

studied induce expression of *c-Fos* in the caudate-putamen, but not all induce this gene in the nucleus accumbens (1). Activation of the nucleus accumbens is neither necessary nor sufficient for addiction.

Richard E. Harlan

Department of Anatomy, Tulane University School of Medicine, New Orleans, LA 70112, USA. E-mail: harlanre@mailhost.tcs.tulane.edu

Meredith M. Garcia

Department of Otolaryngology, Tulane University School of Medicine

References

1. R. E. Harlan and M. M. Garcia, *Mol. Neurobiol.* **16**, 221 (1998).

Scientists in the Courtroom

The 2 April article "Court views engineers as scientists" by Jeffrey Mervis (News of the Week, p. 21) includes a curious quote from Richard Meserve, the attorney for the U.S. National Academy of Engineering (NAE), which filed a brief in the U.S. Supreme Court case *Kumho v. Carmichael*. The attorney states that experts "ought to be embarrassed if a judge finds their testimony not acceptable." This presumes that judges are never biased and never misunderstand the scientific issues. Ironically, in struggling with issues of scientific evidence, some courts have promulgated pseudo-science, for instance, holding that it takes a doubling of epidemiological risk to imply that a toxic substance is more likely than not to have caused an individual's disease. This is scientifically false (1). The statement that a scientist should be embarrassed by a negative judge's ruling also presumes that other scientists would agree with the decision, and it presumes that higher courts will not overturn the decision. But most important, the statement ignores the fact that scientists are often barred from testifying for reasons having nothing to do with the reliability of their science. Instead, the judge rules that the expert's science is not relevant to the legal issues in the case.

No judgment about a scientist's worth should be made merely on the basis of a statement that a judge barred his or her expert report from a proceeding. This will only discourage scientists from bringing their knowledge to the courtroom.

Jan Beyea

Consulting in the Public Interest, 53 Clinton Street, Lambertville, NJ 08530. USA. E-mail: jbeyea@cipi.com

References

1. J. Beyea and S. Greenland, *Health Phys.* **76**, 269 (1999).

Origin of the Japanese Population

I read with great interest the article by Dennis Normile (News of the Week, 5 Mar., p. 1426) about the origin of the Japanese population. Recently, there has

been an increasing interest in the origin of Japanese (1) and Chinese (2) populations. Relevant to this question, we have identified a splicing mutation that causes glycogen storage disease 1a (GSD1a), 727G RT, in the glucose-6-phosphatase gene. The incidence of the mutation in our local Chinese population is 1 in 385 (3). This same mutation has also been identified in the Japanese population with an incidence of 1 in 432 (4). The 727G RT mutation accounts for a majority of the GSD1a cases in both Hong Kong Chinese and Japanese. Interestingly, this mutation is absent in other ethnic populations. We have also identified the polymorphism 1176C/T in the 3' untranslated region of the same gene (5). All studied 727G RT mutant alleles are linked to the polymorphic marker 1176C in both Chinese and Japanese populations (seven Chinese and nine Japanese; $P = 0.0000047$) (6).

Thus, it is most likely that the 727G RT mutations in Japanese and Chinese populations descend from a single event. This observation supports the notion that Japanese and Chinese GSD1a patients share a common ancestor, providing an interesting complement to the anthropological evidence for the origin of these two populations. Our finding is consistent with other recent molecular genetic findings (1) indicating that the Japanese derived from the Chinese population. The ancient mutation we describe in the glucose-6-phosphatase gene will enhance the tracking of the origin of the modern Japanese population by determining its prevalence in Chinese from different provinces of China (2).

Ching-Wan Lam

Department of Chemical Pathology, Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong, China. E-mail: ching-wanlam@cuhk.edu.hk

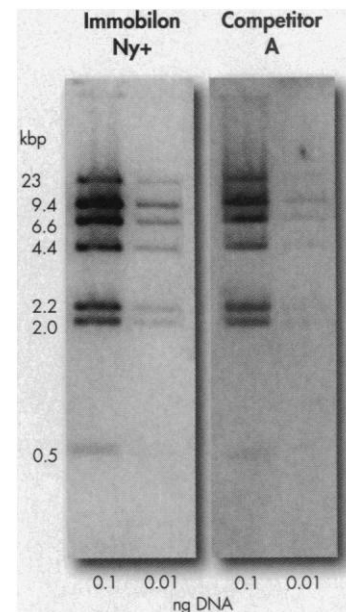
References

1. H. Oota *et al.*, *Am. J. Hum. Genet.* **64**, 250 (1999); A. Piazza, *Nature* **395**, 636 (1998).
2. J. Y. Chu *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **95**, 11763 (1998).
3. C.-W. Lam *et al.*, *Clin. Genet.* **53**, 184 (1998).
4. M. Okubo *et al.*, *ibid.* **51**, 179 (1997).
5. C.-W. Lam *et al.*, *ibid.* **53**, 502 (1998).
6. L. J. Wong *et al.*, *Hum. Genet.* **103**, 199 (1998); M. Okubo *et al.*, *ibid.* **104**, 193 (1999).

A Fidgeter's Calculation

J. A. Levine *et al.* (Reports, 8 Jan., p. 212) fed extra calories to human subjects and attributed the lack of weight gain in some of them to their fidgeting. Since my wife describes me as a consummate fidgetarian, I initially thought that one of life's little mysteries, the fact that I do not gain weight easily, had been solved. However, I am also a muscle biophysicist by trade, so I decided to pursue this

MILLIPORE



Identification of sub-picogram amounts of DNA

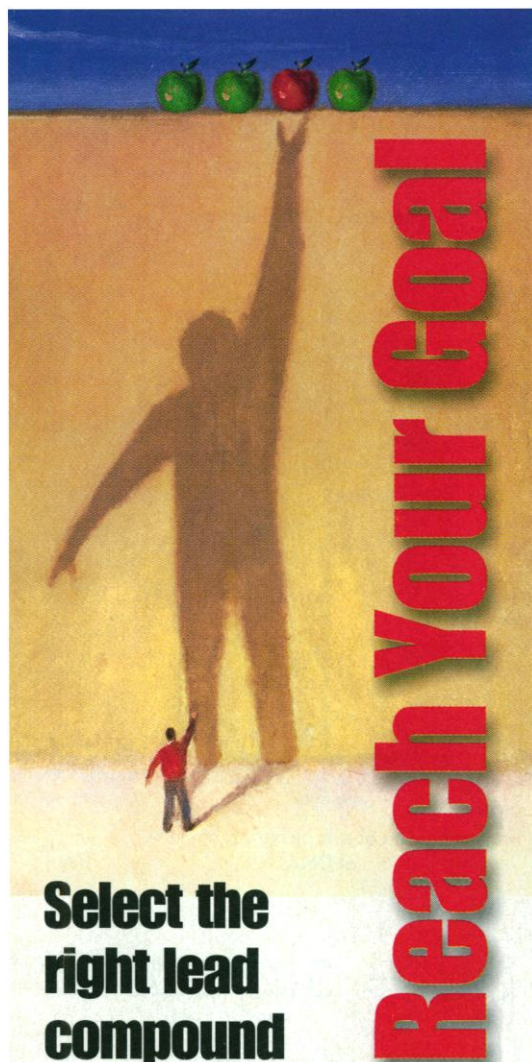
pure signal

For superior band intensity and lower background, try the latest in nucleic acid transfer membranes — Immobilon-Ny+. This advanced, positively charged, web-supported nylon membrane is optimized for superior nucleic acid fixation and reprobing.

Immobilon-Ny+ is ideal for Southern transfers and colony/plaque lifts. When compared to other nylon membranes, it provides a 50% improvement in signal strength, five times better after 13 rounds of probing.

To place an order call Fisher Scientific at 1-800-766-7000 (800-234-7437 in Canada). In Europe fax +33 3.88.38.91.95. In Japan call (03) 5442-9716. In Asia call (852) 2803-9111. For more information call Technical Service at 800-MILLIPORE. www.millipore.com/immobilon

Circle No. 49 on Readers' Service Card



Your objective is to generate metabolically stable, orally bioavailable pharmaceuticals that aren't significantly metabolized by polymorphic cytochrome P450s or cause drug-drug interactions by P450 inhibition. GENTEST Corporation's *in vitro* testing services support your efforts from discovery through registration. Of course after 15 years, GENTEST continues to be your best source for innovative products for the study of human *in vitro* drug metabolism in your own lab: cryo-preserved hepatocytes, microsomes, heterologously-expressed enzymes, antibodies, substrates, inhibitors and metabolite standards. Call us or visit our website to learn more about our comprehensive line of products and services.



United States and Other Countries

GENTEST Corporation
6 Henshaw Street • Woburn, MA 01801
Telephone: (781) 935-5115
Toll Free: (800) 334-5229
FAX: (781) 938-8644
Email: info@gentest.com

Visit us on the Internet: www.gentest.com
Circle No. 19 on Readers' Service Card

SCIENCE'S COMPASS

concept of fidgeting and caloric intake one step further.

A simple biophysical calculation can estimate the energy expended by a single fidget. For example, I observed one of my own favorite fidgets, which involves the swinging of my lower leg (1). The energy expended by this fidgeting is only a small fraction, or about 0.2%, of the total energy consumed by the subject. This estimate is for a simple type of fidget, but what about other forms of fidgeting, for instance, getting up to get a glass of water? The energy expended in walking by a 75-kilogram subject is about 150 kilojoules per kilometer (2). Assuming that the subject covered a distance of 2 kilometers during trips between desk and water cooler, the energy expended would be about 300 kilojoules per day, which accounts for less than 10% of the extra caloric intake.

The approximations used above are simplistic, but they are unlikely to alter the result by a magnitude required to explain the lack of weight gain by some subjects. The data reported by Levine *et al.* make a considerable contribution to our understanding of human metabolism, but the hypothesis that nonexercise activity thermogenesis accounts for a lack of weight gain is not realistic. The calculations presented above suggest that other mechanisms for disposing of the extra calories must exist. Fidgeting alone will burn insufficient calories to affect weight gain, indicating that people should not quit their health clubs or refrain from working on their exercycles.

Roger Cooke

Department of Biochemistry and Biophysics, University of California, San Francisco, CA 94143-0448, USA. E-mail: cooke@cgl.ucsf.edu

References and Notes

1. The swing involves the movement of my foot a distance of about 10 centimeters while I keep my knee stationary. It requires a time, estimated by averaging over 30 seconds, of about 1 second per fidget (± 0.2 seconds, 1 observation). I approximated my lower leg as a cylinder with a mass of 3 kilograms (the use of approximations is infamous in the field of biophysics). I estimated the kinetic energy generated per fidget by assuming that the center of mass of my leg achieved a peak velocity of 0.2 meters per second (5 centimeters were traversed in 0.5 seconds, and I assumed peak velocity to be twice the average). I determined the kinetic energy [$(1/2) \text{ mass} \times \text{velocity}^2$] to be 6×10^{-2} joules (this is a 33% underestimate because of the center-of-mass approximation). Studies of the efficiency of skeletal muscle suggest an overall efficiency (from fuel to mechanical work) of 20 to 30% (3). If one uses the more conservative efficiency rate of 20%, the energy expended in a single fidget is 0.3 joule per fidget. Assuming an upper limit of 1 fidget per second for 8 hours per day, I estimate that about 8 kilojoules per day are expended by fidgetarians like myself. This estimate can be compared with the excess calories consumed by the subjects in Levine *et al.*'s study: about 4000 kilojoules per day.
2. T. A. McMahon, *Muscles, Reflexes, and Locomotion* (Princeton Univ. Press, Princeton, NJ, 1984).
3. R. C. Woledge, N. A. Curtin, E. Homsher, *Energetic Aspects of Muscle Contraction* (Academic Press, London, 1985); J. Bangsbo, *Sports Med.* **22**, 299 (1996).

Response

Cooke has extrapolated from his calculations regarding the energy expenditure of his foot-tapping to conclude that changes in nonexercise activity thermogenesis (NEAT) cannot account for the resistance to fat gain we observed with overfeeding. Although observation of a complex object can result in appreciation of its components, consideration of a series of components in isolation may not enable the complex object to be fathomed (1). Using Cooke's calculations, it is not possible to explain how some individuals expend up to 800 kilocalories per day in spontaneous physical activity while confined in a small 3.3- by 2.5-meter calorimeter chamber (2). The most likely explanation for this discrepancy is that fidgeting represents only one component of NEAT. Other components include sitting, standing, and ambulating. Each of these activities significantly increases energy expenditure: sitting by about 10%, standing by about 40%, and walking by two- to threefold (3). Because sedentary individuals spend approximately 80 to 90% of waking time sitting, standing, or walking, these activities account for 40 to 60% of the total daily energy expenditure and the majority of NEAT (4). Fidgeting-like activities may add a further 20% to energy expenditure (5). Also, the energy expended in these activities is highly variable, with severalfold interindividual variability in the extra calories expended sitting, writing, and performing clerical work (3, 6). These data, combined with great variations in the levels of physical activity, help explain the severalfold differences in daily NEAT between individuals (7). We do not suggest that people quit their health clubs or exercise programs; however, it is noteworthy that increasing NEAT activities has health benefits similar to those of structured aerobic exercise (8).

Appreciation of the numerous and varied components of NEAT confirms the feasibility of our suggestion that modulation of NEAT has a substantive impact on energy balance and weight gain.

James A. Levine

Michael D. Jensen

Department of Medicine, Endocrine Research Unit, Mayo Clinic, and Mayo Foundation, Rochester, MN, 55905, USA. E-mail: jensen.michael@mayo.edu

References

1. Aristotle, *Metaphysics* (Univ. of Michigan Press, Ann Arbor, MI, 1952).
2. E. Ravussin, S. Lillioja, T. E. Anderson, L. Christin, C. Bogardus, *J. Clin. Invest.* **78**, 1568 (1986).
3. C. V. Bouten, K. R. Westerterp, M. Verduin, J. D. Janssen, *Med. Sci. Sports Exerc.* **26**, 1516 (1994).
4. P. O. Astrand and K. Rodahl, *Textbook of Work Physiology; Physiological Basis of Exercise* (McGraw-Hill, New York, 1986).
5. M. J. Dauncey, *Can. J. Physiol. Pharmacol.* **68**, 17 (1990).
6. J. D. Webster, G. Welsh, P. Pacy, J. S. Garrow, *Br. J. Nutr.* **55**, 1 (1986).
7. A. E. Black, W. A. Coward, T. J. Cole, A. M. Prentice, *Eur. J. Clin. Nutr.* **50**, 72 (1996).
8. R. E. Andersen *et al.*, *J. Am. Med. Assoc.* **281**, 335 (1999).