Golowasch, J., Abbott, L.F., and Marder, E. (1999). J. Neurosci. *19*, RC33.

Harris-Warrick, R.M., Coniglio, L.M., Levini, R.M., Gueron, S., and Guckenheimer, J. (1995). J. Neurophysiol. *74*, 1404–1420.

LeMasson, G., Marder, E., and Abbott, L.F. (1993). Science *259*, 1915–1917.

MacLean, J.N., Zhang, Y., Johnson, B.R., and Harris-Warrick, R.M. (2003). Neuron *37*, this issue, 109–120.

Marder, E., and Prinz, A.A. (2002). Bioessays *24*, 1145–1154.

Maynard, D.M. (1972). Ann. N Y Acad. Sci. *193*, 59–72.

Stemmler, M., and Koch, C. (1999). Nat. Neurosci. *2*, 521–527.

Thoby-Brisson, M., and Simmers, J. (2002). J. Neurophysiol. *88*, 2942–2953.

Tierney, A.J., and Harris-Warrick, R.M. (1992). J. Neurophysiol. *67*, 599–609.

Turrigiano, G., Abbott, L.F., and Marder, E. (1994). Science *264*, 974–977.

From Humble Neural Beginnings Comes Knowledge of Numbers

Following a recent report that monkey prefrontal cortex contains cells that represent number concepts, Neider and Miller investigated the scale used to code numbers. In this issue of *Neuron*, they report that prefrontal cells use the same scale (Weber's Law) used by sensory neurons to code stimulus intensity, suggesting how abstract cognitive operations may arise from simpler building blocks that humans share with other animals.

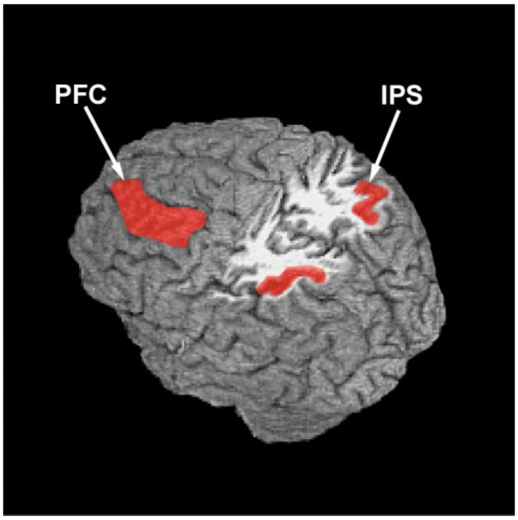
A horse known as "Clever Hans" lived in Berlin around the turn of the 20th century. Hans' claim to fame was that he was seemingly able to solve mathematical problems, such as adding two numbers. Noted scientists traveled to Berlin to test Hans' fascinating ability. They would write an equation on a board and wait for him to paw the ground with his hoof. When Hans reached the answer, he would stop. Ever since Clever Hans was shown to be solving problems in ways that did *not* involve performing calculations (i.e., "cheating"), scientists have been skeptical of accounts of numerical proficiency by animals. In this issue of *Neuron*, following their recent report of monkey prefrontal cells acting as "number detectors" (Nieder et al., 2002), Nieder and Miller explore the neural code employed by prefrontal cells to represent numerosity (Neider and Miller, 2003). Their results provide insight into how abstract cognitive operations may arise from simpler neural principles that humans share with monkeys and probably other species.

The surprising result from the Nieder and Miller study is that the building blocks of the cognitive sense of numerosity may derive from very basic neural mechanisms for representing the magnitude of sensory inputs. Sensory judgments often follow Weber's law (Walraven et al., 1990), namely, $\Delta I/I = c$, where ΔI is the "just noticeable difference" intensity of a stimulus in order for it to be detected over a background stimulus of intensity I (c is a constant). For example, detecting a light increment over a background field is known to follow Weber's law. Likewise, the responses of sensory neurons, such as retinal ganglion cells, also approximate Weber's law, and the coding of sensory input in this way (approximately luminance contrast) greatly expands the dynamic range of the cells. This allows the cells to largely preserve sensitivity to inputs whose range can vary over many orders of magnitude (e.g., retinal illumination changes over at least 7 log units). Nieder and Miller found that numerosity is also coded by prefrontal neurons according to Weber's law.

Monkeys were trained to perform a delayed match-to-sample task that required them to judge whether successive visual displays contained the same number of items. To perform this task, monkeys must abstract the quantity of items from visual displays that vary widely in appearance, and then hold that information in memory over a short delay. Stimuli were comprised of black dots on a gray background. To prevent the monkeys from memorizing the displays, the location and size of the dots were randomized. But how do we know that the monkeys were solving this task in a way that truly reflects abstracting quantity, rather than utilizing low-level visual features (a kind of Clever Hans trick)? To eliminate this possibility, prior to the experiments, monkeys were tested with several control stimuli, including displays with the total area and circumference equated across different quantities, displays of low and high dot density, and displays in which the dots were replaced with triangles, squares, or ovals. Overall, the performance of the monkeys on the controls indicated that they were indeed judging quantity (Nieder et al., 2002).

In the present series of experiments, monkeys made more errors when the numerosities of the match and sample stimuli were very close and performed progressively better as the numerical distance between the two stimuli increased. This behavior, known as the *numerical distance effect*, is also observed in humans and other species. The monkeys also exhibited the *numerical size effect*, namely, that for equal numerical distance, discrimination between two numbers gets worse as their numerical size increases. In terms of neuronal responses, roughly a third of the cells studied exhibited selectivity for numerosity, such that activity declined progressively with increasing numerical distance from a preferred number (i.e., the one eliciting maximal activity). Moreover, the neural data mirrored the behavioral numerical distance and size effects insofar as the neural tuning curves also exhibited an inverted V-shape that became less selective (wider) with increasing preferred numerosity. The critical new finding was that the neural responses appeared to follow Weber's law, such that increasing the numerical distance between numerosities by a given fraction improved discriminability. Thus, it appears that the coding of an abstract feature such as numerosity relies on representations that follow a basic principle of sensory physiology, and in this manner the transition between perception and cognition may be more gradual. As Nieder and Miller suggest, from an evolutionary point of view, it might have been adaptive to build on existing principles of lower-level sensory processing to develop representations of information that are more cognitive.

The location of the cells in prefrontal cortex suggests



Imaging Studies in Humans Suggest that the Posterior Parietal Cortex (Especially the Intraparietal Sulcus) Is a Crucial Region for the Representation of Numbers

However, the prefrontal cortex, which was investigated by Nieder and Miller in monkeys, is also recruited during numerical tasks.

that, in monkeys, prefrontal cortex plays an important role in encoding numerosity, although it is not yet known if it is actually the most critical site. In humans, deficits in processing numbers, known as *acalculia* (Grafman and Rickard, 1997), are most often associated with lesions of the inferior parietal cortex (Dehaene and Cohen, 1997). In some cases, comprehending, producing, and calculating with numbers are all impaired. In other cases, however, the deficit may be selective for calculation, with reading, writing, spoken recognition, and production of Arabic digits and number words not being affected. Overall, studies of patients with brain lesions suggest the existence of a dedicated neural system for certain aspects of number processing, with the inferior parietal cortex occupying a central node of this system.

Converging evidence that number processing builds upon basic brain systems comes from developmental studies in humans and behavioral studies in simpler animals. Non-verbal tests indicate that children as young as 1.5–4 years of age have mastered number conservation. Moreover, violation-of-expectation paradigms have shown that even 5-month-old infants have developed numerical expectations analogous to the operations $1 + 1 = 2$ and $2 - 1 = 1$ (Wynn, 1992). Related studies reveal that several species exhibit elementary arithmetic abilities comparable to those of human infants (Dehaene et al., 1998), including rats, pigeons, raccoons, dolphins, parrots, monkeys, and chimpanzees. They can all discriminate the numerosity of various sets, including visual objects presented simultaneously or sequentially, as well as sequences of sounds.

In humans, neuroimaging studies have also helped map out regions important for performing arithmetic calculations. An early positron emission tomography (PET) study showed that, when subjects repeatedly subtracted three from a given number, activation (relative to rest) increased bilaterally in the prefrontal and inferior parietal cortex (Roland and Friberg, 1985). Subsequent studies have confirmed this early report but emphasize the importance of the intraparietal sulcus (IPS), bilaterally, as a key site for the encoding of numbers (Simon et al., 2002). A recent fMRI study by Naccache and Dehaene (2001), for example, used the phenomenon of repetition suppression to probe the coding of numbers. Both imaging and neurophysiological studies show that when the same visual stimulus is repeated over time, the evoked responses are steadily reduced (Miller and Desimone, 1991). Naccache and Dehaene (2001) showed that repetition suppression for numbers occurs in the IPS independent of the stimulus attributes (e.g., "six" versus "6"), indicating that the representation is at an abstract level. Moreover, repetition suppression was observed even when subjects were not aware of the initial exposure, which was masked and very brief (43 ms), indicating that such number representations are invoked "automatically." Thus, neuroimaging studies, in line with findings with patients with lesions, point to the posterior parietal cortex as a key region for the representation of numbers (see Figure). Determining the relative roles of parietal and prefrontal areas in humans and monkeys (see also Sawamura et al., 2002) in the representation of numbers awaits further studies.

Some of the most advanced cognitive capacities of humans, such as the ability to manipulate numbers and understand language, have long been regarded as unique and therefore not amenable to study in animals. However, the Miller and Neider study is one piece of the growing evidence that even the most abstract, cognitive operations in humans may borrow basic building blocks from neural circuits evolved to perform simpler behavior in animals. For example, the number cells studied by Nieder and Miller might be analogous to "mirror neurons" described by Rizzolatti et al. (2001) in a portion of monkey prefrontal cortex. The mirror neurons respond not only in association with the monkey's actions, but also in association with the monkey observing comparable actions of other organisms and even inanimate objects. These cells are found in a location corresponding to Broca's area in the human brain, a region long known to be important for language. Broca's area is especially important for understanding language related to actions and verbs, and it is possible to imagine how such a system evolved from a neural system for understanding the actions of others in lower animals.

Humans may have some abilities, however, that are truly unique. The knowledge of numerical quantities and their relations, for example, is only the core of the concept of number. Other aspects include digit identification, numeral comprehension and production, the spatial layout of multidigit calculations, rote arithmetic memory, and more abstract mathematical reasoning. Algebraic knowledge [e.g., $(a + b)^2 = a^2 + 2ab + b^2$] can be intact in patients with brain damage which impairs number knowledge, suggesting a dissociation of the neural systems. Thus, although sensory mechanisms might provide building blocks with which to build more abstract representations, such as numerosity, understanding the neural bases of high-level cognition will pose formidable challenges to neuroscientists working with humans and other animals for years to come.

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Selected Reading

Dehaene, S., and Cohen, L. (1997). Cortex *33*, 219–250.

Dehaene, S., Dehaene-Lambertz, G., and Cohen, L. (1998). Trends Neurosci. *21*, 355–361.

Grafman, J., and Rickard, T. (1997). In Behavioral Neurology and Neuropsychology, T.E. Feinberg and M.J. Farah, eds. (New York: McGraw-Hill), pp. 219–225.

Miller, E.K., and Desimone, R. (1991). Science *254*, 1377–1379.

Naccache, L., and Dehaene, S. (2001). Cereb. Cortex *11*, 966–974.

Nieder, A., and Miller, E.K. (2003). Neuron *37*, this issue, 149–157.

Nieder, A., Freedman, D.J., and Miller, E.K. (2002). Science *297*, 1708–1711.

Rizzolatti, G., Fogassi, L., and Gallese, V. (2001). Nat. Rev. Neurosci. *2*, 661–670.

Roland, P.E., and Friberg, L. (1985). J. Neurophysiol. *53*, 1219–1243.

Sawamura, H., Shima, K., and Tanji, J. (2002). Nature *415*, 918–922.

Simon, O., Mangin, J.-F., Cohen, L., LeBihan, D., and Dehaene, S. (2002). Neuron *33*, 475–487.

Walraven, J., Enroth-Cugell, C., Hood, D.C., MacLeod, D.I.A., and Schnapf, J.L. (1990). In Visual Perception: The Neurophysiological Foundations, L. Spillmann and J.S. Werner, eds. (San Diego: Academic Press), pp. 53–101.

Wynn, K. (1992). Nature *358*, 749–750.