storms, acts as a source of energy to excite

Why does the jet stream across the United

### ATMOSPHERIC SCIENCE

# Record-breaking winters and global climate change

Rising greenhouse gas emissions may have played a role in the severe 2013-2014 winter in the U.S. Midwest

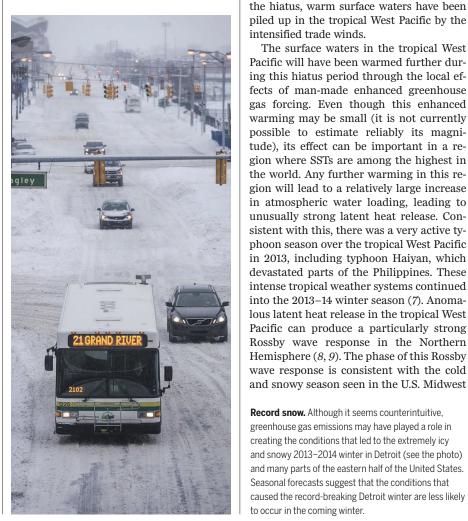
**Bu Tim Palmer** 

ust when it looked like spring was arriving this year, the U.S. Midwest slipped back into winter, and Detroit recorded its snowiest season ever (see the photo). Has global warming gone into reverse, or could human emissions of greenhouse gases actually be responsible for this particular record being broken? Although the chances of cold winters can in general be expected to decrease with global warming, climate change linked to the particular circulation patterns that have prevailed in the past decade or so could have played an important role in this recordbreaking winter.

Climate anomalies such as a colder-thanaverage winter or spring are commonly viewed as part of the natural variability of climate but will become less common as the concentration of greenhouse gases increases in the atmosphere. A simple analogy is to imagine a well-shuffled deck of cards. There is a 0.5 chance of drawing a black card. Now let us throw away five black cards, reshuffle the deck, and draw another card at random. The chance of drawing a black card is now 0.45. Now throw away another five black cards, and the chance is reduced to 0.38. For the purposes of this analogy, a black card represents a cold winter, the shuffling and random drawing is the chaotic variability of climate, and the process of throwing away the black cards mimics the effect of greenhouse gas emissions into the atmosphere. Just like the deck of cards, the chances of cold seasons will in general decrease. Indeed, observational studies show exactly this (1).

Given this overall decreasing tendency in cold winters, it seems impossible to argue that the record-breaking snowy winter in the Midwest could be connected to climate change. However, there is a plausible link. To understand this link we must consider the atmospheric circulation patterns that were associated with this winter and ask whether there is evidence that climate change might

have increased the likelihood of these patterns. Large-scale atmospheric circulation patterns are controlled by the position of the jet stream. The Northern Hemisphere jet stream flows from west to east at midlatitudes; it deviates from a line of latitude through a series of ripples called Rossby waves. Regions above which the jet stream is flowing from the north are likely to experience cold weather. Conversely, in regions above which it flows from the south, the weather is likely to be relatively warm. The larger the amplitude of the Rossby waves, the more anomalous the weather is likely to be at the surface.



particularly large-amplitude Rossby waves in the Northern Hemisphere jet stream, with just the right phase to produce cold weather in the Midwest and East Coast. In the 2013-2014 winter, SSTs have been particularly warm in the tropical West Pacific (3). Since the late 1990s, global mean temperatures have been rising quite slowly. This pause or "hiatus" in global warming is linked to an increase in the westward trade winds across the tropical Pacific (4). The ocean currents, forced by these intensified trade winds, have been drawing down much of the excess heat associated with human cli-

mate change to the deep ocean (5, 6). How-

ever, one region that has not been cooling is

the tropical West Pacific. Over the period of

The surface waters in the tropical West Pacific will have been warmed further during this hiatus period through the local effects of man-made enhanced greenhouse gas forcing. Even though this enhanced warming may be small (it is not currently possible to estimate reliably its magnitude), its effect can be important in a region where SSTs are among the highest in the world. Any further warming in this region will lead to a relatively large increase in atmospheric water loading, leading to unusually strong latent heat release. Consistent with this, there was a very active typhoon season over the tropical West Pacific in 2013, including typhoon Haiyan, which devastated parts of the Philippines. These intense tropical weather systems continued into the 2013-14 winter season (7). Anomalous latent heat release in the tropical West Pacific can produce a particularly strong Rossby wave response in the Northern Hemisphere (8, 9). The phase of this Rossby wave response is consistent with the cold and snowy season seen in the U.S. Midwest

Record snow. Although it seems counterintuitive, greenhouse gas emissions may have played a role in creating the conditions that led to the extremely icv and snowy 2013–2014 winter in Detroit (see the photo) and many parts of the eastern half of the United States. Seasonal forecasts suggest that the conditions that caused the record-breaking Detroit winter are less likely to occur in the coming winter.

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and East Coast. If this line of argument is correct, the extremely cold and snowy season in parts of the United States may indeed have been caused at least in part by increased greenhouse gas concentrations.

The linkages described here are fundamentally different to another proposed mechanism, in which reduced Artic sea ice is hypothesized to influence jet stream variability (10). The latter hypothesis has been subject to considerable criticism (11). By contrast, the linkages proposed here are consistent with dynamical theory (8), and global climate models have been shown to be especially sensitive to small perturbations in the tropical West Pacific (9).

As this analysis indicates, it is simplistic to say that climate change makes the planet uniformly warmer. Earth's climate is a complex system, and its response to some external forcing will not be linear. Because of this complexity, sophisticated climate models are needed to test the correctness and robustness of climate mechanisms. Running these models is computationally expensive but crucial for advancing understanding of current and future climate.

Current seasonal forecast models suggest that a new (warm) phase of the El Niño/ Southern Oscillation phenomenon may begin later this year, when the trade winds will finally weaken. If an El Niño event is on the way, the hiatus period may be coming to a close. If so, the upside is that the residents of the U.S. Midwest will be much less likely to have to suffer very cold winters. The downside is that global temperatures are likely to start to rise again, with many undesirable consequences for humans across the planet (1). The only way to reduce the risks associated with man-made climate change, in Detroit or elsewhere, is to cut greenhouse gas emissions. ■

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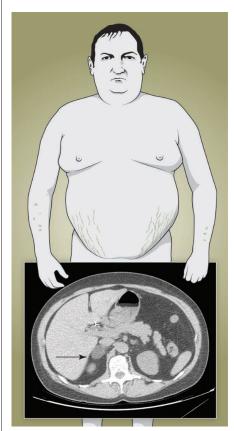
**MEDICINE** 

## A unified cause for adrenal Cushing's syndrome

Mutations in a signaling protein underlie a class of functional adrenal tumors

By Lawrence S. Kirschner

n the cartoon adventure Falling Hare, aviator Bugs Bunny is vexed by a series of aerial mishaps, causing his airplane to crash. After spending the episode trying to understand the origin of his problem, Bugs hits on the obvious solution: a gremlin. Four papers-two on pages 913 and 917 in this issue of Science (1, 2), a third in the New England Journal of Medicine (3), and a fourth in Nature Genetics (4), all from different groups-describe the use of whole exome sequencing (WES) to reach similar conclu-



**Disease symptoms.** A patient with typical features of Cushing's syndrome, including moon facies, abdominal obesity, striae, and peripheral muscle wasting. The CT image highlights (arrow) a typical adrenocortical adenoma. If this tumor secretes cortisol, there is an approximately 50% chance that it harbors a PRKACA L206R mutation.

sions regarding the molecular origin of cortisol-producing adrenocortical adenomas. Just like Bugs' sudden recognition of the gremlin's underlying role in his predicament, the surprisingly consistent answer to the question of the underlying cause of these tumors is no longer obscure; rather, it is a mutation in the catalytic subunit of the signaling subunit of the cyclic-AMP (cAMP)-dependent protein kinase, protein kinase A (PKA).

The four groups each studied benign cortisol-producing adrenocortical tumors. Like individuals receiving large doses of glucocorticoids for treatment of pulmonary or rheumatologic disorders, patients with endogenous hypercortisolism develop Cushing's syndrome, characterized in part by abdominal adiposity, purplish stretch marks (striae), and an increased risk for diabetes, hypertension, and osteoporosis (see the first figure).

The PKA signaling cascade is a central player in cellular signaling and is conserved in all eukaryotes. The PKA holoenzyme is a heterotetramer consisting of two catalytic (C) subunits and two regulatory (R) subunits. When intracellular cAMP levels rise. two molecules bind cooperatively to each regulatory subunit and release PKA-C, which is then able to phosphorylate targets in the cytoplasm and nucleus. In humans, there are three PKA catalytic subunit genes (PRKACA, -CB, and -CG), as well as a homologous gene on the X chromosome (PRKX). There are four regulatory subunits (PRKAR1A, -1B, -2A, and -2B) divided into class I and II based on their physicochemical properties. Of these components, PRKACA and PRKARIA are expressed ubiquitously and exhibit the highest protein levels in most tissues; thus, they are thought to be the predominant players in mediating cAMP action. The cAMP/PKA axis is normally tightly regulated upstream at the level of cAMP generation and downstream by cAMP degradation.

The role of PKA signaling in mammalian physiology is complex, and the phenotypic outputs from pathway activation are highly context specific. In the normal adrenal cortex, activation of PKA has long been known to promote both cellular growth and hormone secretion. Pituitary ACTH (adrenocortico-

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