in 10^{10} of Earth's mass is gravitational energy⁹, this result implies that the accelerations of gravitational energy and matter differ by less than a few parts per 10^4 .

Archibald and colleagues' study breaks new ground because the gravitational energy inside a neutron star can account for as much as 20% of the body's mass¹⁰. The authors' results therefore imply that the accelerations of gravitational energy and matter differ by no more than a few parts per 10^5 — a tenfold improvement over the bound from lunar laser ranging.

More importantly, the authors have provided what is known as a strong-field test of general relativity. Unlike the Solar System, for which Einstein's theory predicts only small deviations from Newton's theory of gravity, the motion of a neutron star in a gravitational field invokes full general relativity in all its complex glory. Einstein's theory passes this strong-field test with flying colours.

Because general relativity predicts a null effect, the grading is a simple pass or fail. But for alternative theories, invoking strong-gravity effects substantially complicates the interpretation of the results. Archibald *et al.* demonstrate this complexity using scalar–tensor theories as an example. For these theories, the interpretation of the results depends on the internal structure assumed for the neutron star and on the values chosen for quantities known as coupling constants. The authors show that their results improve on certain pre-existing constraints on the parameters that govern these theories — some arising from Solar System measurements and some from data on binary systems containing a pulsar. Although the theories are not completely quashed, their hopes for validity have been made that much fainter. ■

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DEVELOPMENTAL BIOLOGY

Fat gets a brake

Single-cell transcriptional profiling of stem and progenitor cells in fat tissue identifies distinct cell subpopulations, one of which inhibits fat growth by signalling to neighbouring cells. SEE LETTER P.103

DAVID A. GUERTIN

Fat tissue has a remarkable capacity for growth. It can expand in two ways: by increasing the size of individual fat cells (adipocytes), and by making adipocytes from progenitor cells through the process of adipogenesis. Fat is essential for metabolic fitness, but having too much fat in the wrong places can be harmful. Obesity is a precursor to serious medical conditions such as type 2 diabetes, cardiovascular disease and cancer, which are ravaging health-care systems worldwide. Key to combating obesity is understanding how mature adipocytes develop from precursor cells, but the identity of these precursors has so far been elusive. On page 103, Schwalie *et al.*¹ define three populations of fat-precursor cell, one of which unexpectedly functions to suppress adipocyte production.

The origin of the body's adipocytes has been a mystery, complicated by the fact that fat tissues, called depots, contain many cell types other than adipocytes. In addition, adipocytes at different anatomical locations originate from different early embryonic precursors². There is also metabolic variation between fat depots around the body, and even between adipocytes in the same depot^{3–5}.

A pool of adipocyte stem and progenitor cells (ASPCs) can be isolated from fat depots using a technique called fluorescence-activated cell sorting (FACS), which separates cells on the basis of specific cell-surface proteins^{6,7}. Many of the surface markers currently used to isolate ASPCs through FACS were selected because they distinguish stem-like cells from other tissues. However, the pools isolated when trying to obtain ASPCs using this method contain a mixture of cell types, and the molecular profiles of the true stem and progenitor cells within the mix has remained largely undefined.

Schwalie and colleagues started with a mixture of 208 ASPCs isolated from mouse fat tissue using FACS. They performed

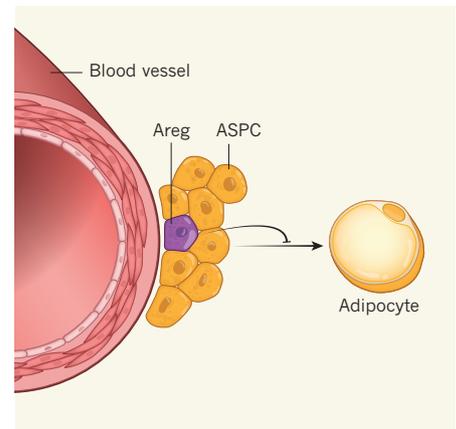


Figure 1 | A cell population that inhibits fat growth. A pool of adipocyte stem and progenitor cells (ASPCs) that is found around blood vessels gives rise to fat cells, which are called adipocytes. Schwalie *et al.*¹ identified a subpopulation of cells within the ASPC pool, dubbed Aregs. These cells release signals to inhibit the formation of adipocytes from ASPCs.

single-cell RNA sequencing to determine which genes are expressed in each cell. Using computer algorithms to group the cells according to their gene-expression profiles, the authors discovered that at least three distinct subpopulations exist within the ASPC pool. They then confirmed the existence of these three subpopulations using an alternative cell-isolation strategy combined with a different method of grouping ASPCs by their gene-expression signatures.

Most of the ASPCs fell into two of three groups discovered by the authors. The first group, designated P1, expressed high amounts of stem-cell markers. The second group, designated P2, expressed many genes that regulate the early steps of adipocyte formation. But it was the smallest group, P3, representing less than 10% of the cell population, that drew the authors' attention. Unlike the other groups, P3 cells did not form mature adipocytes when