from the northern North Atlantic, where 14C reservoir ages of surface waters varied strongly during the last glacial and deglacial periods (that is, before 10,000 calendar years B.P.).

The new results based on the stratigraphic method can be used successfully to calibrate 14C ages (see the figure). Between 33,000 and 41,000 calendar years B.P., whereas previous records disagree by up to 5000 calendar years, the new data sets agree within the errors. This confirms the reliability of the stratigraphic method applied to these two distant and very different marine environments. The correct calibration curve thus probably runs between the Lake Suigetsu and Bahamian speleothem data sets.

These new results have important implications for archaeology. Consider the prehistoric paintings in the Chauvet Cave of southern France, which were created at about 31,000 14C years B.P. (13) (red horizontal arrow in the figure). According to the new stratigraphic data (10, 12) and other results presented in Wellington, the calibrated age is almost 36,000 calendar years B.P. (black vertical arrow). The earlier Bahamian speleothem data yield ~38,000 calendar years B.P. (purple vertical arrow) and the Lake Suigetsu record gives ~33,000 calendar years B.P. (green vertical arrow), dates that are respectively too old and too young.

The new radiocarbon results also have wide implications for geochemistry and geophysics. For example, the observed differences between the 14C and true ages reflects deviations of the atmospheric 14C/12C ratio, the long-term trend of which is modulated by the geomagnetic field. A well-known magnetic excursion, the Laschamp event, dated by Ar-Ar at ~41,000 calendar years B.P. (14), resulted in an abrupt increase of cosmogenic nuclide production (such as 10Be, 36Cl, and 41Ca). The new data from the Cariaco Basin (10) and the Iberian Margin (12), together with previous coral data (15), indicate that the atmospheric 14C/12C ratio reached a maximum of about 700 per mil above the modern one at ~39,000 to 41,000 calendar years B.P. Taking into account a millennium-scale phase shift linked to the carbon cycle, the calendar age for the Laschamp event is thus ~40,000 to 42,000 calendar years B.P.

This is fully compatible with recent determinations, in the very same Iberian Margin core, of a 10Be maximum (16) and a magnetic paleointensity minimum (17) at ~41,000 to 42,000 calendar years B.P. Further independent confirmation of this calibration point comes from 10Be and 36Cl concentration maxima in ice sections dated at ~41,000 calendar years B.P. in the Greenland Summit ice cores (18, 19).

Significant progress is expected in the near future from the stratigraphic method for two main reasons. First, the recently drilled NorthGRIP ice core (20) will soon provide improved accuracy and precision for the calendar time scale up to 50,000 calendar years B.P., which is the backbone of the stratigraphic method. Second, additional data will allow researchers to verify and complement the emerging agreement observed between several data sets beyond 26,000 calendar years B.P. (see the figure). In the framework of the international IMAGES program, the research vessel Marion Dufresne has recently drilled several new sediment cores from the Iberian Margin and Cariaco Basin. This should increase the 14C data base and permit measurement of other interesting parameters such as 10Be concentrations and magnetic paleointensity. The hope is that a complete calibration curve, reaching back to 50,000 calendar years B.P., will be presented during the next International Radiocarbon Conference in Oxford, UK, in 2006.

References and Notes

1. 1th International Radiocarbon Conference, 1 to 5 September 2003, Wellington, New Zealand. A series of papers by the INTCAL Working Group led by Paula Reimer from the Lawrence Livermore National Laboratory will be published in Radiocarbon, providing full technical details on INTCAL04 and COM-PARE04.


21. Work at CEREGE is supported by CNRS and the European Community (HPRN-CT-2002-0221).
transcription factor. When transfected into cultured CREST, some fusion proteins (including CREST) caused activation of a Gal4-dependent reporter gene only when the neurons became depolarized. CREST does not possess a DNA binding domain. Rather, it appears to be a transcriptional coactivator that interacts with DNA binding proteins to increase the transcription of target genes.

In primary cultured neurons, the CREST-Gal4 fusion protein stimulated transcription in response to Ca\(^{2+}\) entry either through voltage-sensitive Ca\(^{2+}\) channels or through NMDA receptors after glutamate was applied to neurons. Deletion of different protein domains suggested that the amino terminus of CREST represses transcription in the basal state, whereas the carboxyl terminus mediates Ca\(^{2+}\)-dependent activation. Aizawa et al. (4) found further that CREST interacts in vitro with CBP (CREB binding protein) and p300, both histone acetyltransferases believed to cause transcriptional activation by opening up chromatin. The evidence that CREST is essential for dendritic development comes from mice that are deficient in CREST. These mice are viable at birth, but their brains are smaller than those of wild-type animals, and only 20% of the mice reach adulthood. Golgi staining to reveal the morphology of individual neurons indicates a substantial reduction in dendritic growth and branching. Interestingly, in cortical pyramidal neurons the deficit appears specific to basal rather than apical dendrites. Does CREST act directly and in a cell-autonomous manner to direct development of dendrites? This question is difficult to address in vivo, but the authors used in vitro cultures of neurons from animals lacking CREST to prove their case. Depolarization of neurons stimulates dendritic growth and branching of cultured cortical neurons from wild-type animals by about threefold. Remarkably, cultured neurons from CREST-deficient animals, while exhibiting comparable dendritic growth and branching under quiescent conditions, fail to show a boost in dendritic growth and branching in response to depolarization. Reintroduction of a CREST transgene into the mutant neurons rescued these defects. So, at least in culture, CREST is required within individual neurons for depolarization-induced dendritic development.

This study raises a number of interesting questions. First, how do Ca\(^{2+}\) signals actually activate CREST? Ca\(^{2+}\) can regulate the phosphorylation of transcription factors through protein kinases and phosphatases; Ca\(^{2+}\) can trigger translocation of transcription factors from the cytosol to the nucleus; it also can bind to and directly activate transcription factors (5). One of the best-characterized Ca\(^{2+}\) effectors is nuclear Ca\(^{2+}\)-calmodulin–dependent kinase IV (CaMKIV). Targets of CaMKIV include the transcription factor CREB and the coactivator CBP (6). Indeed, previous studies from the same group have shown that constitutively active CaMKIV is sufficient to induce dendritic growth in cultured neurons at least in part through CREB and CBP (3). In vivo, CaMKIV activation is likely to be complemented by sustained MAP kinase signaling (5). Is CREST directly regulated by Ca\(^{2+}\)? It does not possess a Ca\(^{2+}\) binding site, resides solely in the nucleus irrespective of Ca\(^{2+}\) levels, and there is no evidence yet that it is regulated by phosphorylation. The only clue comes from its binding to CBP. Might Ca\(^{2+}\) activation of CREST actually occur indirectly through CBP and perhaps CREB? This remains a viable hypothesis. Of course, different transcriptional complexes can assemble at different promoters, so the fact that CREB and CBP interact in one context does not mean that they must do so at CREST-regulated genes.

How does CREST regulate transcription of specific genes? Because it does not bind to DNA, it must associate with other transcription factors to achieve this. Aizawa, Ghosh and their colleagues point to the interaction of CREST with the CBP coactivator as a potential source of specificity, but CBP must also rely on other proteins to assemble at specific promoters. One such transcription factor has already been mentioned: CREB. Identifying which DNA binding proteins partner with CREST should help to explain why only a subset of genes show Ca\(^{2+}\)-dependent transcription despite the diverse functions of CREST’s binding partner, CBP.

One interesting implication of the Aizawa et al. study is that there appears to be a transcriptional program dedicated to activity-dependent regulation of dendritic growth. What kind of target genes might CREST regulate to produce these effects? Potential targets for dendritic growth include a diverse array of secreted molecules, cell surface receptors, cytoskeletal regulators, and other signaling proteins (1), some of which are known to be Ca\(^{2+}\)-dependent (7). Recently, other transcription factors have been shown to be intrinsic regulators of different aspects of dendritic development, including dendritic-tree complexity (8, 9) and dendritic targeting specificity (10). How similar are intrinsic and activity-regulated transcription programs? Identifying targets...
of these transcription programs is an important direction for future research. Finally, in addition to developmental expression, CREST is also expressed in a subset of adult neurons implicated in plasticity (4). This observation is consistent with the notion that the same molecules and mechanisms that help to build dendritic trees during development might also be used to modify their structures after learning and experience.

References and Notes


PERSPECTIVES

Weak Faults—Rotten Cores
Robert E. Holdsworth

When Earth’s crust deforms, earthquakes can be triggered by displacements along fault zones. Such fault zones can be sites of repeated deformation for hundreds of millions of years, suggesting persistent weakness relative to the adjacent crust. In addition, data on surface heat flow and stress orientations around crustal-scale fault zones such as the San Andreas fault in California indicate that they are much weaker than expected from laboratory models of friction. Yet despite 30 years of research, the causes of the inferred weakness—and even the existence—remain controversial (1, 2).

One problem is that much of the geophysical data cited as evidence for weakening lacks sufficient resolution to determine its underlying mechanical causes. Recently, additional insights have been gained from geological studies of ancient fault cores exposed at the surface and laboratory experiments on the deformation of materials that closely resemble fault rocks. These studies reveal that weakening originates at the scale of individual grains in mid-crustal fault networks whose natural interconnectivity then helps to transmit such effects to larger scales.

Two classes of continental faults are particularly likely to be weak over long time scales: low-angle normal faults (3) and reactivated faults (4). The ancient deep roots of these structures are often exhumed and exposed at the surface by major periods of tectonic activity. Assuming that the ancient examples are representative of what happens at depth today, direct study of weakening mechanisms operating within these faults may be possible, especially where they cut through the main load-bearing foliations or mineral alignments suggesting ductile flow (see the figure, B). This results from pervasive fluid influx that alters the load-bearing mineral phases. The alteration produces fine-grained aggregates of weak, platy minerals (micas, clays) that align to form an interconnected network (see the figure, C) (4). Fluid influx also triggers widespread stress-induced dissolution-precipitation deformation mechanisms in the preexisting, finely crushed fault rocks. The permanent weakening effect caused by all these processes is vividly illustrated by the preferential localization of most subsequent displacements into the foliated fault cores (7).

The microphysics of faults. (A) Right side, experimentally derived strength-versus-depth profiles for intact rock (5) based on traditional brittle-plastic rheology. Left side, strength profile for a vertical fault, with a broadened mid-crustal “frictional-viscous” regime characteristic of a weak, fluid-infiltrated and altered fault zone (9). (B) Natural example of brittle cataclasite breccia overprinted by mica-rich foliation, representing a transition to frictional-viscous behavior. (C) Scanning electron microscope image of foliated fault rock in which the mica-rich layers formed by alteration of feldspars form an interconnected weak layer at the microscopic scale. Images in bottom panel are of fault rocks from core of Median Tectonic Line, Japan (taken by S. Jefferies and M. Albers).

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References and Notes

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