increased atherosclerosis compared with mice that were able to express hypocretin. Giving hypocretin to mice that had sleep disruption reduced white blood cell production and decreased the severity of atherosclerosis, suggesting that reduced hypocretin levels have a major role in atherosclerosis driven by sleep fragmentation.

Probing further, McAlpine *et al.* found that sleep disruption decreased hypocretin levels in the animals' blood and bone marrow. This protein has two receptors in cells, one of which is highly expressed in the subset of bone marrow cells that gives rise to neutrophils. These pre-neutrophils responded to decreased amounts of hypocretin by increasing the production of colony-stimulating factor 1 (CSF-1), a protein that promotes the production of white blood cells from stem cells in the bone marrow. The authors also found that CSF-1 deficiency in bone marrow cells counteracted the increased production of monocytes and the accelerated atherosclerosis caused by hypocretin deficiency or sleep fragmentation. These results suggest that the reduction of hypocretin levels caused by sleep disruption stimulates CSF-1 production, and that this increases the production of monocytes and promotes atherosclerosis.

Although the hypocretin–CSF-1 pathway seems to be the major mechanism linking sleep fragmentation to the production of white blood cells and atherosclerosis, there are hints that other mechanisms could also be involved. For example, McAlpine *et al.* observed that CSF-1 deficiency in bone marrow cells did not reduce the elevated numbers of neutrophils in blood caused by hypocretin deficiency or sleep fragmentation. This suggests that other, CSF-1-independent, pathways increase neutrophil production during sleep disruption. Of note, neutrophils can contribute to the formation of atherosclerotic plaques, even if their role is less important than that of monocytes. Furthermore, in addition to increasing monocyte numbers in blood, CSF-1 affects the artery wall directly, for example by stimulating the maturation of monocytes into macrophage cells[6]. This influence of CSF-1 on artery walls might have contributed to the protective effects of CSF-1 deficiency in mice with sleep fragmentation.

McAlpine *et al.* observed a decrease in hypocretin expression and an increase in the production of white blood cells only after 12 weeks of sleep disruption. Although this might suggest that the brain undergoes structural changes that lead to loss of hypocretin-producing neurons, this possibility was not supported by the authors' assessment of the number of dead cells in the hypothalamus. Narcolepsy can be caused by the loss of hypocretin-producing neurons[5], and one of the hallmarks of this disease is fragmented sleep[7]. Together with the present study's findings, which indicate that sleep fragmentation causes hypocretin deficiency, this suggests that a bidirectional relationship might exist between the two conditions.

Although sleep disruption did not affect the animals' body weight, it reduced food intake, as expected when hypocretin levels are low. The maintenance of body weight despite reduced food intake implies that the mice used less energy. Given that hypocretin increases energy expenditure through signalling by the hormone leptin[8], these findings indicate that hypocretin deficiency might lead to reduced leptin signalling in mice that have sleep fragmentation. Moreover, white blood cell production is increased in leptin-deficient mice[9]. This suggests that metabolic disturbances beyond those studied by McAlpine *et al.* might contribute to the increased production of these cells and the worsening atherosclerosis in mice with sleep disruption.

Study of the relationships between sleep disorders and metabolic and cardiovascular disorders is in its infancy. McAlpine *et al.* have uncovered a previously unknown mechanism that has possible therapeutic implications. The drug suvorexant, a blocker of hypocretin receptors, was approved in 2014 for the treatment of insomnia. The present study raises the question of whether such therapies could have harmful cardiovascular consequences. Effects observed in mouse studies often do not translate well to humans, and suvorexant did not increase total white blood cell counts in one observational human study[10]. Nevertheless, continued surveillance of people receiving this drug might be warranted. Future studies might further unravel the links between sleep disorders and cardiometabolic risk, and lead to new therapeutic strategies for treating these highly prevalent disorders. ■

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CITATION METRICS

Small-team science is beautiful

The application of a new citation metric prompts a reassessment of the relationship between the size of scientific teams and research impact, and calls into question the trend to emphasize 'big team' science. See Letter p.378

PIERRE AZOULAY

The current infatuation with large-scale scientific collaborations and the energy they can bring to a scientific domain owes much to the robust correlation that exists between citation impact and team size. This relationship has been well documented in the emerging 'science of science' field[1]. On page 378, Wu *et al.*[2] use a new citation-based index to nuance this conventional wisdom. They find that small and large teams differ in a measurable and systematic way in the extent of the 'disruption' they cause to the scientific area to which they contribute.

Scientists have long had a love–hate relationship with citation metrics. When it comes to recognizing and promoting individuals (or even teams), why would researchers ever rely on proxies of questionable validity, rather than engage with the scientific insights proposed in a paper or by a particular scientist? And yet, precisely because they encode the recognition of one's peers, citations occupy a central place in the complex web of institutions and norms that allow for the smooth functioning of the scientific enterprise.

But what is the meaning of a citation? Scientists cite previous work for many reasons. Sometimes their purpose is to acknowledge an intellectual debt. More rarely, it is to criticize the work that came before them[3]. Citation behaviour can also reflect strategic considerations, such as currying favour with referees or editors, or status-based considerations, as when an author cites well-known authorities in the field without engaging with the substantive content of their work. Moreover, citation counts are obviously affected by field size and cross-domain citation norms, which makes it

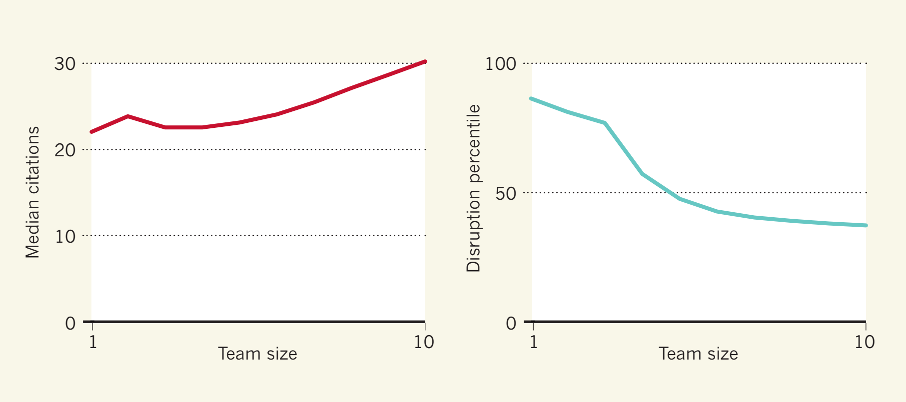

Figure 1 | Small teams make more-disruptive contributions to science than do large teams. Wu *et al.*[2] show that median citations to scientific articles (red curve) increase with team size, whereas articles' average disruption percentile (blue curve), as measured using a citation-based index[6], decreases as team size increases. This analysis is based on 24,174,022 research articles published in 1954–2014 and indexed on the Web of Science database. Similar associations were seen for patents and software-code snippets (not shown). (Adapted from ref. 2.)

difficult to compare scientists across fields or subfields.

Some new citation metrics have been proposed since the turn of the century, such as the *h* index[4] and the Relative Citation Ratio[5], but these alternatives have their own drawbacks. The *h* index is defined only for authors, not individual papers, and understates the impact of an author's most highly cited work. The Relative Citation Ratio normalizes an article's citations by a measurement of 'expected citations' given the article's field, but determining to which field an article belongs can be a subjective decision.

In this context, the article by Wu and colleagues comes as a breath of fresh air. The authors describe and validate a citation-based index of 'disruptiveness' that has previously been proposed for patents[6]. The intuition behind the index is straightforward: when the papers that cite a given article also reference a substantial proportion of that article's references, then the article can be seen as consolidating its scientific domain. When the converse is true — that is, when future citations to the article do not also acknowledge the article's own intellectual forebears — the article can be seen as disrupting its domain.

The disruptiveness index reflects a characteristic of the article's underlying content that is clearly distinguishable from impact as conventionally captured by overall citation counts. For instance, the index finds that papers that directly contribute to Nobel prizes tend to exhibit high levels of disruptiveness, whereas, at the other extreme, review articles tend to consolidate their fields.

Armed with this new measure, Wu *et al.* document a robust and striking empirical fact: the type of work performed by large teams and small teams differs markedly, with small teams being much more likely than large teams to publish disruptive articles (Fig. 1). This finding holds for articles, patents and computer-code snippets deposited on the web-based hosting service GitHub. It holds across all quantiles of the citation distribution. In the case of articles, it also holds across scientific disciplines, from biology to the physical sciences, as well as the social sciences.

A sceptic could object that large and small teams might differ in unobserved ways that are correlated with disruptive potential. In particular, scientists who prefer to work in small teams might be predisposed to upset the intellectual apple cart in their domains. Strikingly, however, the relationship documented by Wu *et al.* also holds within the corpus of work of individual scientists. The authors' analysis of a large sample of approximately 38 million name-disambiguated scholars and their published works shows that the same individual scientists participate in more consolidating projects when they operate in large teams than when they work in small teams.

These results are important in three respects. First, they provide us with a new, validated metric with which to evaluate the impact of policies or interventions that might affect the rate and direction of scientific progress, such as new funding mechanisms.

Second, they are a corrective to the zeitgeist that tends to view collaborations — across laboratories and especially across disciplines — as an inexorable trend that science funders should embrace and celebrate. Wu *et al.* invite us to recognize that sustained scientific progress requires both radical and incremental contributions, and that the investigations that lead to these contributions are probably better carried out by different types of team.

Third, the results show that researchers need not choose between a slavish devotion to citation metrics and ignoring citation data altogether. Rather, scientists should support the development of more-informative metrics and be careful about how these are interpreted and used.

As is the case with any new metric, the

50 Years Ago

Populations of red kangaroos that suffered badly in the Australian droughts of 1965–67 now seem to be increasing again. By 1967 there were so few in north-western New South Wales that the Division of Wildlife Research of the Commonwealth Scientific and Industrial Research Organization had to stop regular sampling of the population. When in March that year heavy rain produced the best growth of pasture for many years, an aerial survey showed that, despite the abundance of food, numbers of kangaroos had not been increased, as on previous occasions, by immigrants from surrounding areas. The density of kangaroos in this part of New South Wales was then the smallest since surveying began in 1964. But happily, after more rain in 1967, red kangaroos began breeding again and the population had begun to recover by March 1968.
From *Nature* 22 February 1969

100 Years Ago

Within the limits of a short article it is not possible to do justice to our feathered friends. The services rendered by homing-pigeons to the Army, Navy, and Air Forces have been invaluable, and numerous stories of their gallantry and devotion, under fire and even when wounded, have already appeared in the daily newspapers. Canaries, long recognised as the miners' friends in detecting the presence of poisonous underground gases, have played their part in the war by being used in the trenches and dug-outs when the presence of German poison-gas was suspected. It is not so generally known that parrots, in the earlier days of the war, were employed on the Eiffel Tower to give warning of the approach of enemy aircraft. Sea-gulls, on more than one occasion, betrayed the presence of submarines and mines and thus prevented disaster to our sailors.
From *Nature* 20 February 1919

disruptiveness index should not be embraced uncritically. Because it relies on citations to articles, it can be calculated only after enough time has passed since publication for citations to accumulate. This limits the applicability of the index in areas in which citations build up slowly, or its use as a tool for evaluating the impact of recent policies. Moreover, Wu and colleagues' article leaves open the question of mechanisms: why would small teams be more likely to perform disruptive work? How much overlap is there between the skills, backgrounds and experience of the members of small teams and those of large teams? Are differences in talent between collaborators more or less pronounced in small scientific teams than in large collaborations? These questions await further examination. ■

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NUCLEAR PHYSICS

Origin of neutron and proton changes in nuclei

The structure of a neutron or a proton is modified when the particle is bound in an atomic nucleus. Experimental data suggest an explanation for this phenomenon that could have broad implications for nuclear physics. SEE LETTER P.354

GERALD FELDMAN

In 1983, it was discovered that the internal structure of a nucleon — a proton or a neutron — depends on its environment[1]. That is, the structure of a nucleon in empty space is different from its structure when it is embedded inside an atomic nucleus. However, despite vigorous theoretical and experimental work, the cause of this modification has remained unknown. On page 354, the CLAS Collaboration[2] presents evidence that sheds light on this long-standing issue.

The advent of nuclear physics dates back to the days of Ernest Rutherford, whose experiments in the early 1900s on the scattering of α-particles (helium nuclei) by matter revealed a compact, dense core at the centre of atoms[3]. Since then, physicists have been working to understand the structure of the atomic nucleus and the dynamics of its component parts. Similarly, since the revelation in the late 1960s that nucleons themselves have internal constituents called quarks[4,5], extensive work has focused on studying this deeper underlying structure.

For decades, it was generally thought that nucleons in nuclei were structurally independent of each other and were essentially influenced by the average nuclear field produced by their mutual interactions. However, a lingering question had been whether nucleons were modified when inside a nucleus; that is, whether their structure was different from that of a free nucleon. In 1983, a startling discovery by the European Muon Collaboration (EMC) at the particle-physics laboratory CERN near Geneva, Switzerland, provided evidence for such a nucleon modification[1]. The modification, known as the EMC effect, manifested itself as a variation in the momentum distribution of quarks inside the nucleons embedded in nuclei. This result was verified by subsequent experiments at the SLAC National Accelerator Laboratory in Menlo Park, California[6,7], and at the Thomas Jefferson National Accelerator Facility (Jefferson Lab) in Newport News, Virginia[8].

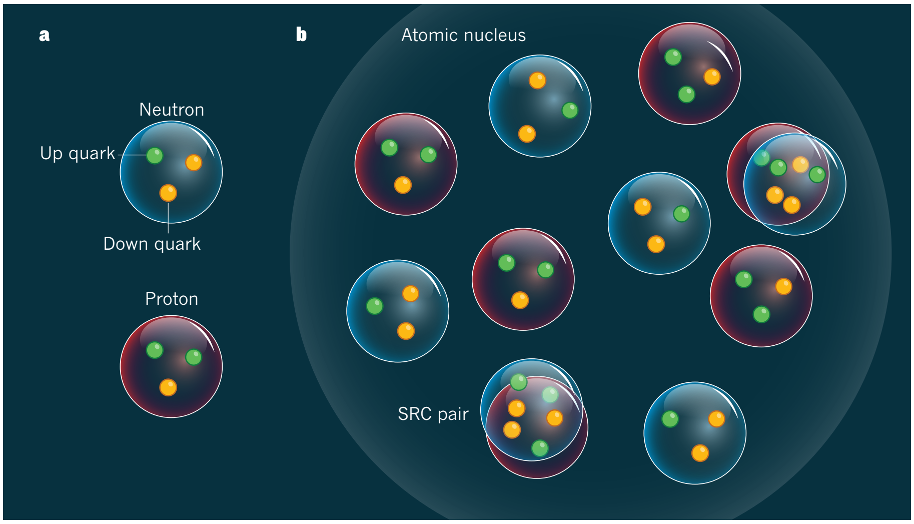

Figure 1 | Modified protons and neutrons in nuclei. **a**, Nucleons — neutrons and protons — are composed of elementary particles called quarks. Neutrons contain one 'up' quark and two 'down' quarks, whereas protons contain two up quarks and one down quark. **b**, In atomic nuclei, nucleons can briefly interact in what are known as short-range correlated (SRC) pairs. The CLAS Collaboration[2] reports evidence that these interactions alter the internal structure of the nucleons inside the nucleus.

Although the existence of the EMC effect is now firmly established, its cause has been elusive. Current thinking offers two possible explanations. The first is that all nucleons in a nucleus are modified to some extent because of the average nuclear field. The second is that most nucleons are not modified, but that specific ones are substantially altered by interacting in what are called short-range correlated (SRC) pairs over brief time periods (Fig. 1). The current paper provides definitive evidence in favour of the second explanation.

The EMC effect is measured in experiments in which electrons are scattered from a system of particles, such as a nucleus or a nucleon. The electron energies are selected so that the quantum-mechanical waves associated with the electrons have a wavelength that matches the dimensions of the system of interest. To study the interior of a nucleus, energies of 1–2 GeV (billion electronvolts) are needed. To probe the structure of a smaller system, such as a nucleon, higher energies (smaller wavelengths) are required, in a process called deep inelastic scattering (DIS). This process was central to the discovery of the quark substructure of nucleons[4,5], which resulted in the 1990 Nobel Prize in Physics[9].

In DIS experiments, the rate at which scattering occurs is described by a quantity called the scattering cross-section. The magnitude of the EMC effect is determined by plotting the ratio of the per-nucleon cross-section for a given nucleus to that for the